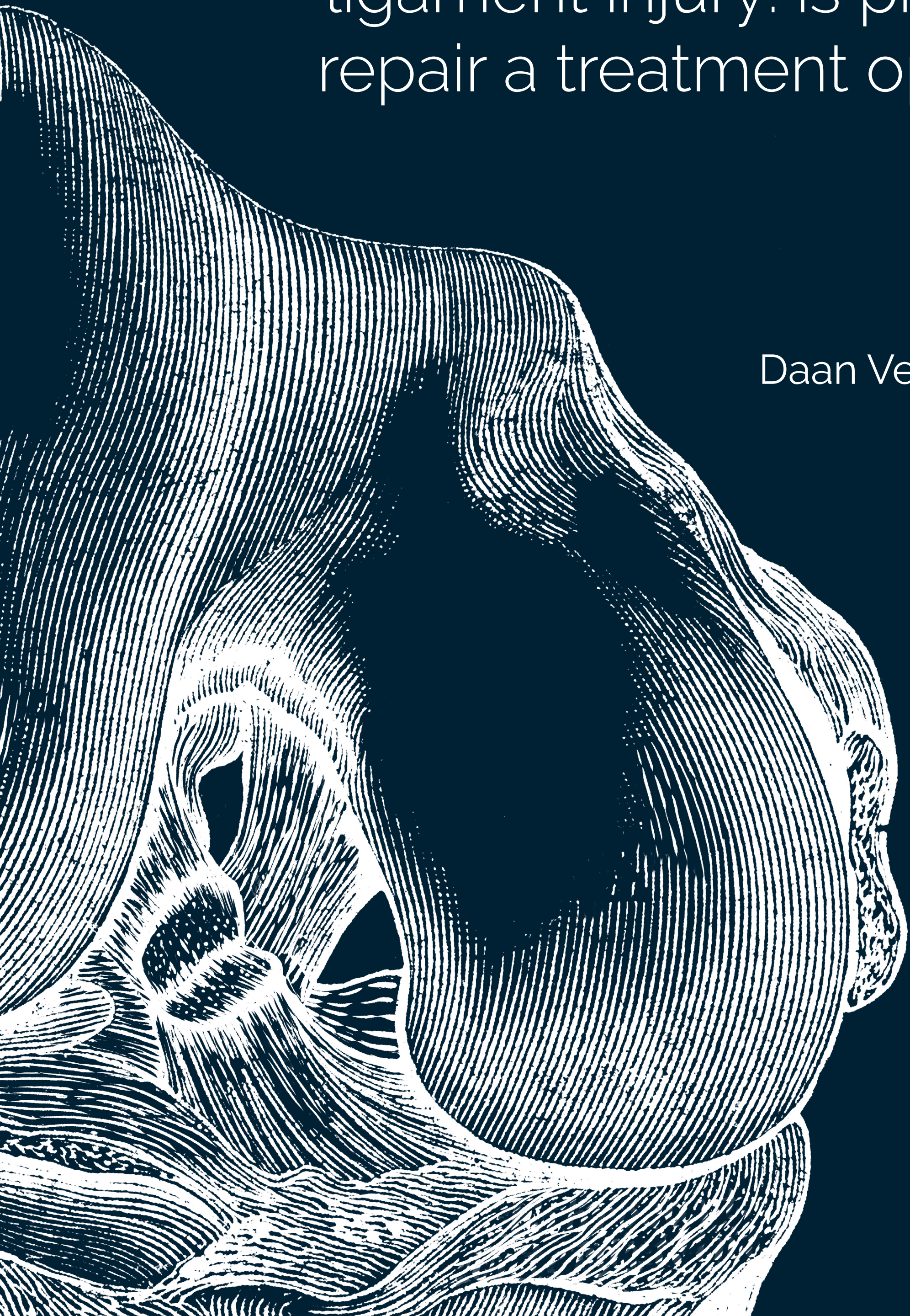
Acute anterior cruciate ligament injury: is primary repair a treatment option?

Daan Vermeijden



Acute anterior cruciate ligament injury: is primary repair a treatment option?

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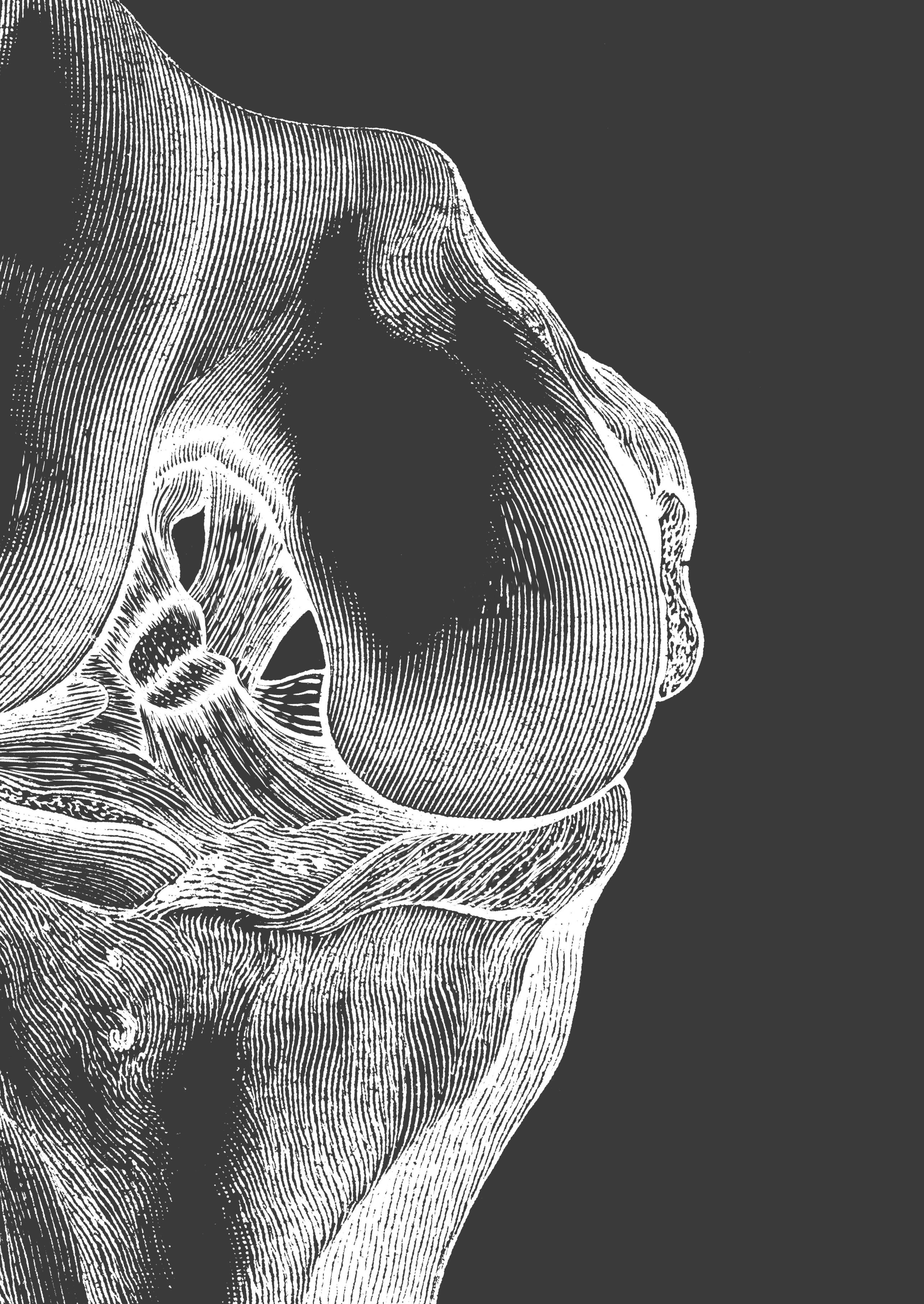
Part 1

Introduction



Chapter 1

General introduction and thesis outline

Acute anterior cruciate ligament (ACL) tears remain among the most common musculoskeletal injuries, especially in younger and active patients.[1] Over the last decades, this ligament has been one of the most heavily researched topics in sports medicine.[2,3] As sports participation is increasing worldwide, the number of acute ACL tears and surgical treatments have also risen, since it is estimated that more than 10,000 ACL surgeries are performed in the Netherlands.[4,5] This leads to increased health care costs and a high burden on society, with an estimated annual cost of more than 55 million euros in the Netherlands each year.[6,7]

Anatomy and function

The ACL is one of the major ligaments in the knee that connect the femur to the tibia. Situated in the center of the knee joint, the ACL runs obliquely from the anterior part of the intercondylar eminence at the distal side towards the posterolateral aspect of the intercondylar fossa of the femur on the proximal side. The ligament consists of a microstructure of dense connective tissue, predominantly collagen type I, which provides stiffness and tensile strength.[8] This is important as the ACL functions as a primary stabilizer by resisting excessive anterior tibial translation, internal rotation, and hyperextension of the knee. The ACL has two non-isometric bundles, an anteromedial bundle (AMB) and a posterolateral bundle (PLB).[9] Both have their specific function; the AMB primarily resists anterior tibial translation during knee flexion, while the PLB primarily resists internal tibial rotation and anterior translation at near full extension.[10]

Blood and nerve supply

The ACL is protected by a synovial layer ensuring that the ligament is not in contact with the knee's synovial fluid.[8] This synovial layer contains a rich network of blood vessels, of which the majority originates from the middle genicular artery.[11,12] The ACL also receives blood supply at the distal insertion side through the inferior medial and lateral geniculate arteries.[11] The nerve supply to the ACL originates from the tibial nerve, where branches of the tibial nerve run from distal towards the femoral origin of the ACL. These fibers have an important function in controlling normal joint movement due to their proprioceptive function, in which mechanoreceptors provide feedback on the positioning and movement of the knee joint.[13]

Etiology of acute ACL tears

Sports injuries are the most frequent cause of ACL injuries, but this can also occur during any other trauma, such as car accidents or falls from height. Nevertheless, most patients tear their ACL during a pivoting moment without physical contact (70%).[14] The knee is then close to full extension and placed in valgus position while the foot externally rotates.[15] Although less frequent, severe hyperextension of the knee can also lead to injury by excessively increasing stress on the ligament.[15] At the time of injury, some patients describe hearing and feeling a sudden "pop" and experiencing severe pain with a giving way sensation of the knee.

Current management of acute ACL tears

Management of acute ACL injuries starts with a precise diagnosis based on thorough patient history, physical examination, and additional diagnostic tests, such as standard knee radiographs and magnetic resonance imaging (MRI). The main treatment goal is restoring normal knee function, preventing secondary knee damage, and enabling return to normal activities.[16,17]

Treatment contains both conservative and operative strategies and is often made by shared decision-making.[18,19] Conservative treatment involves a structured rehabilitation to gradually reinforce lower limb muscles to cope with daily instability.[20] For older and less active patients, several studies have shown that this could lead to satisfying outcomes.[21–23] However, for those with high demand, such as young and active patients, this often leads to persistent instability complaints, and are advised to undergo surgery.[23] The Dutch guideline recommends performing ACL reconstruction (removing the torn ACL and replacing it with a graft) if symptomatic instability is still present after formal physiotherapy or activity level adjustment.[24]

There are several advantages of treating most patients conservatively first. With this treatment protocol, ACL surgery is not performed in all patients, which is important as approximately half of patients do not require surgery within five years after injury, as shown in the KANON trial.[21] This prevents surgical complications and decreases surgical costs.

Nonetheless, there are some major disadvantages of delaying surgery as this increases the time from injury to surgery and increases the risk of meniscal or chondral lesions.[23,25] In addition, delayed surgery increases the recovery time and indirect costs by requiring longer sick leave time after failed non-operative treatment.[26] Finally, the COMPARE trial, contradictory to the KANON trial, showed superior outcomes of early surgery compared to initial rehabilitation and subsequent surgery.[22]

Therefore, it has been suggested that early surgery should be considered in younger patients participating in higher-impact sports, as in this patient group non-operative treatment is associated with high incidence of treatment failure (>80%), increased risk of meniscal and chondral damage and a longer total time to return to sports.[23] Hence, it is important to identify if and which patients should be treated with early surgery, which also has the advantage of potentially performing ACL repair in a subset of patients.[27,28]

Modern-day ACL repair

Altough historically abandoned,[29–35] ACL repair can now be performed using minimally invasive arthroscopic procedures (rather than open procedures) while focusing on early mobilization (rather than cast immobilization) in selected patients only.[36–39] This procedure has been advocated for selective patients with proximal tears since these tear types may have better healing capacity due to better vascularization at the proximal end of the ligament.[12,40,41] Midsubstance tears, on the other hand, have less healing capacity since it is thought there is premature loss of a stable fibrin-platelet clot as the synovial fluid washes this away.[42–44]

ACL repair can be performed with or without augmentation. The augmentation of the repair functions as a restraint for failure of the construct. Although initial studies have reported on outcomes ACL repair without augmentation, more recent studies have suggested reinforcing the repaired ligament with either static or dynamic augmentation.[45] With static augmentation, the ligament is augmented by a 3 mm high-strength tape, whereas a spring-screw system is used in dynamic augmentation. Of all described procedures, a recent systematic review with meta-analysis showed that primary repair with static augmentation has the lowest failures and the least complications.[28] This thesis will, therefore, (mainly) focus on the outcomes of ACL repair with static augmentation.

It should also be noted that there are some potential advantages of repairing a torn ACL rather than reconstructing it. With primary repair, the native ligament and its proprioceptive functions might be maintained, potentially restoring native kinematics and preventing osteoarthritis development.[46–48] Furthermore, there is no need for graft harvest, which prevents donor-site morbidity.[49–51] Revision surgery of failed repairs has been found to be an uncomplicated single-stage primary reconstruction procedure as no 'bridges have burned'.

Current repair evidence

Recent research on ACL repair has shown promising short-term outcomes after selectively performing ACL repair in the (sub)acute setting; these outcomes are maintained at mid-term follow-up.[28,38,52,53] As repair surgery is minimally invasive, it has previously been shown that these patients regain a full range of motion earlier and have less complications than those undergoing ACL reconstruction,[49] potentially leading to a shorter and less intensive rehabilitation period. From a biomechanical perspective, this procedure effectively restores anterior tibial translation directly after surgery.[46] It remains, however, unclear what is the ideal patient to benefit from a a primary ACL repair and whether it is safe to treat acute ACL tears early (given the poor historically reported outcomes). This fundamental knowledge will help to further define the future role of primary repair as a treatment option for patients with acute ACL tears.

Aims of this thesis

This thesis aims to assess if patients with acute ACL injuries should be treated early and to evaluate if there is indeed a role for primary repair in the treatment algorithm for (some of) these patients. Therefore, this thesis will assess the current treatment of acute knee ligament injuries, patient selection of primary ACL repair, and the outcomes of this procedure. These issues and their relevance are briefly introduced below.

Outline of this thesis

Part I: Acute treatment of ACL injuries

In recent years, several repair techniques have been proposed, including repair using suture anchors, internal bracing, and dynamic intraligamentary stabilization (DIS).[28] In **chapter 2**, an overview is presented assessing the rationale behind modern ACL repair, the different treatments for various tear types, and the available evidence for these procedures.

Primary repair is often performed in the acute setting. However, in the case of non-repairable ACL tears, it is unknown if acute reconstruction can be performed without significantly increasing the risk for complications. **Chapter 3** assesses the advantages of early versus delayed ligament knee injury surgery.

Part II: Patient selection for ACL repair

Based on both historical and more recent studies, strict patient selection is paramount for achieving successful outcomes with ACL repair. Part II of this thesis aims to understand which patients are eligible for this procedure.

Although vascularity is key for ACL healing,[40] relative perfusion of the ACL has not been extensively evaluated. In **chapter 4,** the healing capacity of the ACL is assessed by assessing the relative blood perfusion of the ligament›s proximal, middle, and distal thirds using quantitative MRI in cadavers.

To understand which patients are eligible for ACL repair, hence how and where ACLs commonly tear, **chapter 5** assesses which factors predict a proximal tear location of the anterior cruciate ligament. This includes several demographical risk factors, anatomical risk factors, and injury mechanisms.

Magnetic resonance imaging (MRI) has become an important tool for diagnosing ACL and concomitant injuries.[54] MRI cannot only indicate whether ligaments are torn, but it can also distinguish between different tear locations.[39] In **chapter 6,** an MRI measurement protocol is proposed that enables orthopedic surgeons to predict which patients are eligible for ACL repair.

Part III: Outcomes after ACL repair

Part III of this thesis focusses on the outcomes of modern-day arthroscopic primary ACL repair. This includes several aspects, including objective outcomes, such as failure and reoperation rates, and various patient-reported outcomes measurements (PROMS).

As mentioned, primary repair with static augmentation has the lowest failure and the least complication rates of all described repair techniques in the literature.[28] In **chapter 7,** the latest outcomes of this procedure in the literature are systematically presented.

Numerous studies have shown that failure rates of ACL reconstruction in young patients are high (10 to 28%).[55–58] In **chapter 8,** the failure rates and patient-reported outcomes measures (PROMs) following primary ACL repair of proximal tears in different age groups are assessed.

Successful return to sports (RTS) is thought to be one of the most important indicators of success after ACL surgery.[59–61] In **chapter 9,** the RTS rates and the timeline of rehabilitation milestones following primary ACL repair are reported.

As the native ligament is preserved, normal kinematics are potentially restored, leading to a more normal feeling of the knee joint than reconstructive surgery. In **chapter 10,** the extent to which patients forget their operative knee joint daily between both groups is investigated.

Anterior cruciate ligament reconstruction is associated with moderate to severe postoperative pain in the first days after surgery and requires the use of long-acting nerve blocks and severe pain killers.[62,63] **Chapter 11** assesses postoperative pain and daily opioid use between ACL repair and ACL reconstruction and investigates if ACL repair could also be performed without using perioperative nerve blocks.

Although it is recommended that primary repair should be performed in the acute or subacute phase, the ideal treatment window is debatable, as it has been suggested that some tears may even be repairable within the chronic phase.[64] In **chapter 12,** it is assessed whether primary repair of proximal ACL tears in the delayed setting leads to similar outcomes as compared to ACL repair in the acute setting.

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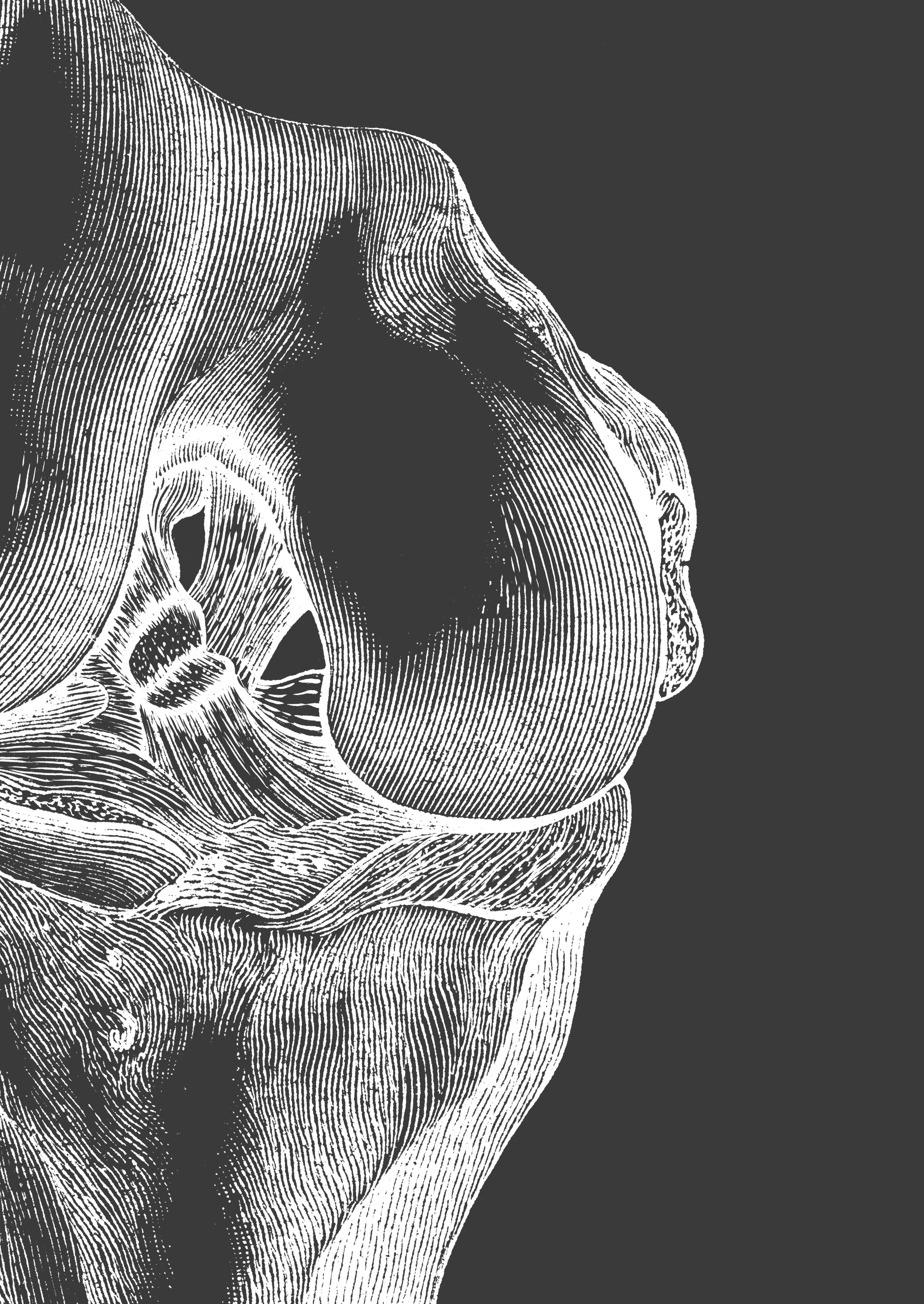
Part 2

Acute treatment of ACL injuries



Chapter 2

Primary repair of anterior cruciate ligament injuries: current level of evidence of available techniques

Vermeijden HD, van der List JP, O'Brien RJ, DiFelice GS

JBJS reviews. 2021 May 6;9(5).

Abstract

Recently, there has been a resurgence of interest in primary anterior cruciate ligament (ACL) repair that has the potential to preserve native tissue using a more minimally invasive approach. Multiple repair techniques for different tear types have been reported over the last decade.

From a healing perspective, proximal tears can be reinserted directly toward the femoral wall due to better intrinsic healing capacity than midsubstance tears. These procedures can be classified further as direct suture repair with or without static or dynamic augmentation. Due to limited healing capacity, current evidence does not support direct repair of midsubstance tears. In many instances biological augmentation is needed to enhance the healing potential of the ACL.

While ACL repair is certainly not an effective surgical approach for all tears or in all patients, this procedure can be an effective and less morbid alternative to ACL reconstruction in carefully selected patients.

Overall current reported level of evidence of published studies ranges from low to moderate, and therefore there is a need for higher-quality, comparative studies in which outcomes of larger patient groups are compared to the current gold standard of ACL reconstruction

Introduction

Mayo Robson performed the first open surgical treatment of a cruciate injury in 1897, when he primarily repaired a proximally avulsed anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) tear.[1] It wasn't until the 1970s, however, that open primary ACL repair became a widespread treatment for ACL injury in athletic populations. Despite encouraging early clinical outcomes, Feagin and Curl were in 1976 the first to describe a deterioration of open repair outcomes at mid-term follow-up (5 years).[2] As time passed, multiple other studies also showed substantial deterioration at mid-term follow-up.[3] As operative arthroscopy gained acceptance in the 1980s, there was a heightened interest in reconstructive techniques to address a growing athletic population suffering ACL injuries. In the 1990s, open primary repair was mostly abandoned in favor of ACL reconstruction which, to date, is still the surgical standard for the ACL deficient knee in active patients.[4]

Recently, there has been a resurgence of interest in ACL repair.[5] In contrast to the historically disappointing clinical results of non-selective, open ACL repair; emerging research suggests that improved outcomes may be expected by applying modern-day arthroscopic and rehabilitative techniques to selective patients eligible for various tear location-dependent suture techniques.[6] Over the last decade, multiple different repair techniques have been reported.[5] This article will first review the rationale behind modern-day ACL repair, then review the different currently used treatments for various tear types, and finally assess the available evidence for these procedures.

Rationale behind primary repair

Multiple reasons have contributed to the aforementioned resurgence of interest in ACL repair. First, improved outcomes as compared to the historical outcomes can be expected due to several modern-day advancements including a minimally invasive arthroscopic approach and utilizing immediate post-operative mobilization (versus historical casting and immobilization).[6] Secondly, there are some potential advantages of repairing a torn ACL rather than reconstructing it: the native ligament can be preserved which preserves the blood supply and potentially preserves the proprioception, and there is no need for graft harvest which prevents donor-site morbidity.[5] Another reason for the renewed interest is that revision surgery has now been found to be an uncomplicated single-stage primary reconstruction procedure.[7]

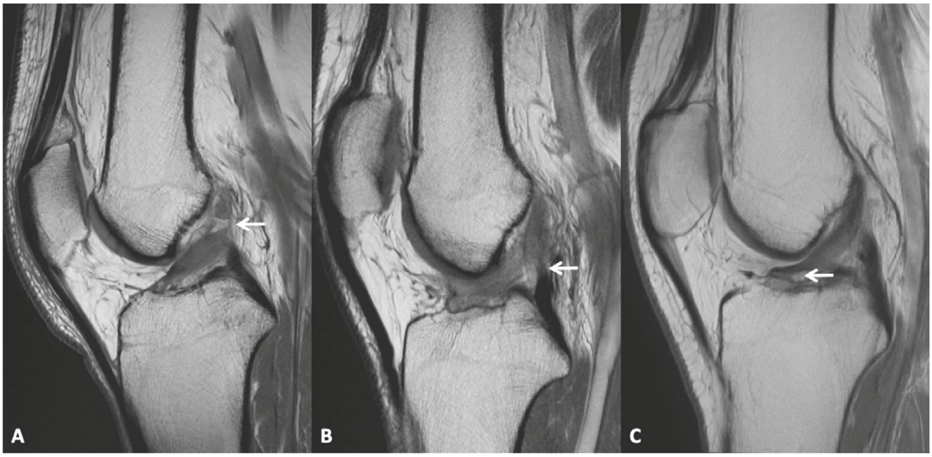
ACL tear locations with different treatment principles

In recent years, various tear location-dependent repair techniques have been reported. Variances in healing capacity of different tear locations can explain the rationale behind these different techniques.

Proximal tears

Proximal tears are generally defined as tears in the proximal 25% of the ACL (leaving >75% of the distal ACL intact) and occur in roughly 10–43% of all ACL tears (Figure 1A).[8] From a healing standpoint, both better vascularity and increased intrinsic healing capacity are present within this quarter of the ACL as compared to the midsubstance.[9] A histological study suggested that proximal tears may have an intrinsic healing response similar to that of the medial collateral ligament (MCL).[10] Moreover, disrupted ACLs have been shown to reattach to the posterior cruciate ligament (PCL) or to the intercondylar notch roof, implying that healing response characteristics may exist.[11] However, although this healing response is well-documented, this does not restore the ACL's biomechanical function. Several surgeons and investigators have therefore promoted the concept of inducing and promoting self-healing of torn ACLs by re-approximation of proximal tears toward the femoral wall using sutures,[6] although it remains unknown if the native complex microanatomy can actually be restored. Two general fixation methods have been described to ultimately fix the reapproximated ACL at its anatomic insertion site, including transosseous tunnel fixation using a cortical button or direct fixation using suture anchors.[6]

Figure 1. Two examples of sagittal T1-weighted MRI images of patients with ACL tears *(arrow)*.



(A) A 36-year-old female with proximal tear with excellent tissue quality; (B) A 24-year-old male with midsubstance tear; (C) A 21-year-old male with distal avulsion tear with excellent tissue quality.

Midsubstance tears

Midsubstance tears are defined as tears within 25–75% of the distal-proximal distance of the ACL and occur in roughly 52% of all tears (Figure 1B).[8] As opposed to proximal tears, the healing capacity of midsubstance tears is limited.[10] Midsubstance tears have a lower likelihood of healing due to poorer blood supply[5], whereas the integrity of the synovial sheet may also be related as improved outcomes following repair have been reported in in one-part tears with intact synovial coverage as compared to more-part ACL tears.[12] Although it is known that ACL insertions sites are better vascularized, ligament perfusion is primarily supplied by periligamentous capillaries within the synovial sheet, which can be disrupted when the ligament is torn at the midsubstance.[12] Furthermore, a stable fibrin-platelet clot, which is necessary for healing, is less likely to form at the injury site of midsubstance tears, given the continuous flow of synovial fluid that prematurely breaks down this clot.[13] Therefore, it is thought that midsubstance tears cannot be repaired directly and that some form of biological augmentation is necessary for successful healing.[7] Other investigators have therefore pursued suture repair with implementation of biological augmentation, such as scaffolds, to stabilize the blood clot and enhance the healing potential of the ruptured ends of the ligament.[7,14]

Distal tears
Distal tears are defined as tears in the distal 25% of the ACL and occur in approximately 4% of all ACL tears (Figure 1C).[8] In contrast to proximal tears, distal tears are most commonly associated with bony avulsions rather than soft-tissue avulsion type tears, especially in the osteoporotic or skeletally immature population,[15] in which nearly all patients younger than 10 years have a bony component (93%).[16] For these tear types, open or arthroscopic reduction and internal fixation remains the preferred surgical treatment, but there is no consensus regarding the optimal fixation method.[17]

Primary repair for proximal tears

Although initial studies reported on non-augmented repair techniques, more recent studies have advocated reinforcing the repaired ligament with either static or dynamic augmentation to confer additional stability during the early healing phase.[6] With static augmentation, the ligament is augmented by a 3 mm braid whereas in dynamic augmentation, an addition elastic link is utilized.[5] From a biomechanical perspective, all described techniques have been demonstrated to effectively restore control of anterior tibial translation at time zero.[18,19] The clinical outcomes of direct suture repair with and without static and dynamic augmentation will be discussed per level of evidence. In addition, the available evidence will be summarized using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group system.[20]

Suture repair without augmentation
Level I/II studies: No recently published or currently ongoing level I or II evidence studies were identified.

Level III studies: One study with 20 repair patients have reported their outcomes of direct suture repair without augmentation.[21] Achtnich et al. compared the outcomes of suture anchor repair and ACL reconstruction. At a mean follow-up of 28 months, a 15% failure rate was observed in the repair group, while no failures occurred in the reconstruction group ($p = 0.231$). Nevertheless, functional and subjective outcomes were excellent regardless of treatment strategy. Magnetic resonance imaging (MRI) showed homogeneous signals in 86% of the 20 patients treated with suture repair.

Level IV studies: Six studies were identified that reported outcomes of non-augmented repair suture repair.[22–26] DiFelice et al. reported good results following double suture anchor repair in 11 patients with one failure (9%) and excellent subjective outcomes at mean follow-up of 3.5 years.[25] In their follow-up study, they showed that the clinical outcomes maintained at mid-term follow-up.[26] Similarly, others have also reported similar short-term results using transosseous tunnel techniques since both Ferretti et al. and Mukhopadhyay et al. reported no failures at short-term follow-up.[24,27] When evaluating studies with longer follow-up, Nau et al. reported two revisions (3.3%) following suture repair in 60 patients within 72 hours after injury at minimum of five-year follow-up.[22] In contrast, a small retrospective case series of 13 patients reported high failure rates (25%) following single push-lock suture anchor repair at mean follow-up of 79 months.[23]

Conclusion: Although direct suture repair without augmentation can lead to good outcomes with reported slightly higher failure rates, but similar subjective results as compared to ACL reconstruction, there is **low evidence** to support this based on the fact that most studies are level IV studies.

Suture repair with static augmentation

Level I/II studies: No level I or II studies were identified. Currently, there is a multi-center, randomized controlled trial (RCT) comparing suture repair with Internal Bracing, dynamic intraligamentary stabilization (DIS) repair, and ACL reconstruction for acute proximal tears ongoing to assess clinical efficacy and economic benefits.[28]

Level III: Two studies have reported their outcomes of direct suture repair with augmentation.[29,30] Jonkergouw et al. assessed the role of suture augmentation in the first 56 consecutive patients treated with suture anchor repair.[29] Although lower failure rates were observed in those patients treated with the Internal Bracing cohort (7.4% versus 13.8%, respectively) versus the non-augmented suture repair, this study was not powered to assess statistical significance. Ortmaier et al. reported good outcomes in their matched-pair analysis between 24 patients treated with Internal Brace repair and 25 with hamstring autografts and 20 quadriceps autografts.[30] The authors reported no failures or reoperations at a minimum follow-up of 12 months, while no significant differences were observed between groups regarding pain and knee satisfaction scores. Furthermore, overall return to sports (RTS) participation rate was high (91.3%) and did not differ between treatment groups.

Level IV: Five studies were identified. Mackay et al. were, in 2015, the first reporting outcomes of 68 patients undergoing suture repair with Internal Bracing.[31] They reported four re-interventions (6.0%) and only one failure (1.5%) at one-year follow-up. Furthermore, radiographic and arthroscopic evaluation confirmed evidence of healing of the repaired ACL. At two-years, there were two failures (4.8%) in their cohort of 46 repair patients.[32] Furthermore, the Knee injury and Osteoarthritis Outcome Score (KOOS) scores improved significantly from baseline in all cases ($p < 0.001$), but a significant decrease in Marx Activity Scale was also observed (12.3 to 8.3; $p < 0.001$). Kalina et al., evaluated the outcomes of 20 patients treated with Internal Brace repair and reported three failures (15%) at a minimum follow-up of 12 months.[33] Furthermore, the mean International Knee Documentation Committee (IKDC) subjective score was 89, Lysholm score was 91, and Tegner scores decreased from 8.2 preinjury to 7.4 postoperatively. Douoguih et al. reported the two-year outcomes of 27 patients treated with Internal Brace repair and noted four failures (15%).[34] Finally, Schneider et al. noted a 3% revision rate and good to excellent subjective outcomes in patients treated with Internal Brace repair at mean follow-up of 21 months.[35]

Conclusion: Although direct suture repair with augmentation can lead to good outcomes with similar reported failure rates and subjective outcomes as compared with those reported in the ACL reconstruction literature, there is **low evidence** to support this based on the fact that most studies are level III & IV studies.

Suture repair with dynamic augmentation

Level I/II studies: Two RCTs were identified that assessed clinical outcomes of DIS.[36,37] Hoogeslag et al. reported their findings of 48 patients either receiving DIS or ACL reconstruction.[36] At two-year follow-up, lower failure rates were reported in the DIS group (8.7% versus 19.0%, respectively), but this study was not powered to assess statistical significance. Contradictory, a higher number of other adverse events were reported in the DIS group. These findings were confirmed in another level I study of 85 patients treated with either DIS repair or ACL reconstruction, with no significant differences in failure rates (16.3% versus 12.5%, respectively) and subjective outcome scores at two years.[37] Again, a higher number of adverse events were associated with the DIS approach.

Level III: Two studies were found.[38,39] Bieri et al. performed a matched cohort study of 106 patients treated either with DIS or ACL reconstruction.[39] They reported a 11% revision rate in the DIS group and 7% in the reconstruction group, while hardware removal was significantly more common following DIS procedure (36% versus 6%, $p < 0.001$, respectively). Interestingly, DIS patients returned to work nearly one month earlier than reconstruction patients. Haberli et al. assessed the outcomes of 173 patients treated with DIS with either hardware removal (n = 47) or no additional procedure (n = 126).[38] The authors reported no significant differences in objective laxity and subjective outcomes at two year follow-up. Therefore, they concluded that hardware could be removed safely without adverse consequences for knee stability.

Level IV: Sufficient data has been published for the DIS procedure only, with multiple case-series reporting on more than 650 cases.[5] Although initial studies reported outcomes of both proximal and midsubstance tears, more recent studies have indicated that this technique should only be performed in proximal tears.[40] A recent meta-analysis found a mean failure rate of 11%, reoperation rate of 10%, and hardware removal rate of 29%, while subjective outcomes were >85% of maximum scores following this procedure for proximal tears only.[6] One explanation for this high complication rate could be explained by the large spring device that is implemented (length, 30 mm; diameter, 10 mm), which can potentially increase the risk of scar tissue, range of motion (ROM) deficits, and arthrofibrosis.[41] Future studies are therefore necessary to assess the added value of this spring device.

Conclusion: Although there have been two level I studies looking at the DIS procedure versus reconstruction, there is **moderate** evidence for acceptable failure rates given that the studies reported significantly varied numbers. In addition, there is **moderate** evidence that subjective outcomes are similar to those of ACL reconstruction and **moderate** evidence that complications and reoperations are higher following the DIS procedure. Furthermore, it should be noted that designers or first-adopters have conducted most of the published DIS studies.

Primary repair with augmentation for midsubstance tears

As previously mentioned, ligament-to-ligament healing is hypothesized to be limited.[10] Therefore, some researchers are attempting to repair midsubstance tears using bioinductive scaffolds to enhance the biological healing potential of the torn ACL.[42] One of these options is the Bridge-Enhanced ACL Repair (BEAR) procedure, which focuses on midsubstance ACL repair using a collagen-based scaffold that has been soaked in platelet-rich autologous plasma. This scaffold is then placed between the torn ends of the ACL to facilitate ligamentous healing by anchoring the clot in place. Others, however, have advocated using protective collagen I/III membrane, acting as a scaffold and sutured to the ACL surface to improve the midsubstance ACL tear results.[14]

Suture repair with collagen scaffold
Level I/II: After a pilot study of 10 patients in which they concluded that the treatment was safe,[13,43] the research group performed the first RCT with 100 patients treated with BEAR or ACL reconstruction using hamstring autografts (median age of 17 years).[7] At two-year follow-up, higher failure rates were observed in the BEAR group (14% versus 6%, respectively), but this study was not powered on failure rate. All failed BEAR procedures were converted to uncomplicated ACL reconstructions with excellent short-term outcomes, while revision reconstruction surgery was performed in those with failed ACL reconstructions. Furthermore, side-to-side differences measured by KT-1000 (1.61 mm versus 1.77 mm) and IKDC Subjective score (88.9 versus 84.8) were similar between both groups. Additionally, the authors showed that hamstring strength indices were significantly higher in the BEAR group, respectively (98% versus 63%). Therefore, they concluded that ACL repair with BEAR implant resulted in similar outcomes to those of ACL reconstruction and that future studies evaluating this technique are justified.

Level III: One study by Evangelopoulos et al. was identified that reported their outcomes of DIS repair with and without the application of protective collagen membrane on 56 patients.[14] At final follow-up, a significantly lower total complication rate was reported when applying the membrane (8.7% versus 78.8%). This included a lower failure rate (0% versus 18%) and lower extension deficit rate (9% versus 33%) in the membrane group (n = 23) compared to the membrane-free group (n = 33). The membrane was identified as the only independent variable associated with reduced complications. Due to the overall high complication rate, they discouraged the DIS procedure for midsubstance tears but also identified a potential beneficial role for membrane application during ligament healing.

Level IV: No studies were identified.

Conclusion: There is **low to moderate** evidence that failure rates for collagen augmentation procedures are higher than ACL reconstruction, based on one large level I study and pilot studies. Furthermore, there is **moderate** evidence that subjective outcomes are similar between both procedures and **moderate** evidence that hamstring strength, due to avoidance of donor-site morbidity, is higher following collagen augmentation, respectively.

Primary repair for distal tears

As previously mentioned, various fixation methods exist to treat bony avulsions, including screws, sutures, and K-wires. Since multiple studies have assessed outcomes of these tear types, only recent studies and larger case-series will be reviewed.

Level I/II studies: No studies were identified.

Level III: When reviewing the literature, Melugin et al. compared surgical fixation of bony fragments with ACL reconstruction for soft-tissue tears in 40 pediatric patients.[44] At mid-term follow-up, a 5% failure rate was observed in the repaired group compared to 15% failure rate in the reconstructed group (p = 0.410). On the contrary, the arthrofibrosis rate was higher in the repaired group (20% vs. 2.5%, respectively), while subjective outcomes were excellent in both. Callanan et al. reported the outcomes of 68 pediatric patients with bony avulsion tears treated with either suture or screw fixation.[45] In both groups, 3% of patients sustained a reinjury; however, 24% of the suture and 34% of the screw group underwent subsequent surgery for arthrofibrosis. When reviewing other studies, several authors also reported low failure rates and excellent subjective outcomes but reported high risk for arthrofibrosis after distal bony avulsion tear fixation using various techniques.[46,47]

Level IV: A systematic review reported acceptable outcomes in 580 pediatric patients treated for bony avulsions using various repair techniques in 26 studies.[17] Overall, 1.7% of patients had non-union. Arthrofibrosis occurred in 11% of patients, while ROM loss was reported in 22%. More recently, Leie et al. reported the mid-term outcomes of 48 patients (mean age 24.5 years) treated for bony avulsion fractures using K-wires.[48] At final follow-up, 10.4% of patients sustained a reinjury, while no reoperations (0%) were reported. Mean IKDC subjective and Lysholm score were 86 and 92. Several other case-series supported these outcomes by reporting similar short and mid-term outcomes.[49,50]

Conclusion: There is **low** evidence that distal ACL repair leads to low failure rates and good subjective outcomes given that only level III and IV studies have been published. Additionally, there is **moderate** evidence that there is increased risk for postoperative stiffness following this procedure.

Eligiblity for repair

Learning from both historical and more recent studies, it is now known that strict patient selection is paramount for achieving successful outcomes with primary repair. Over the last decade, several factors, besides tear type and tissue quality, that predict eligibility for repair have been identified.

Older patients

When specifically evaluating eligibility for repair of proximal ACL tears, Van der List et al. showed that older patients are more likely to be treated with primary repair.[51] One of the reasons for this finding is that proximal tears are more frequently found in patients >35 years than in those <35 years (23% versus 8%).[8] Our analysis is based on an age related decrease in blood supply, although the exact reason remains unclear. It does appear that older patients are good candidates for repair, given the relatively lower demand of these patients, and excellent reported outcomes. Nevertheless, it is well known that a certain percentage of these patients can achieve successful results solely with non-operative treatment consisting of physical therapy.[52] A recent study showed that non-operative treatment after ACL injury failed in 90% of patients younger than 25 years, 56% aged 25 to 40 years, and 33% older than 40 years.[53] Therefore, further studies are needed to determine which patient characteristics are indicated for early repair surgery and if this procedure is indeed superior over non-operative treatment, especially in the older patient population.

Surgical timing

When considering primary repair, it is recommended to perform surgery in the (sub)acute phase (within 12 weeks post-injury[54]) since the ligament can potentially retract and scar.[6] Although the ideal treatment window has yet to be established, most studies have reported performed primary repair within 3 weeks post-injury.[6] A recent case-control study, however, found patients more likely to be treated with primary repair if surgery was performed within four weeks post-injury (OR 3.3, $p < 0.001$) instead of those treated after four weeks.[51]. Furthermore, it should be noted that recent studies showed that acute ACL reconstruction surgery is not associated with increased risk for complications, including arthrofibrosis or postoperative stiffness as was previously assumed.[55]

Gender

When reviewing gender-specific outcomes, it has been shown that gender is not predictive for the possibility of undergoing primary repair.[51] Furthermore, no differences in clinical outcomes between genders have been observed.[40]

Criteria for successful outcomes

In recent years, several factors have been identified that substantially affect clinical outcomes following primary repair, such as younger age and activity levels. These factors will be reviewed in more detail in this section.

Pediatric patients

Treatment of ACL tears in children and adolescents remains challenging, mainly due to the presence of open physes.[56] There are certainly some theoretical advantages of primary repair over reconstruction in this patient group since growth disturbances can potentially be avoided, and the risk of OA may be decreased.[57] Previously published studies in younger patients, however, have shown inconsistent results following repair. Dabis et al. reported excellent outcomes in their cohort of 20 pediatric patients (mean 12.6 years) treated with primary repair with Internal Bracing at two-year follow-up.[58] In their study, there were no failures, no side-to-side difference, and no complications. By contrast, Gagliardi et al. reported that 13 of 22 pediatric patients (41%) failed following primary repair as compared to 6 of 151 (4%) patients following reconstruction.[56] In our experience, we have also observed significantly higher failure rates in patients younger than 18 years old and therefore only recommend isolated ACL repair in younger patients on a very limited basis.

Anterolateral structures

Recently, there has been a resurgence of interest in injuries and treatment of anterolateral structures.[59] Comparative studies showed that concomitant anterolateral ligament or lateral extra-articular procedures are associated with significantly lower failure risks following ACL reconstruction.[59] Therefore, improved outcomes may also be expected when combining treatment of anterolateral structures and ACL repair, especially in younger and high-risk patients.

This is an exciting area of research and future studies are needed to assess if this combination will improve the clinical outcomes of ACL repair surgery.

Activity levels

An important predictive role of activity level on this procedure's success has been observed since higher failure rates have been reported in patients performing highly active sports than to those playing recreational sports.[19] A recent case-series showed that among 60 patients treated with primary suture repair, 85% returned to any sports, 70% returned to knee-strenuous sports, 60% returned to preinjury level, and identified older age, which is generally associated with lower activity levels, as a positive predictor for returning to preinjury sport level.[60] Highly active patients should therefore be well informed of the potentially increased risk for treatment failure when discussing primary repair as a treatment option.

Summary

Currently, the surgical standard for treating ACL injuries is ligament reconstruction. In recent years, however, various modern-day tear location-dependent ACL repair techniques have been proposed. From a healing perspective, proximal tears can be reapproximated directly toward the femoral wall due to their better intrinsic healing capacity than midsubstance tears. Midsubstance tears, on the contrary, seem to require biomechanical augmentation to improve their healing potential. While ACL repair is certainly not effective for all patients, this procedure seems to be an effective and less morbid alternative to ACL reconstruction for treating carefully selected ACL injured patients. The current reported level of evidence, however, is low to moderate and there is a clear need for high-quality studies in which outcomes of larger groups of patients are compared to the current gold standard.

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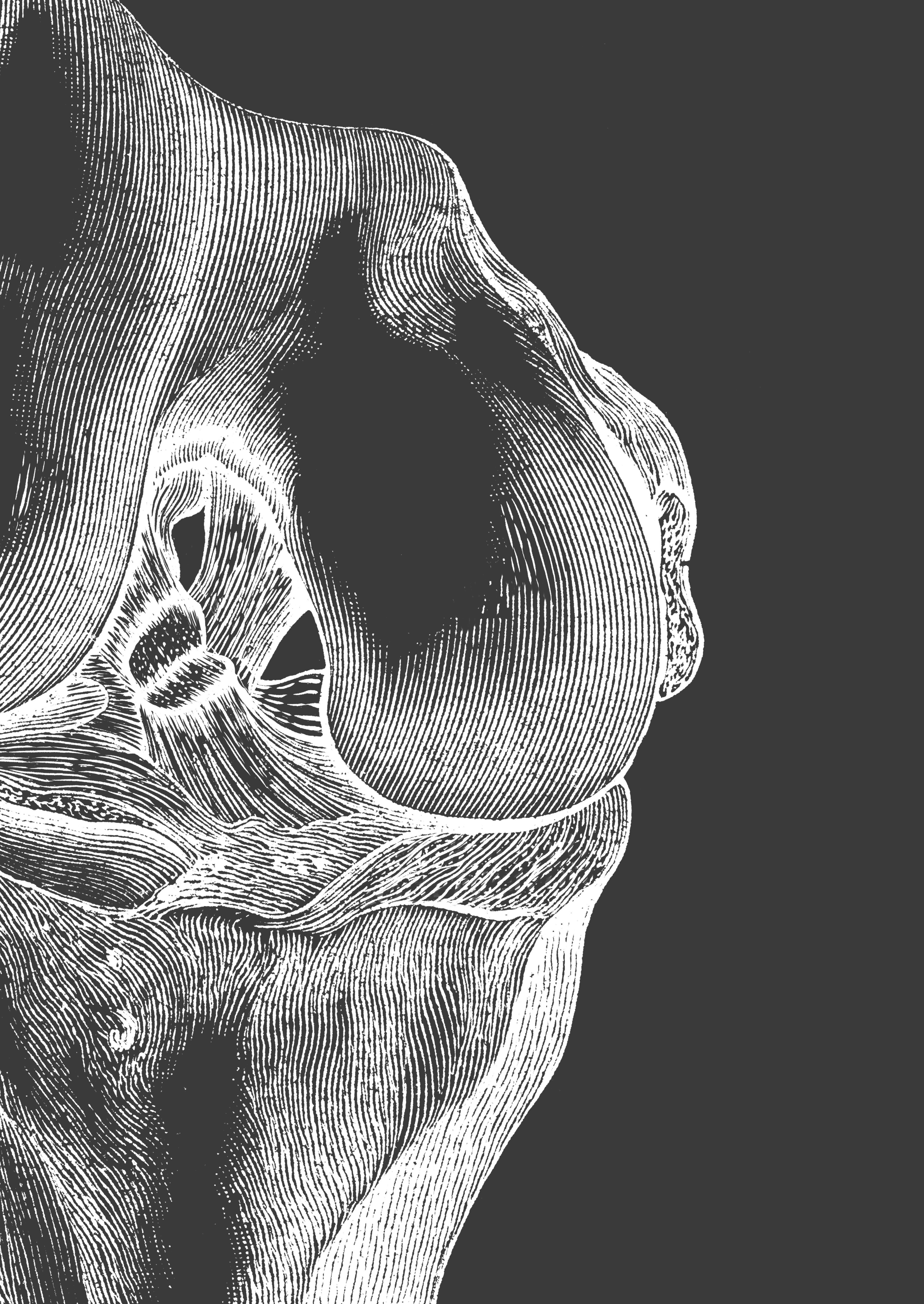

Chapter 3

Early and delayed surgery for isolated ACL and multiligamentous knee injuries have equivalent results: A systematic review and meta-analysis

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Abstract

Background
Early surgery of acute ligamentous injuries has recently shown good clinical and functional outcomes.

Purpose
To assess the advantages of early versus delayed surgery in patients undergoing either isolated ACL or multiligamentous knee (MLIK) surgery.

Study-design
Meta-analyses of Level I, II and III studies.

Methods
A systematic search was performed using PubMed, EMBASE, and Cochrane for studies reporting outcomes of timing of surgery after isolated ACL reconstruction or in the MLIK setting using accelerated rehabilitation protocols. Two separate analyses were conducted to differentiate between early and delayed treatment (3 week and 6-week cutoff). Collected outcomes included meniscal or chondral lesions, failure and reoperation rates, range of motion (ROM) deficits, other complications, muscle strength, instrumented laxity, and functional outcomes. Outcomes were reported in risk ratios (RR) or mean differences (MD) with 95% confidence intervals [CI].

Results
For timing of isolated ACL surgery, 16 studies were included with a total of 2093 patients. There was high-grade evidence that there were no differences in meniscal or chondral lesions, failure and reoperation rates, stiffness, ROM deficits, complications, muscle strength, instrumented laxity, and functional outcomes between patients treated early and late (all $p>0.05$). When only including studies that set no preoperative criteria for early surgery, the findings were similar.

Regarding MLIK surgery, 14 studies were included with a total of 1172 patients. Low evidence was noted for the following: patients treated early had significantly less meniscal (RR, 0.7, $p=0.04$) and chondral injuries (RR, 0.5, $p<0.001$), while no differences were found in reoperation rates, complications, stiffness, ROM deficits, muscle strength, instrumented laxity, and functional outcomes between both groups. Besides higher Lysholm scores in the early group for the 3-week analysis (MD, 6.8; $p=0.006$), there were no differences between both cutoff analyses.

Conclusion
This systematic review with meta-analysis found no difference in clinical and functional outcomes between early and delayed surgery for isolated ACL injuries. For MLIK injuries, there were also no differences in surgical outcomes between early and delayed surgery.

Introduction

Acute ligamentous knee injuries can either be present in isolation or in the setting of a multiligament injured knee (MLIK).[1,2] Most acute knee injuries, however, involve a single ligament injury, with the anterior cruciate ligament (ACL) being one of the most frequently injured knee structures.[3] As ligamentous knee injuries often result in functional impairment, surgical treatment is generally recommended in active patients to restore knee stability and reduce the risk of further injuries.[4] However, there is currently no consensus regarding the optimal timing of these procedures.[5]

Historically, ligamentous injuries of the knee were treated as “knee emergencies” with open repair procedures and post-operative casting.[6] However, this led to unacceptably high rates of stiffness and arthrofibrosis due to the immobilization.[7] Subsequently, surgical treatment of acute knee injuries was often delayed to reduce the risk of arthrofibrosis and stiffness.[8] The disadvantage of delaying these procedures is that this increases the time from injury to surgery, may consequently lead to quadriceps atrophy,[9] and potentially increases the risk of meniscal and chondral damage.[10,11] Therefore, it might be advantageous to indicate patients early for surgery to enable a faster return to work or sports activities. Furthermore, recent studies with modern surgical techniques and rehabilitation protocols did not associate early surgery with higher risk for postoperative stiffness (Table 1).[12] A recent meta-analysis also compared the outcomes of early and delayed surgery following both single anterior cruciate ligament and MLIK injuries.[13] In this study, however, the cutoff between early and delayed surgery was not clearly defined and there was overlap in cutoffs between included studies (ranging from 48 hours to 1-year postinjury).[13]

Table 1. Potential advantages and disadvantages of acute knee surgery

Advantages of acute surgery	Disadvantages of acute surgery
Decreased risk for further meniscal injury	Delayed surgery might improve pre-operative ROM
Decreased risk for further chondral lesions	Increased risk for complications (arthrofibrosis and postoperative stiffness)
Decreased risk for degenerative joint changes	Subset of patients may be surgically overtreated
Shorter time injury to RTS	Patients might not be psychologically prepared for surgery
Earlier RTW and RTS, thus cost-effective	
Potential for ligament repair	
No muscle atrophy and deconditioning	

RTS indicates return to sports; RTW, return to work; ROM, range of motion.

The purpose of this meta-analysis was to assess the possible advantages of early versus delayed knee surgery in patients undergoing either (i) isolated ACL surgery or (ii) in the MLIK setting using clearly defined cutoffs. It was hypothesized that there would be no increased risk for postoperative stiffness and ROM deficits following early treatment with modern-day surgical and rehabilitation protocols, while clinical and functional outcomes would be similar between early and delayed treatment.

Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were used to perform this systematic review with meta-analysis.[14]

Literature search

A systematic search was performed on December 12, 2020, using the electronic search engines PubMed, Cochrane Library, and Embase with the search algorithm *'(anterior cruciate ligament OR posterior cruciate ligament OR medial collateral ligament OR lateral collateral ligament OR multiligament injured knee OR knee dislocation) AND (reconstruction OR repair OR treatment OR surgery) AND ((early OR acute) AND (delayed OR chronic) OR timing)'* for randomized, non-randomized, and comparative cohort studies reporting outcomes of early and delayed surgery after isolated ACL reconstruction or in the MLIK setting. The search was limited to identify English studies only and published between January 1, 2000, and December 1, 2020. After duplicates were removed, two reviewers (XAY and HVD) independently reviewed all studies for titles and abstracts and then reviewed full-texts of eligible studies for inclusion. Furthermore, the reference lists of relevant studies were screened for additional studies not identified by the initial search strategy. Consensus was ultimately reached on the inclusion and exclusion of all studies, and a third reviewer was not needed.

Inclusion criteria for this study included (i) surgical treatment of isolated ACL injuries or MLIKs, (ii) early vs. delayed treatment group, (iii) follow-up of outcomes (e.g. clinical or functional outcomes), (iv) and comparative studies. Exclusion criteria included (i) incorrect or not specified timing protocol, (ii) no accelerated rehabilitation protocol (i.e. no immediate full ROM for isolated ACL surgery studies or more than 2-week knee immobilization after MLIK surgery), (ii) pediatric patient population, (iii) partial tears only, (iv) revision knee surgery, (v) studies with <10 patients, and (vi) non-comparative studies, biomechanical studies, or reviews. In case several studies reported on similar patient cohorts, it was first assessed if study data of multiple studies could be combined or used. Otherwise, the smallest cohort study or with the shortest follow-up was excluded.

Methodological quality of studies

Level of evidence was determined using the adjusted Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence.[14] To assess the methodological quality of studies, two different tools were used. The PEDro (Physiotherapy Evidence Database) tool was used for level I randomized clinical trials (RCT),[15] while the Methodological Index for Non-Randomized Studies (MINORS) instrument was used for non-randomized comparative studies.[16] For both tools, the mean scores with their percentage of the maximum score were reported.

Data extraction

Data was first collected in Excel 2017 (Microsoft Corp., Redmond, WA, USA). Collected study demographics included author names, year of publication, and number of patients. Collected patient demographics included age at time of surgery, gender, timing of surgery (early versus delayed), any meniscal or chondral damage (grade ≥ 1 classified by any grading system), treatment (repair, reconstruction or conservative treatment for each major knee ligament), and length of follow-up. For MLIK studies specifically, the Schenck knee dislocation (KD) classification was used to identify different injury patterns. Collected outcomes consisted of treatment failure (defined as rerupture or symptomatic instability), reoperations (defined as surgical intervention besides revision surgery), or any complication besides failure and reoperations (defined as any undesirable and unexpected result of surgery). In addition, isokinetic muscle strength at 180° degrees/sec and ROM (both passive knee motion and motion deficits) were collected. Postoperative stiffness was defined as a ROM deficit >5° as compared with the contralateral knee.[17] Furthermore, instrumented laxity, either using KT-1000 measurements or Rolimeter arthrometer, was collected. Collected functional outcomes included the Lysholm Knee score,[18] International Knee Documentation Committee (IKDC) objective and subjective score,[17,19] preinjury and postoperative Tegner score,[18] and the Single Assessment Numeric Evaluation (SANE).[20] Finally, the time to return to work and sports activities was collected.

For study purposes, the results will be presented in 2 parts. The outcomes of early versus delayed isolated ACL reconstruction will be presented first. Then, the results of early versus delayed knee surgery in patients undergoing MLIK surgery will be discussed.

Statistical analysis

RevMan Version 5.4 (Nordic Cochrane Center, Copenhagen, Denmark) and Excel 2017 were used for statistical analysis. Since multiple different cutoffs for early and delayed treatment have been reported, two separate analyses were conducted to present the most comprehensive information available. A 3-week cutoff time point was used in the first analysis, while a 6-week cutoff time point was used for the second analysis.[21,22] To avoid overlap of time intervals between both analyses, studies within the 3-week cutoff with their delayed group treated between 3 and 6 weeks postinjury were excluded for overall analysis. Dichotomous variables were compared using the Mantel-Haenszel test and expressed as risk ratios (RRs) with a 95% confidence interval [CI], while continuous variables were compared using the inverse variance method and expressed as mean differences (MDs) with a 95% CI. A random-effects model was used for all analyses, and forest plots were used to report the synthetic results. If means and standard deviations (SD) were not available, they were calculated according to previously defined methods, and sensitivity analyses excluding these studies were subsequently performed.[23] All tests were two-sided, and a $p < 0.05$ was considered statistically significant.

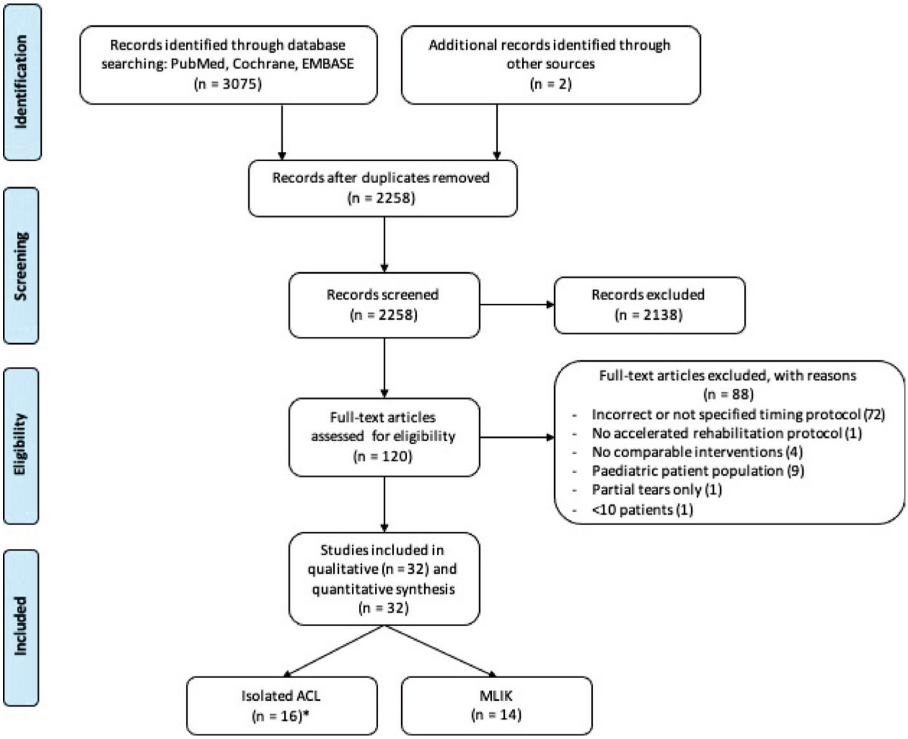
Not all figures of the analyses could be included in the manuscript. The appendix shows the Forest plots of all 51 analyses for isolated ACL and MLIK treatments.

Results part 1 – isolated ACL surgery

Study selection and characteristics

The results of the literature search are shown in Fig. 1, according to the PRISMA statement. After removing duplicates and reviewing title, abstract, and full-text of the articles, a total of 16 studies were ultimately included.[24,25,34–39,26–33] In regards to different cutoffs for early and delayed treatment, 11 studies were included in the 3-week cutoff analysis,[24–28,32,34,35,37,39] while five were included in the 6-week cutoff analyses.[29–31,33,38]

Figure 1.



A PRISMA flowchart of the included studies is shown. Asterisk indicates that study data of previously reported patients have been merged into one study for this meta-analysis.

A total of 2093 patients were included, with 864 in the early and 1229 in the delayed group. For the 3-week cutoff, 487 patients underwent early reconstruction with a mean time between injury to surgery of 7.8 ± 2.3 days, while 523 were treated late after 317.4 ± 67.0 days. For the 6-week cut-off, 377 patients were treated early (mean 24.4 ± 10.3 days), and 706 were treated late (mean 408.2 ± 176.5 days). Overall, mean age at surgery was 27.3 ± 6.3 years, 66% was male gender, and mean follow-up was 1.4 years (range of means: 0.5 to 3.0 years).

Quality of studies

Five level I RCTs were included.[24–28] Four studies were level II prospective studies,[31,32,34,36] whereas seven studies were level III retrospective studies.[29,30,33,35,37–39] The methodological quality of five RCTs scored 5.4 out of 10 points using the PEDro, representing 54% of the maximum points possible (Table 2).

Using the MINORS criteria, 11 comparative studies scored a mean of 18.4 ± 1.6 points, corresponding to 76.7% of the maximum possible (Table 3). Statistical heterogeneity among included studies was high regarding study design, surgical technique, reported outcomes, and follow-up length.

Table 2. Quality assessment of included RCTs' using the PEDro Scale

Authors	Year	Journal	Evidence	Study design	1	2	3	4	5	6	7	8	9	10	11	Total
Comparative isolated ACL reconstruction studies																
Bottoni et al. [21]	2008	Am J Sports Med	I	RCT	1	1	1	1	0	0	0	1	0	1	1	6
Manandhar et al. [22]	2018	J Clin Orthop Trauma	I	RCT	1	0	0	0	0	0	0	1	0	1	1	3
Meighan et al. [23]	2003	J Bone Joint Surg	I	RCT	1	1	1	0	0	0	1	1	1	1	0	6
Raviraj et al. [24]	2010	J Bone Joint Surg	I	RCT	1	1	0	1	0	0	1	1	0	1	1	6
Von Essen et al. [25, 59][a]	2020	KSSTA	I	RCT	1	1	1	1	0	0	0	1	0	1	1	6

RCT, Randomized Controlled Trial; [a] Data of previously reported patients have also been used in this meta-analysis.

The criteria of PEDro Scale with 0 points when not satisfied, 1 when clearly satisfied. Maximum score is 11 points.

1. Eligibility criteria were specified (this item does not contribute to total score)
2. Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received).
3. Allocation was concealed.
4. The groups were similar at baseline regarding the most important prognostic indicators.
5. There was blinding of all subjects.
6. There was blinding of all therapists who administered the therapy.
7. There was blinding of all assessors who measured at least one key outcome.
8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups
9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case data for at least one key outcome was analyzed by "intention to treat".
10. The results of between-group statistical comparisons are reported for at least one key outcome
11. The study provides both point measures and measures of variability for at least one key outcome

3

Table 3. Quality assessment of included studies using the Methodological Index for NonRandomized Studies (MINORS) criteria

Authors	Year	Journal	Evidence	Study design	1	2	3	4	5	6	7	8	9	10	11	12	Total
Comparative isolated ACL surgery studies																	
Baba et al.[a] [26]	2017	OJSM	III	Cohort	2	2	0	2	2	2	1	2	2	2	1	2	20
Bierke et al. [27]	2020	Arch Orthop Trauma Surg	III	Cohort	2	2	0	2	0	2	1	2	2	2	2	2	19
Burnett et al. [28]	2019	Iowa Orthop J.	II	Cohort	2	2	2	1	0	2	2	0	2	2	1	2	18
Chua et al. [29]	2020	J Knee Surg,	II	Cohort	2	2	2	2	0	2	2	2	2	2	1	2	21
Goradia et al. [30]	2001	Arthroscopy	III[c]	Cohort	2	1	0	2	2	2	1	0	2	2	2	2	18
Herbst et al.[b] [31]	2017	KSSTA	II	Cohort	2	2	2	2	0	1	2	1	2	2	1	2	19
Hu et al. [32]	2017	JCLA	III	Cohort	2	2	0	2	0	1	2	0	2	2	2	2	17
Hur et al. [33]	2017	Indian J Orthop,	II	Cohort	2	2	2	2	0	2	2	0	2	2	2	2	20
Karruppiah et al. [34]	2016	J Orthop,	III	Cohort	2	2	0	1	0	1	2	0	2	2	2	2	16
Papastergiou et al. [35]	2007	KSSTA	III	Cohort	2	2	0	2	0	2	2	0	2	2	1	2	17
Sterret et al. [36]	2003	Orthopedics	III	Cohort	2	2	0	2	0	2	1	0	2	2	2	2	17
Comparative MLIK studies																	
Billieres et al. [37]	2020	Orthop Traumatol Surg Res	III[c]	Cohort	2	2	0	2	2	2	0	0	2	2	0	2	16
Hanley et al. [38]	2017	J Knee Surg	III[c]	Cohort	2	2	0	2	0	2	2	0	2	2	0	2	16
Harner et al. [39]	2004	J Bone Joint Surg	III	Cohort	2	2	0	2	0	2	1	0	2	2	2	2	17
LaPrade et al. [40]	2019	Am J Sports Med	III[c]	Cohort	2	2	0	2	0	2	1	0	2	2	0	2	15
Liow et al. [41]	2003	J Bone Joint Surg	III[c]	Cohort	2	2	0	2	2	2	2	0	2	2	0	0	16
Moatshe et al. [42]	2017	OJSM	III	Cohort	2	2	0	1	0	2	2	0	2	2	0	2	15
Shamrock et al. [43]	2020	J Knee Surg,	III[c]	Cohort	2	2	0	2	0	2	2	0	2	2	1	2	17
Shelbourne et al. [44]	2007	Am J Sports Med	III[c]	Cohort	2	2	0	2	0	2	1	0	2	2	0	2	15
Subbiah et al. [45]	2011	J Orthop Surg	III[c]	Cohort	1	2	0	1	2	1	1	0	2	2	0	2	14
Sundararajan et al.[a] [46]	2018	Orthop J Sports Med.	III	Cohort	2	2	0	1	0	2	2	0	2	2	0	2	15

Table 3. Quality assessment of included studies using the Methodological Index for NonRandomized Studies (MINORS) criteria *(Continued)*

Authors	Year	Journal	Evidence	Study design	1	2	3	4	5	6	7	8	9	10	11	12	Total
Comparative isolated ACL surgery studies																	
Tzurbakis et al. [47]	2006	KSSTA	III	Cohort	2	2	0	2	0	2	1	0	2	2	0	2	15
Wajzifz et al. [48]	2014	Orthop Traumatol Surg Res.	III[c]	Cohort	2	2	0	2	2	1	2	0	2	2	0	2	17
Zhang et al. [49]	2013	Orthop Surg.	III	Cohort	2	2	0	2	0	2	1	0	2	2	0	2	15
Zhang et al. [50]	2020	OJSM	III	Cohort	2	2	0	2	0	2	1	0	2	2	0	2	15

[a] Patients treated in the subacute phase have been excluded for this meta-analysis; [b] Patients were divided into three groups based upon meniscal treatment, and those with isolated ACL reconstructions and ACL reconstructions with meniscal repair have been included separately in this meta-analysis; [c] This study reported being a level IV case series but we have classified this comparative study as level III cohort study.

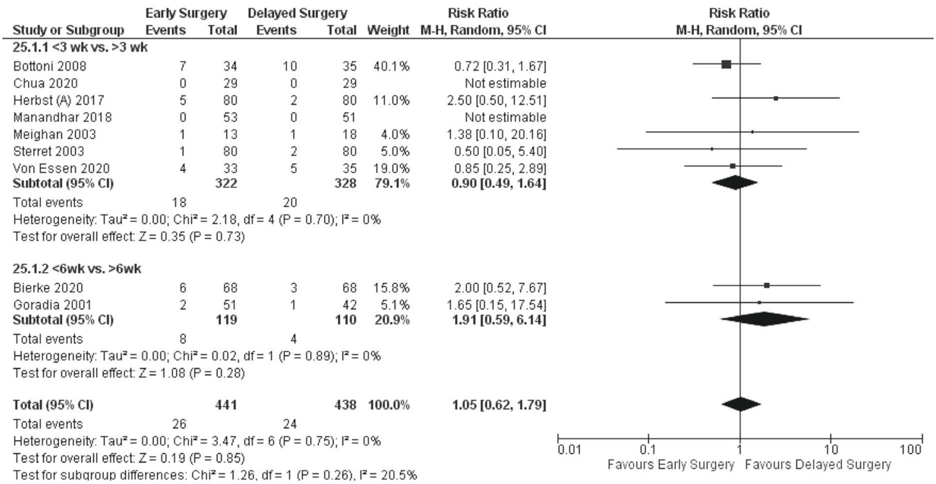
The criteria of MINORS with 0 points when not reported, 1 when reported but not adequate, and 2 when reported and adequate. Maximum score is 16 for non-comparative studies and 24 for comparative studies.

1. A clearly stated aim: the question addressed should be precise and relevant in the light of available literature.
2. Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion).
3. Prospective collection of data: data were collected according to a protocol established before the beginning of the study.
4. End points appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome which should be in accordance with the question addressed by the study. In addition, the end points should be assessed on an intention-to-treat basis.
5. Unbiased assessment of the study end point: blind evaluation of objective end points and double-blind evaluation of subjective end points. Otherwise, the reasons for not blinding should be stated.
6. Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events.
7. Loss to follow-up less than 5%: all patients should be included in the follow-up. Otherwise, the proportion lost to follow-up should not exceed the proportion experiencing the major end point.
8. Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% CI, according to the expected incidence of the outcome event, and information about the level for statistical.
9. An adequate control group: having a gold standard diagnostic test or therapeutic intervention recognized as the optimal intervention according to the available published data.
10. Contemporary groups: control and studies group should be managed during the same time period.
11. Baseline equivalence of groups: the groups should be similar regarding the criteria other than the studied endpoint. Absence of confounding factors that could bias the interpretation of the results.
12. Adequate statistical analyses: whether statistics were in accordance with type of study with calculation of confidence intervals or relative risk.

Outcomes early vs. delayed treatment

For all patients, no significant difference was found between early versus delayed treatment in meniscal injury (6 studies; RR, 0.9, p = 0.29) and chondral lesions (8 studies; RR, 0.8, p = 0.28). Similarly, there were no significant differences in treatment failure (12 studies; RR, 1.2, p = 0.61), reoperations (9 studies; RR, 0.9, p = 0.77), postoperative stiffness (9 studies; RR, 1.1, p = 0.8; Fig. 2), other complications (9 studies; RR, 0.7, p = 0.40), total knee motion (4 studies; MD 2.3°, p = 0.43), mean flexion deficit (4 studies; MD, -0.5°, p = 0.18), mean extension deficit (7 studies; MD, -0.2°, p = 0.37), and objective instrumented laxity (4 studies; MD, -0.3 mm, p = 0.33) between both groups. Significantly higher IKDC subjective scores (2 studies; MD, 3.0; p = 0.003) and postoperative Tegner scores (8 studies; MD, 0.4; p = 0.002; Fig. 3) were found in patients treated early, while (near)normal IKDC objective scores rates (4 studies; RR, 1.0; p = 0.57), and Lysholm scores (7 studies; MD, 1.4; p = 0.15) were similar. Furthermore, significantly higher mean extension strength was found in patients treated early (2 studies; MD, 3.0%; p = 0.03, respectively), whereas no statistical difference was found in flexion strength (2 studies; MD, 4.4%; p = 0.07). Lastly, acute surgery resulted in less sick-leave days as compared to delayed surgery (1 study; MD, -31.6 days; p = 0.003).

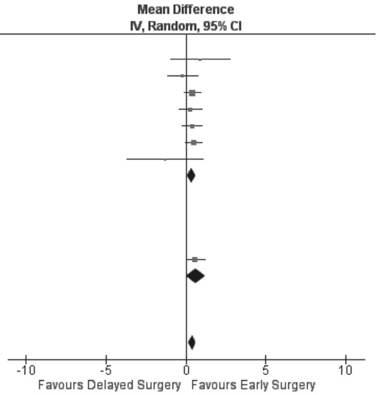
Figure 2. Postoperative Stifness Isolated ACL



Forest plot of the events of overall postoperative stiffness between acute vs. delayed isolated ACL surgery. Postoperative stiffness was defined as a range of motion deficit >5° as compared with the contralateral knee.

Figure 3. Postoperative Tegner Scores Isolated ACL

Study or Subgroup	Early Surgery Mean	SD	Total	Delayed Surgery Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
31.1.1 <3 wk. vs >3 wk.								
Bottoni 2008	5.8	3.9	34	4.9	3.9	35	1.8%	0.90 [-0.94, 2.74]
Chua 2020	5.8	2.2	29	6	1.5	29	6.7%	-0.20 [-1.17, 0.77]
Herbst (A) 2017	6.7	1.3	50	6.3	1.4	50	22.3%	0.40 [-0.13, 0.93]
Herbst (B) 2017	6.6	1.3	30	6.3	1.5	30	12.4%	0.30 [-0.41, 1.01]
Hur 2017	6	1.6	48	5.6	1.5	43	15.4%	0.40 [-0.24, 1.04]
Manandhar 2018	4.2	1.5	53	3.7	1.3	51	21.6%	0.50 [-0.04, 1.04]
Von Essen 2020	7	5.9	33	8.3	3.7	35	1.1%	-1.30 [-3.66, 1.06]
Subtotal (95% CI)			**277**			**273**	**81.4%**	**0.35 [0.07, 0.63]**
Heterogeneity: Tau² = 0.00; Chi² = 3.84, df = 6 (P = 0.70); I² = 0%								
Test for overall effect: Z = 2.47 (P = 0.01)								
31.1.2 <6 wk vs. >6 wk								
Goradia 2001	7.3	1.4	51	6.7	1.6	52	18.6%	0.60 [0.02, 1.18]
Subtotal (95% CI)			**51**			**52**	**18.6%**	**0.60 [0.02, 1.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.03 (P = 0.04)								
Total (95% CI)			**328**			**325**	**100.0%**	**0.40 [0.15, 0.65]**
Heterogeneity: Tau² = 0.00; Chi² = 4.42, df = 7 (P = 0.73); I² = 0%								
Test for overall effect: Z = 3.10 (P = 0.002)								
Test for subgroup differences: Chi² = 0.58, df = 1 (P = 0.45), I² = 0%								



Forest plot of the difference in overall postoperative Tegner scores between acute vs. delayed isolated ACL surgery.

When comparing outcomes following different cutoffs, it was noted that early treated patients had less chondral lesions (3 studies; RR, 0.5, p = 0.002) and lower complication rates (1 study; RR, 0.6, p = 0.006) than those treated late in the 6-week cutoff time point. On the contrary, these parameters were similar for the 3-week cutoff time point analysis (all p > 0.5). No other statistical differences were found between both cutoffs, although it should be noted that IKDC subjective scores, mean extension and flexion deficit, ROM, flexion and extension strength, and sick leave days were only reported in the 3-week cutoff time point analysis.

Sensitivity analysis including only studies with non-estimated means and SDs confirmed these outcomes. In addition, sensitivity analysis including only studies in which no exclusion criteria were set regarding swelling, ROM limitations, pain, or other inflammatory parameters also did not show a higher risk for stiffness and ROM deficits after acute surgery.

Results part 2 – MLIK surgery

Study selection and characteristics

Fourteen studies were selected for inclusion after removing duplicates and reviewing title, abstract, and full-text of eligible studies (Fig. 1).[40,41,50–53,42–49] This included 10 studies for the 3-week,[41,42,44,45,47,48,50–53] and four for the 6-week cutoff analyses.[40,43,46,49]

Overall, 1172 patients were included: 690 in the early and 482 in the delayed treatment group. For the 3-week cutoff, 394 patients underwent early treatment with a mean of 7.0 ± 5.0 days after surgery, and 317 were treated late with a mean of 275.4 ± 498.4 days, but this was not further specified for all studies included in the 6-week cut-off analysis. For all patients, mean age at surgery was 33.3 ± 14.2 years, 62% was male gender, and mean follow-up was 2.2 years (range of means 1.0 to 4.3 years). According to the Schenck Classification, most patients sustained a KD-I injury (48%), followed by KD III-L injury (26%), and KD III-M injury (21%).

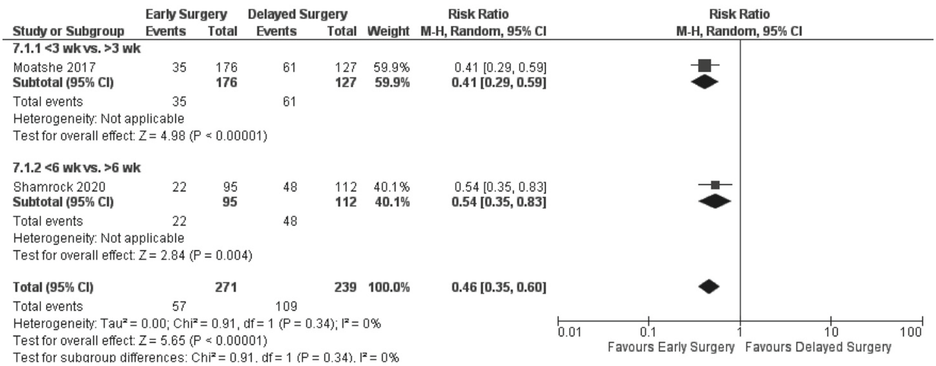
Quality of studies

No level I or II studies were identified. There were 14 levels III non-randomized comparative studies.[40,41,50–53,42–49] These studies scored a mean of 15.6 ± 1.0 points on the MINORS instrument, corresponding to 65.0% of the maximum possible (Table 2). Heterogeneity was present among the included studies.

Outcomes early vs. delayed treatment

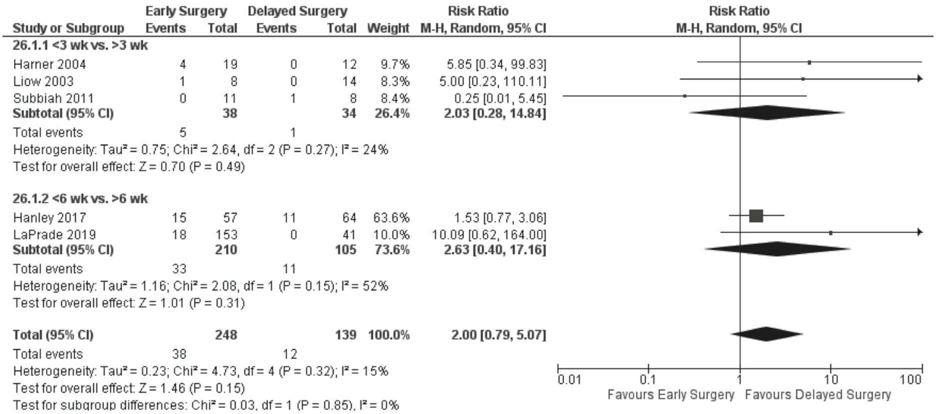
Overall, significantly less meniscal injuries (1 study; RR, 0.7, p = 0.04) and less chondral lesions (2 studies; RR, 0.5, p < 0.001; Fig. 4) were found in patients treated early as compared to those treated late. There were no significant differences in reoperations (3 studies; RR, 0.3, p = 0.49), postoperative stiffness (3 studies; RR, 2.0, p = 0.49; Fig. 5), total knee motion (4 studies; MD 0.0°, p > 0.99), mean flexion deficit (4 studies; MD, 2.2°, p = 0.23), mean extension deficit (4 studies; MD, 0.4°, p = 0.41), and objective instrumented laxity (2 studies; MD -0.9 mm, p = 0.06). Significantly higher Lysholm scores were found in patients undergoing early treatment (10 studies; MD, 4.5; p = 0.01; Fig. 6), while (near)normal IKDC objective scores rates (5 studies; RR, 1.4; p = 0.07), IKDC subjective scores (6 studies; MD, 0.8; p = 0.89), and postoperative Tegner scores (4 studies; MD, 0.1; p = 0.89) were similar between both treatment approaches.

Figure 4. Chondral Injury MLIK



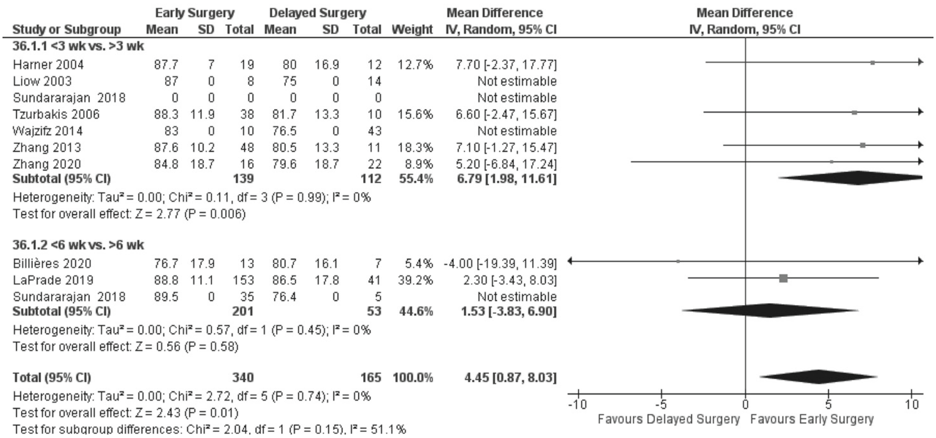
Forest plot of the events of chondral lesions (grade ≥ 1 classified by any grading system) between acute vs. delayed MLIK surgery.

Figure 5. Postoperative Stifness MLIK



Forest plot of the events of postoperative stiffness between acute vs. delayed MLIK surgery. Postoperative stiffness was defined as a range of motion deficit >5° as compared with the contralateral knee.

Figure 6. Lysholm Score MLIK



Forest plot of the difference in Lysholm scores between acute vs. delayed MLIK surgery.

When comparing outcomes following different cutoff time points, patients undergoing early treatment had significantly higher Lysholm scores as compared to those treated in the delayed setting when using the 3-week cutoff time point (7 studies; MD, 6.8; $p < 0.01$; Fig. 6), but this was similar for the 6-week cutoff time point. All other paraments were similar between both cutoffs, including rates of postoperative stiffness. Nevertheless, it should be noted that reoperations, complications, objective instrumented laxity, and IKDC objective scores were only reported in the 3-week cutoff time point analysis, while meniscal injuries were only reported in the 6-week cutoff time point analysis.

The present outcomes were confirmed in a sensitivity analysis involving only studies with non-estimated means and SDs; however, these analyses could not be performed for only studies without inflammatory parameters exemptions before early surgery, since this was either not described or partial resolution of acute inflammation parameters was required before early treatment in all included studies.

Discussion

The main finding of this meta-analysis was that early treatment of acute knee injuries with accelerated rehabilitation protocol results in similar clinical outcomes compared to delayed surgery without increasing the risk for postoperative stiffness and ROM deficits. Furthermore, similar or even higher functional outcomes scores were found in patients treated early compared to late. In this review, a high level of evidence was found for performing isolated ACL injury without increasing the risk of postoperative stiffness, while there was a low level of evidence for the same findings in the MLIK setting.

This meta-analysis supports the findings that early surgery of acutely injured knees is not associated with increased risk for arthrofibrosis and postoperative stiffness. This is contradictory to historical studies,[7] which reported that patients treated acutely had a significantly higher risk of developing arthrofibrosis due to development of adhesions and soft tissue contractures in the immobilized knee. For these reasons, surgical treatment of acutely injured knees was commonly delayed into the inflammation-free period to ensure ROM restoration and soft tissue optimization until the early 1990s.[54] Modern-day rehabilitation and complementary surgical techniques have been shown to prevent these postoperative ROM limitations.[12] It is felt that the adoption of early motion protocols and the relative abandonment of cast immobilization likely played a large part in avoiding post-operative stiffness. Nevertheless, it has been suggested that the acutely injured knee must show signs of improved knee motion and resolving swelling before proceeding with surgery.[55] However, this was not confirmed in the sensitivity analyses for isolated ACL reconstruction, while it should be noted that these analyses could not be performed for MLIK studies. Given these findings, it appears that early surgical treatment of acutely injured ACLs can be safely performed without increasing the postoperative stiffness risk, while further research is warranted in the MLIK setting.

Another important factor in timing of knee surgery is that early tibiofemoral stability restoration might reduce the risk for further meniscal and chondral lesions, potentially leading to decreased risk for posttraumatic osteoarthritis.[10] Although significantly lower secondary injuries were indeed found for MLIK patients treated in the acute setting in this meta-analysis with a RR of 0.74 and 0.46, respectively, this did not differ between early and late treated isolated ACL reconstruction patients. One explanation for this finding might be that the length between injury and surgery was too short for increasing the risk for secondary injuries in the delayed group, as several studies with longer time-intervals have reported significantly higher incidence of secondary injuries in the delayed treatment groups.[56,57] Therefore, based on all available literature, it might be advantageous to indicate patients early for surgery to potentially reduce these risks.

From a cost-effectiveness perspective, it was noted that early isolated ACL surgery leads to shorter sick leave (MD -31.6 days), thereby resulting in a substantial economic advantage of early surgery through a quicker recovery period. An economic analysis of ACL reconstruction's timing using registry-based data only also showed that early surgery was more effective at a lower cost, than rehabilitation plus optional delayed surgery.[58] Based upon economic considerations, early surgery could therefore be preferred over delayed in order to reduce costs. This is only true, however, if one knows that the patients are going to require surgery (e.g. high-level athletes, patients participating in pivoting sports). Otherwise, early surgical treatment causes an overtreatment and thereby increase the overall costs. A recent study has shown that approximately 60% of patients require ACL reconstruction following conservative treatment, but 90% of patients aged younger than 25 years and 83% of patients participating in Tegner level 7 or higher sports require surgery.[10] It is therefore important to be aware that early surgery is only likely to be cost-effective when the likelihood to require surgery is high.

When reviewing functional outcomes in this meta-analysis, it was noted that some patient-reported outcomes in both early treated isolated ACL reconstructed patients (IKDC subjective; MD = 3.0 and Tegner scores; MD, 0.4) and MLIK patients (Lysholm score; MD, 4.5;) were superior over those treated in the delayed setting, while none were inferior for the early treated group. Previous meta-analyses comparing early and late surgery have reported similar findings.[21,22] Nonetheless, it remains unknown if these differences are clinically relevant and if early surgery actually leads to improved functionals outcomes due to methodological limitations of the included studies.

When reviewing the time between injury to surgery, patients treated early underwent surgery 44 days earlier than those treated in the delayed setting among the five included RCTs. Therefore, early indicated patients with isolated ACL injuries treated might return to sports activities approximately six weeks earlier than those treated in the delayed setting, without increasing the risk for inferior outcomes. Since no level I MLIK studies were identified, this was not further assessed for this group.[11]

There are also some disadvantages of treating acutely injured knee early, as initially treating patients nonoperatively after injury has the potential advantage of not performing surgery on all patients.[59] This prevents surgery in a significant subset of patients and prevents a long rehabilitation program and potential surgical complications, thereby also decreasing surgical costs.[59] As previously mentioned, age and activity level are significantly correlated with the success of non-operative treatment of ACL injuries.[10] Therefore, early surgical treatment should be recommended in younger and more active patients to prevent longer delay between injury and surgery, while non-operative treatment might be considered in older patients and those with lower activity levels. Lastly, an additional disadvantage of early surgery is that patients cannot psychologically prepare for surgery and establish recovery goals, as these factors have been shown substantial contributory factors for successful outcomes.[54]

There are several limitations to this study. First of all, randomized and non-randomized studies were included in this meta-analysis, which decreases the overall level of evidence due to low methodological quality. Secondly, this study was limited due to heterogeneity among included studies in study design, reported outcomes, and follow-up length. For example, there was great variability between ROM assessment and how this was reported. Thirdly, not all studies clearly described how their patients were assigned into the early or delayed treatment group, while other studies did not indicate their criteria for proceeding with early surgery. This could have led to selection bias. In addition, it was noted that patients undergoing delayed treatment in the 3-week time-point underwent surgery in a shorter timeframe as compared to those in the 6-week time- point (317.4 vs. 408.2 days), which could have influenced the outcomes in this study. Finally, it should be noted that some of the outcomes were only reported in one or two cohorts with relatively low number of patients and further studies need to confirm these findings.

Conclusion

This systematic review with meta-analysis found no difference in clinical and functional outcomes between early and delayed surgery for isolated ACL injuries. For MLIK injuries, there were also no differences in surgical outcomes between early and delayed surgery.

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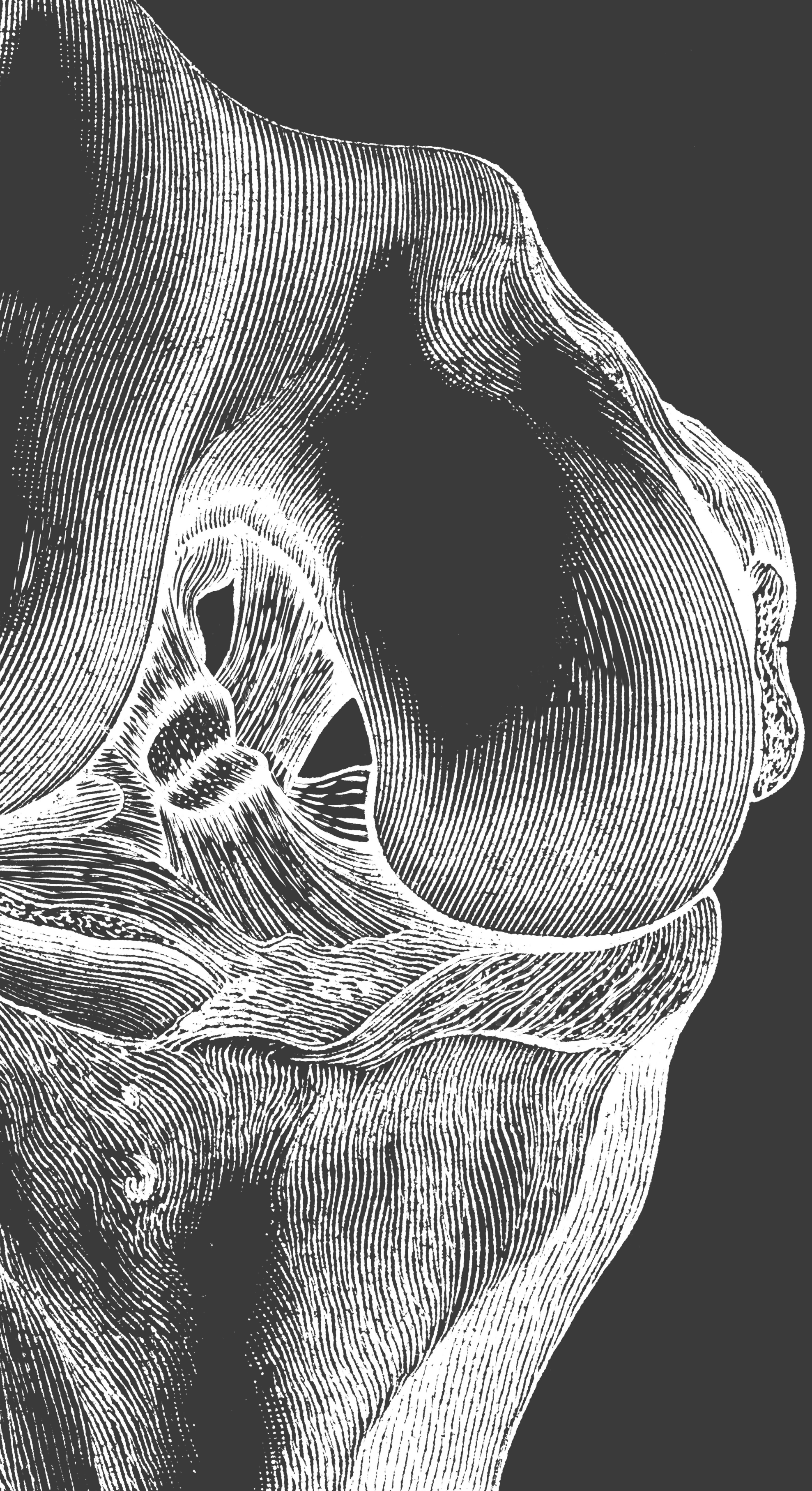
Part 3

Patient selection for ACL repair



Chapter 4

Differential regional of perfusion of the human anterior cruciate ligament: quantitative magnetic resonance imaging assessment

Lin KM, Vermeijden HD, Klinger CE, Dyke JP, Rodeo SA, DiFelice GS

J Exp Orthop. 2022 May 30;9(1):50

Abstract

Background

Surgical reconstruction is the current standard of treatment for ACL rupture in active individuals. Recently, a subpopulation of patients with good outcomes after conservative management has been identified. Additionally, there is renewed interest in primary repair of the ACL for proximal tears. Despite this, ACL biology and healing potential are currently not well understood. Vascularity is paramount in ACL healing; however, previous ACL vascularity studies have been limited to histological and dissection-based techniques. No prior studies have quantified in situ differential perfusion of the human ACL. The study objective was to use contrast-enhanced quantitative Magnetic Resonance Imaging (qMRI) to compare relative perfusion of 3 zones of the in situ ACL: proximal, middle, and distal. We hypothesized that perfusion would be greatest in the proximal third.

Methods

We utilized 14 fresh-frozen human cadaveric knees, 8 females and 6 males, age 25-61 years. The superficial femoral, anterior tibial, and posterior tibial arteries were cannulated; no intraarticular dissection was performed. qMRI was performed using a previously established protocol. Regions of interest corresponding to three ACL zones (corresponding to the proximal, middle, and distal thirds) were identified on sagittal oblique pre-contrast images. Signal enhancement (normalized to tibial plateau cartilage) was quantified to represent regional perfusion as a percentage of total ACL perfusion. Comparative statistics were computed using repeated measures ANOVA, and pairwise comparisons were conducted using the Bonferroni method.

Results

Relative perfusion to the proximal, middle, and distal ACL zones were 56.0% ±17.4%, 28.2% ±14.6%, and 15.8% ±16.3%, respectively ($p=0.002$). Relative perfusion to the proximal third was significantly greater than the middle ($p=0.007$) and distal ($p=0.001$). There was no difference in relative perfusion to the middle and distal thirds ($p= 0.3$). Post-hoc subgroup analysis demonstrated greater proximal perfusion in males (66.9% ±17.3%) than females (47.8% ±13.0%), $p=0.036$.

Conclusion

Assessment of differential regional perfusion of the in situ adult ACL by qMRI found greatest relative perfusion present in the proximal third, nearly 2 times greater than the middle third and 3 times greater than the distal third. Knowledge of differential vascular supply to the ACL is important for understanding pathogenesis of ACL injury and the process of biological healing following various forms of surgical treatment.

Introduction

Anterior cruciate ligament (ACL) injury is common in the active population, with an incidence of 75 per 100,000 person-years.[1] Surgical intervention often is recommended to restore knee stability, prevent further injury, and enable safe return to sport or activity.[2-5] The ACL traditionally was considered to have poor intrinsic healing capacity[6], as early studies of repair, irrespective of tear location, showed poor outcomes.[7,8] The current gold standard for complete ACL rupture is surgical reconstruction. However, a subpopulation of patients with ACL rupture have been found to perform well following nonoperative management.[9] A recent histological study of human tissue suggested that proximal one-third ACL tears, despite being intra-articular structures, may have an intrinsic healing response similar to that of the medial collateral ligament (MCL).[10] Along this line of thought, there has been renewed interest in primary repair of proximal ACL tears[11], with contemporary techniques making use of biological augmentation and various biomechanical constructs, although data remains limited.[12,13] Regardless of treatment strategy, with continued scientific advancement, it is important to understand the biology of the ACL and its pathophysiologic response to injury and healing.

A key component of the healing cascade is vascularity, specifically angiogenic response to injury and surgical treatment, as vascular influx is the first stage of healing in the postnatal human. The ACL is perfused by the middle geniculate artery[14], and perfusion is thought to be greatest at the femoral and tibial insertions.[15] The ligament is nearly entirely supplied by branches traveling through the synovium, rather than through the bony portion of the insertion.[16,17] From a healing standpoint, animal studies have shown that biological augmentation of angiogenesis using stromal cells and various growth factors can improve ACL graft-tunnel healing.[18-20]

While vascularity is known to be integral to ACL healing, previous knowledge has been gained from histological dissection studies or animal models. For greater direct clinical relevance, vascularity should be studied in situ in human tissues using methods that more closely resemble the clinical setting. To date, there are no studies in intact human knees, using standard clinically available imaging modalities, that quantitatively assess ACL vascularity.

The study objective was to quantify the in situ relative vascularity of the adult human ACL by anatomic zone using gadolinium-enhanced MRI. Reliable assessment of relative perfusion using noninvasive imaging could be applied to assessment of patients in the injury setting, as well as evaluation of ligament/graft perfusion and healing post-operatively. Improved understanding of ACL vascularity not only improves the basic science knowledge of ACL biology, but may also carry implications for indications for ACL surgery.

Methods

Specimens

Following institutional review board approval, 14 unmatched human cadaveric knee specimens were acquired (fresh-frozen, sectioned from mid-femur to mid-tibia; Anatomy Gifts Registry, Hanover, Maryland, USA). All specimens were pre-screened excluding any with histories of associated pathology, injury or surgery about the knee. The study included 8 females and 6 males (average age 51.1 years; SD 9.4, range 25-61). Causes of death were suicide (1), neurodegenerative disorder (1), heart failure (1), drug overdose (1), malabsorption syndrome due to gastric bypass (1), multiple sclerosis (1), malignant neoplasm (1), pancreatic cancer (1), lung cancer (1), metastatic renal cancer (1), lyphoma (1), kidney failure (1), throat cancer (1), metastatic thyroid cancer (1). Dissection was performed at our institutional anatomy laboratory and MRI at our academic affiliate, Citigroup Biomedical Imaging Center of Weill Cornell Medicine (New York, NY).

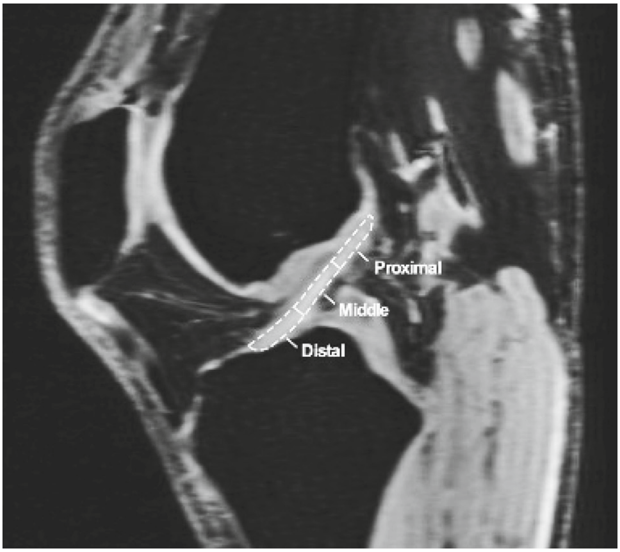
Cannulation procedure
Arterial cannulas (DLP 30000; Medtronic, Minneapolis, Minnesota) were inserted and sutured in place using 2-0 Vicryl sutures (Johnson & Johnson, New Brunswick, New Jersey). Arteries cannulated included the superficial femoral artery (SFA; proximal to the branch-point of the supreme genicular artery), the anterior tibialis artery (ATA; distal to the branch-point of the anterior recurrent artery); and the posterior tibialis artery (PTA; distal to the branch-point of the anterior tibialis artery and proximal to the bifurcation of the peroneal and posterior tibialis arteries).

Quantitative MRI procedure
All MRI scans were performed using a 3.0-T Excite GE MRI scanner (General Electric Healthcare, Milwaukee, Wisconsin) with a quadrature knee coil. The quantitative-MRI (qMRI) protocol consisted of a 20cm field of view, 512x384 matrix size, with 2mm slice thickness. This protocol was utilized pre- and post-infusion of MRI contrast solution. Intravenous (IV) tubing was connected to each arterial cannula (Topspins Inc., IV Smart Set Contrast Tubing, Model 001.4, Ann Arbor, MI) which allowed completion of pre- and post-contrast MRI with both the table and specimen in the same position. This aided secondary qMRI analysis as specimen position and MRI slices were optimally aligned throughout the MRI study. A baseline MRI series was acquired before contrast administration. Contrast solution was manually injected by syringe. MRI contrast solution consisted of Gd-DTPA (Gadolinium-diethylenetriamine pentaacetic acid) mixed with normal saline (3:1 saline to Gd-DTPA). Total infusion volume of 61ml was injected per specimen (35ml via SFA, 13ml via ATA, and 13ml via PTA). Static fat-suppressed and unsuppressed post-contrast T1-weighted three-dimensional gradient-echo images were generated for each MRI exam.

Fat-suppressed MRI images were utilized for qMRI analysis as they better detail Gd-DTPA by eliminating normal bone marrow signal. Computer software, customized by a study investigator (JPD) based on IDL 6.4 (Interactive Data Language, Exelis, Boulder, Colorado), allowed volumetric analysis. For each specimen, MRI examinations were reformatted to the sagittal-oblique plane to capture the entire length of the ACL and allow optimal segmentation for qMRI analysis.

On sagittal-oblique projections, the ACL was divided into three regions of interest (ROI): proximal, middle, and distal (Fig. 1). Entire ACL length was first determined on baseline MRI and divided into 3 zones of equivalent lengths. Signal intensity change within each designated ROI from pre- to post-contrast MRI exams was quantified. Signal intensity was normalized using a baseline of non-enhancing tibial plateau articular cartilage. Weighted means of signal intensity measurements per voxel were calculated to produce a single measurement of signal intensity enhancement for each of the 3 zones. Increase in signal intensity represented the relative increase in vascularity to any particular region. This technique was previously validated for assessment of relative arterial contributions to various anatomic sites.[21-25]

Figure 1.



On sagittal-oblique sections of the ACL, the substance of the ligament was divided into three regions of interest: proximal, middle and distal.

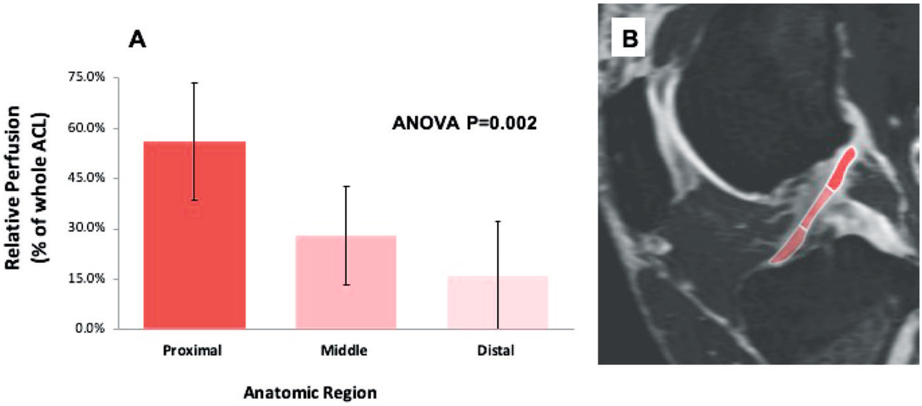
Statistical analysis

The biostatistics department was consulted for statistical analysis. Descriptive statistics (mean and standard deviation) were calculated for all perfusion zones. Mean perfusion was compared across zones using repeated measures ANOVA, and pairwise comparisons were performed using the Bonferroni method. A sample size calculation, to detect difference in relative vascularity between zones, was performed for analysis of a continuous endpoint using 2 samples. As there was no previous data in the literature regarding quantitative relative vascularity of ACL zones to base calculations on, an effect size of 20% (difference in relative perfusion) and standard deviation of 15% were used for calculation, yielding a required sample size of 9 subjects per comparison group to detect a difference of 20% relative perfusion.

Results

All 14 human knee specimens successfully underwent cannulation and the qMRI protocol. The greatest mean relative perfusion was found within the proximal ACL region (56.0%±17.4%); (with 56.0% of the total measured signal enhancement of the entire ACL seen within the proximal aspect of the ACL), followed by the middle region (28.2%±14.6%), and the least relative perfusion was found in the distal region (15.8%±16.3%) (Fig. 2). Repeated measure ANOVA showed significant differences among zones (P=0.002), and pairwise comparisons using the Bonferroni method indicated that perfusion to the proximal third was significantly greater than both middle (P=0.007) and distal thirds (P=0.001). Perfusion to the middle third was not significantly different from the distal third (P=0.281). Descriptive and comparative statistics for differential regional ACL vascularity in the overall study population are presented in Table 1.

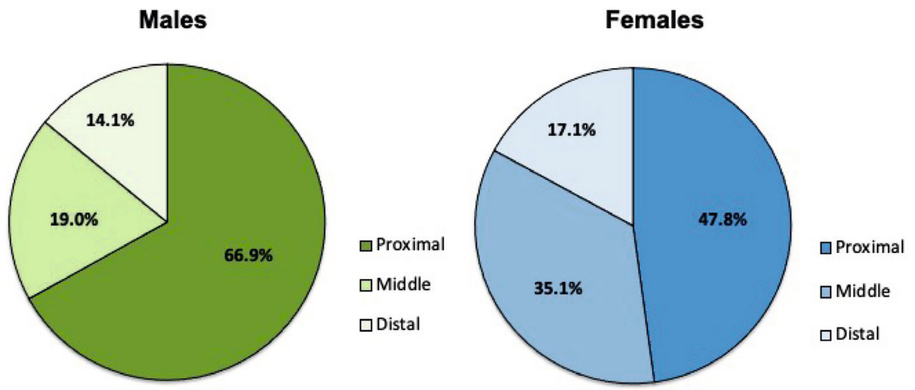
Figure 2.



The greatest mean relative perfusion (as a percentage of the total ACL perfusion) was seen in the proximal ACL region (56%±17.4%), followed by the middle region (28.2%±14.6%), and the least relative perfusion was seen in the distal region (15.8%±16.3%).

Comparison of regional ACL perfusion between genders revealed differences between males and females (Fig. 3). Males were found to have a mean of 66.9% (SD 17.3%) of overall ACL vascularity within the proximal portion (with 66.9% of total measured signal enhancement from the entire ACL seen within the proximal third), 19.0% (SD 12.1%) within the middle portion, and 14.1% (SD 17.5%) within the distal portion. Females were found to have 47.8% (SD 13.0%) of overall ACL vascularity within the proximal portion, 35.1% (SD 12.9%) within the middle portion, and 17.1% (SD 16.4%) within the distal portion. Subgroup comparison of regional ACL perfusion between males and females using t-test showed relative vascularity to the proximal zone was significantly greater in males (P=0.036), while vascularity to the middle region was significantly greater in females (P=0.036), and there was no difference in perfusion to the distal region. Comparative statistics between males and females are in Table 2. It must be noted, however, that despite the statistically significant findings, this subgroup analysis was underpowered, as there were only six males and eight females, whereas a required sample size of nine per group was necessary to detect an effect size of 20%.

Figure 3.



Comparison of regional ACL perfusion between genders revealed differences between males and females.

Discussion

The purpose of this study was to quantitatively compare perfusion of different anatomic ACL regions using gadolinium-enhanced MRI. There were statistically significant differences in regional perfusion, with the proximal third receiving the majority of total perfusion, followed by the middle and distal thirds. In addition, there was a statistically significant difference in regional perfusion between males and females, with males demonstrating greater perfusion proximally than females, although this study was not initially powered for this post-hoc analysis.

To our knowledge, no prior studies have quantitatively assessed human ACL vascularity in situ. The qMRI findings corroborate historical qualitative studies that, using dissection, tissue clearing, and injection techniques, showed that a broader vascular network of small capillaries is seen at the proximal end of the ACL. The vascular supply to the substance of the ACL actually derives from the synovium, rather than through the osseous origin and insertion sites.[15] Prior evidence suggests the greatest concentration of these small vessels is near the femoral origin.[17] The one prior study that attempted to quantify vascularity to differential zones of the ACL utilized intraarticular dissection and placement of probes to measure hydrogen washout in a canine model.[16]

The greater concentration of vessels, and greater relative blood flow to the proximal third of the in situ ACL demonstrated by findings of this study supports the hypothesis that this region may have greater healing potential. This is important clinically in several aspects: (i) indicating patients for operative or conservative management, (ii) surgical technique with respect to the renewed interest in primary repair, and (iii) tissue healing following repair or reconstruction with or without remnant preservation. It is possible that preservation of a stump or remnant of the native ACL insertion may provide improved biological healing potential, in the form of native collagen structure, matrix composition, or vascularity.

There is evidence suggesting some full thickness ACL tears in middle-age female skiers can be managed nonoperatively with good results.[9] It is possible that this is due to avulsion of the ACL from the femoral origin in this particular group. Whether these results can be extrapolated to other demographic groups or other injury mechanisms is unknown, as the literature on nonoperative management of full-thickness ruptures is extremely limited.[26,27] Regarding operative treatment, there is renewed interest in primary repair of the ACL in the setting of partial thickness tears[28] or femoral-sided avulsions.[29] Historically, open primary ACL repair was abandoned due to unacceptably high failure rates at mid-term follow-up.[8] With improved diagnostic capabilities[30] and arthroscopic repair approaches, contemporary rehabilitation protocols (focusing on early mobilization rather than casting and immobilization), and most importantly improved indications, results of selective ACL repair in the recent literature have been generally encouraging[11,31-33], although there are no high quality comparative studies with long-term follow-up and concerns remain regarding the material properties of the repaired ligament.[12,13]

It is not known if the regional differences in vascularity are re-established after ACL graft reconstruction. The reconstructed ACL graft differs in collagen microstructure, non-collagenous extracellular matrix composition, and material properties from the native ACL. The process of ACL graft revascularization is incompletely understood. Although patella bone-tendon-bone autografts heal at the graft-tunnel junction through creeping substitution at the bone-to-bone interface[34], it is unclear during the process of ligamentization when, or if at all, distribution of vascularity returns to that of the native ACL. Furthermore, it is unknown how this process occurs with soft tissue grafts. The finding of increased proximal perfusion is perhaps most relevant to remnant-preserving reconstruction, which has recently become increasingly reported although there is no definitive high quality data supporting its use.[35,36] Based on the present findings, it could be hypothesized that femoral remnant preservation may provide more biologic benefit than tibial remnant preservation, at least from a vascularity standpoint. It is possible that some form of neovascular collateral circulation arises and perfuses the graft via the remnant stump; however, further study is required to elucidate when, how, or if this process occurs. From a tissue-healing standpoint, the presence of greater perfusion to the in situ ACL on qMRI supports the previously hypothesized preferential healing potential in the proximal ACL. Nonetheless, it must be noted that perfusion alone does not equate to healing potential as numerous other factors are involved, including the need for responding cells (either intrinsic or extrinsic cells that repopulate the graft) and the appropriate growth factors and other signaling molecules in the healing tissue.

A notable finding was the greater proximal perfusion in males compared to females. Although post-hoc subgroup analysis of differential vascularity by gender was not properly powered in our study, gender differences are worthy of continued investigation, as it is known that female athletes are 2-10 times more likely than male athletes to suffer ACL injuries.[37] Anatomic factors, including ACL thickness, notch geometry, quadriceps angle, and tibial slope, that differ between genders have been hypothesized to impact ACL injury propensity.[37-39] It is also possible that differences in vascularity may contribute to an observed discrepancy in injury rates, as the current study suggests decreased proximal ACL perfusion in females compared to males, although further study certainly is required to draw this conclusion. Our findings lend support to a recent report that documented accumulated tissue fatigue damage in the femoral enthesis region of ACL tissue from patients with non-contact ACL failure.[40]

There are numerous important limitations to this study, which limit direct clinical relevance of the findings. First, although in situ ACL vascularity is assessed without intra-articular dissection, this is a cadaveric study and thus the results should be cautiously extrapolated to living specimens. Ideally, in situ perfusion would be assessed in a live patient; however, due to ethical and safety concerns, initial use of this technique would first mandate proper safety testing and contrast dose titration. Furthermore, the ACL is a dynamic structure that is exposed to a complex mechanical loading environment, including cyclic compression, tension, and shear, and likely also undergoes physiologic aging, all of which likely affect tissue vascularity, while MRI in this study was done as a single timepoint static examination. ACL vascularity likely changes with age and injury (altering the local microvascular environment), so any results from cadaveric imaging studies of intact ACLs must be cautiously extrapolated to ruptured ACLs in living patients in the clinical setting. From a methodological standpoint, the study sample was limited. Although the main analysis was adequately powered, the subgroup analysis by gender was not. Studies with greater sample size are needed to elucidate true population trends. Furthermore, the average donor age was 51.1 years, placing this cohort at the older side for patients generally seeking consultation for ACL injuries. This introduces sampling bias, as ACL vascularity in a 50-year-old knee may differ from that of a 30- or 15-year-old. Additionally, manual injection of MRI contrast solution introduces a potential source of variability to perfusion pressure which could have been better controlled through the utilization of an MRI-safe pressure-controlled infusion pump. However, the same study investigator performed all MRI contrast solution injections using the same syringe sizes with the same technique in attempt to minimize variability. It is also possible that specimen size may be related to degree of MRI contrast solution uptake within the ACL and other tissues and we did not calibrate the MRI contrast solution with individual specimen size. Finally, in order to improve clinical impact of this research, further work should investigate the role that differential vascularity plays in tissue healing, in the setting of nonoperative management, primary repair, or reconstruction using various graft types. Future vascularity studies should also be done in post-operative knees, with comparison groups, long-term follow-up, and correlation to clinical outcomes, when possible.

Conclusion

Relative perfusion to the in situ human ACL, determined by qMRI in cadaveric knees, differs by anatomic zone, with significantly greater perfusion at the proximal third compared to middle and distal thirds. Although there are important limitations hindering the direct clinical applicability, these findings are valuable for the field of ACL surgery, as differential perfusion carries implications for management of ACL injuries. Increased blood supply is hypothesized to signify greater biologic activity and thus possibly greater healing potential. In context of the literature that has identified a small cohort of patients who have good outcomes following nonoperative management of ACL ruptures, as well as the renewed interest in primary ACL repair, the finding of increased vascularity to the femoral region of the ACL may, in part, provide a physiologic basis. Further research is needed to fully understand the impact of this differential vascularity on injury, healing, and clinical outcomes.

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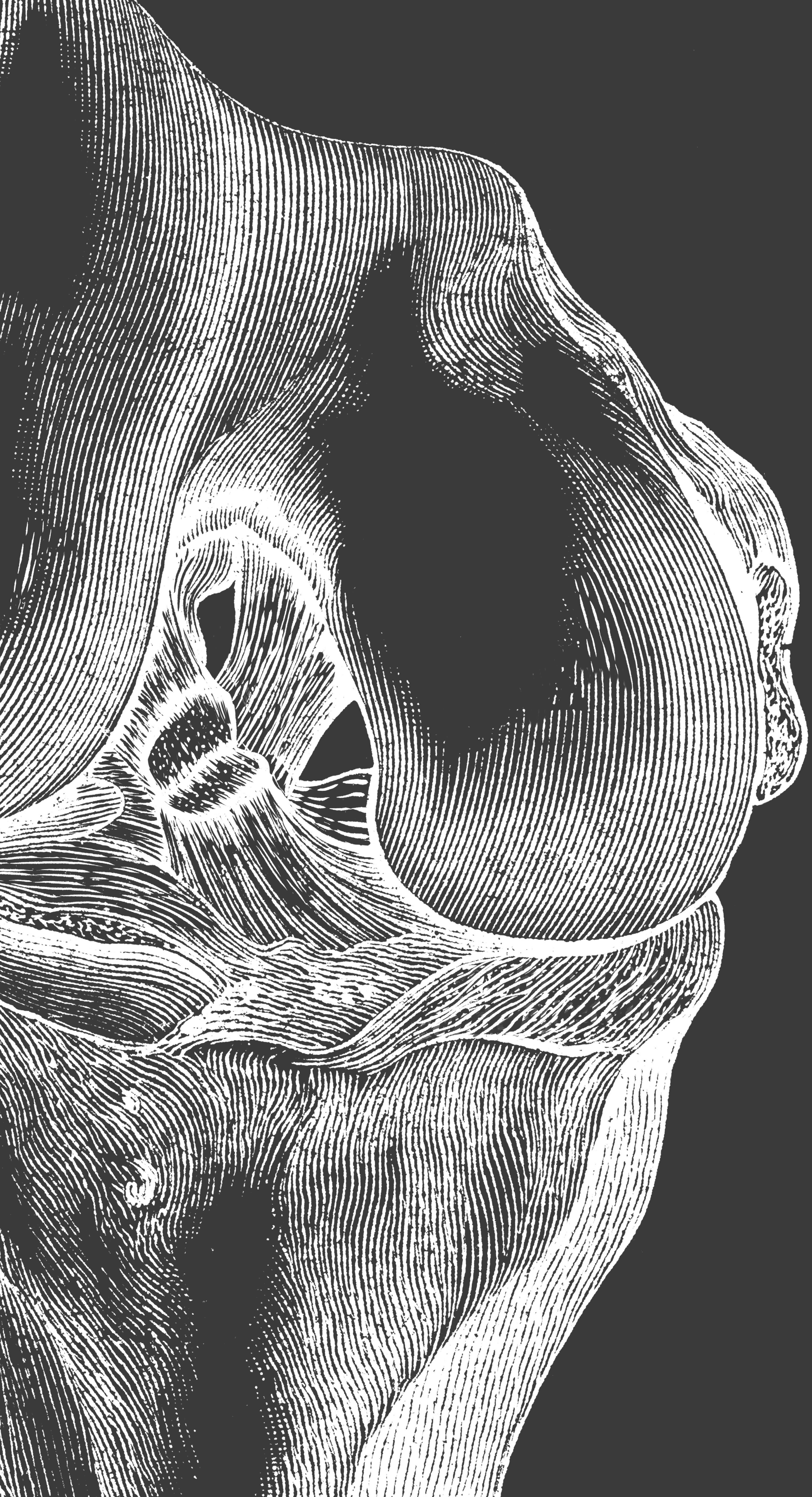


Chapter 5

Age and bone bruise patterns predict tear location in the anterior cruciate ligament

Vermeijden HD, Yang XA, Mintz, DN, Rademakers MV, van der List JP, Kerkhoffs GMMJ, DiFelice GS

ASMAR. 2022 Dec 14;5(1):e41-e50

Abstract

Purpose

To assess the influence of demographical risk factors, anatomical risk factors and injury mechanisms on anterior cruciate ligament (ACL) tear patterns.

Methods

In this case-control study, all patients undergoing knee magnetic resonance imaging (MRI) at our institution for acute ACL tears (within one month of injury) in 2019 were retrospectively analyzed. Patients with partial ACL tears and full thickness posterior cruciate ligament injuries were excluded. On sagittal MRI images, proximal and distal remnant lengths were measured, and tear location was calculated as distal remnant divided by total remnant length. Tear location of previously reported demographical and anatomical risk factors associated with ACL injury were then reviewed, including notch width index (NWI), notch angle, intercondylar notch stenosis, alpha angle, posterior tibial slopes, meniscal slopes, and lateral femoral condyle index (LFCI). In addition, presence and severity of bone bruise were recorded. Finally, risk factors associated with ACL tear location were further analyzed using multivariate logistic regression.

Results

A total of 254 patients (44% male; mean age, 34 years; range, 9–74 years) were included, of which 60 (24%) had a proximal ACL tear (tear at proximal quarter). Multivariate enter logistic regression analysis demonstrated that older age ($p=0.008$) was predictive for more proximal tear location, while open physis ($p=0.025$), bone bruises in both compartments ($p=0.005$), and posterolateral corner injury ($p=0.017$) decreased the likelihood of a proximal tear ($R^2=0.121$, $p<0.001$).

Conclusion

No anatomical risk factors were identified to play a role on tear location. Although most patients have midsubstance tears, proximal ACL tears were more commonly found in older patients. Bone contusions involving the medial compartment are associated with midsubstance tears may indicate that different injury mechanisms play a role in the location where the ACL tears.

Introduction

The current gold standard for surgical treatment of ACL tears is ligament reconstruction.[1] In recent years, however, ACL preservation has received increasing attention, due to the potential advantages of faster recovery, improved proprioception, and preservation of native tissue by obviating the need to harvest grafts.[2,3] Furthermore, several studies have shown that improved outcomes, compared to the historic experience with ACL repair, can be expected after primary repair in patients with proximal tears only,[2] as these tear types have better healing capacity than midsubstance tears.[4] With the resurgence of interest in selective arthroscopic primary repair for proximal tears, it is important to understand which patients are eligible for this procedure.[5]

Although ACL injuries are multifactorial in etiology, several risk factors have been identified that may predispose an individual to ligament rupture.[6] These risk factors include a narrow intercondylar notch, a steeper posterior tibial slope, and a decreased lateral femoral condyle sphericity.[7] Nevertheless, a valgus load combined with internal rotation (IR) is considered the leading cause of injury based on accompanying bone bruises.[8,9] On magnetic resonance imaging (MRI), bone contusions are thought to reflect a static representation of impact at the time of the injury and are typically observed on the lateral femoral condyle (LFC) and the posterior margin of the lateral tibial plateau (LTP).[10] Although these risk factors have been correlated with ACL injuries, it remains unclear if these risk factors also are associated with the tear location of the ACL.

Therefore, the purpose of the present study was to assess the influence of demographical risk factors, anatomical risk factors and injury mechanisms on anterior cruciate ligament (ACL) tear patterns. It was hypothesized that several anatomical factors would be associated with ACL tear location, including a decreased posterior tibial slope, and a stenotic intercondylar notch. Furthermore, it was hypothesized that femoral and tibial bone bruises patterns on MRI would be directly related to different ACL tear patterns.

Materials and methods

Study design and patient selection

Institutional review board approval was obtained prior to study initiation (2020-1497). A search was performed using the electronic radiology patient archiving and communication system (PACS; Sectra Workstation IDS7, version 20.2, Sectra AB, Linköping, Sweden) for all knee MRI scans performed at our institution for acute ACL injuries from January 1, 2019, to December 31, 2019. All radiology reports were screened for the diagnosis of ACL injury.

All patients with acute ACL injuries were included (defined as MRI performed within 31 days after injury). Patients were excluded if screening revealed they (i) sustained a concomitant complete posterior cruciate ligament (PCL) lesion, or a (ii) a partial ACL tear (these specific tears cannot be measured accurately).

MRI procedure

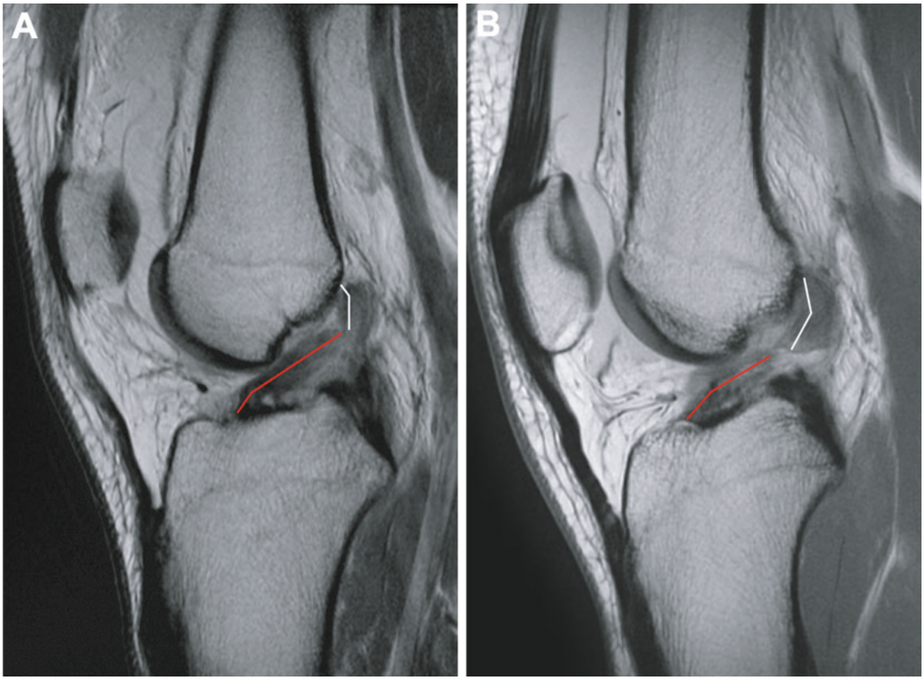
All patients who underwent imaging had undergone a standardized MRI protocol at 1.5-T or 3.0-T (GE Medical Systems, Milwaukee, WI, USA) with an 8-channel knee coil (MedRad, Warrendale, PA, USA). This protocol included two-dimensional fast-spin echo intermedial TE images (proton density, PD) acquired along three standard imaging planes (TR/TE 4,000 to 6,000 milliseconds/25 to 30 milliseconds; ETL 8 to 16; bandwidth, 32 - 62.5 kHz; acquisition matrix, 512x256-416; number of excitations, 1 to 2; field of view, 15 to 16 cm; slice thickness, 3.5 mm with no interslice gap). Furthermore, an additional sagittal inversion recovery (IR) sequence was acquired (TR/TE 5000-8000/18, ETL 8-16, TI 150-180, bandwidth 32-62.5, 256 x192, 1 or 2 NEX, FOV 16-18cm, slice thickness 3.5-4.0 cm).

Variables, outcome measures, data sources, and bias

First, multiple demographic and clinical variables were collected for all patients, including age at time of injury, gender, body mass index (BMI), side, time from injury to MRI, and injury characteristics (type of sport at injury). Next, the length of the distal and proximal remnant of the torn ACL was measured on a sagittal PD image (Figure 1). With this measurement, the distal remnant is assessed by measuring the distance from the anterior tibial insertion site to mid-section of proximal part of the distal remnant, while the proximal remnant was measured from most superior point of femoral attachment site to mid-section of distal part of the proximal remnant. In some cases, multiple measurements on either a single slice or multiple slices were performed to correct for the wavy contour of the ligament. Tear location was then calculated by dividing the distal remnant length by the total remnant length. In a recent reliability study of our group, excellent interobserver reliability was established (intraclass correlation coefficient (ICC) = 0.96; 95% CI, 0.91 – 0.98).

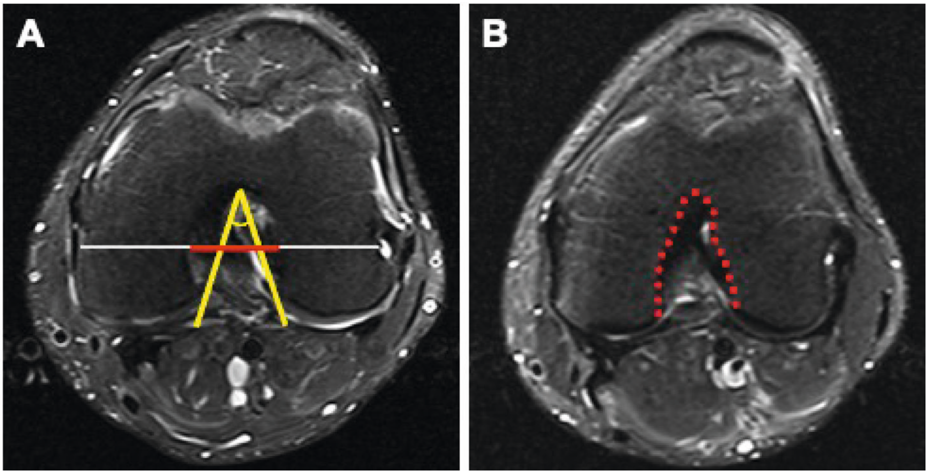
To assess potential anatomical risk factors, previously recognized MRI risk factors associated with ACL injury were analyzed, including notch width index (NWI; Figure 2A),[11] notch angle (Figure 2A), femoral notch morphology (Figure 2B),[12] alpha (α) angle,[13] posterior tibial slopes (Figure 3),[14] meniscal slopes (Figure 3),[15] and lateral femoral condyle index (LFCI),[7] as described in Table 1. All measurement methods have previously shown excellent reproducibility (ICC range 0.89 – 0.99),[7,13,16] and were performed by an experienced orthopaedic research fellow (HDV).

Figure 1.



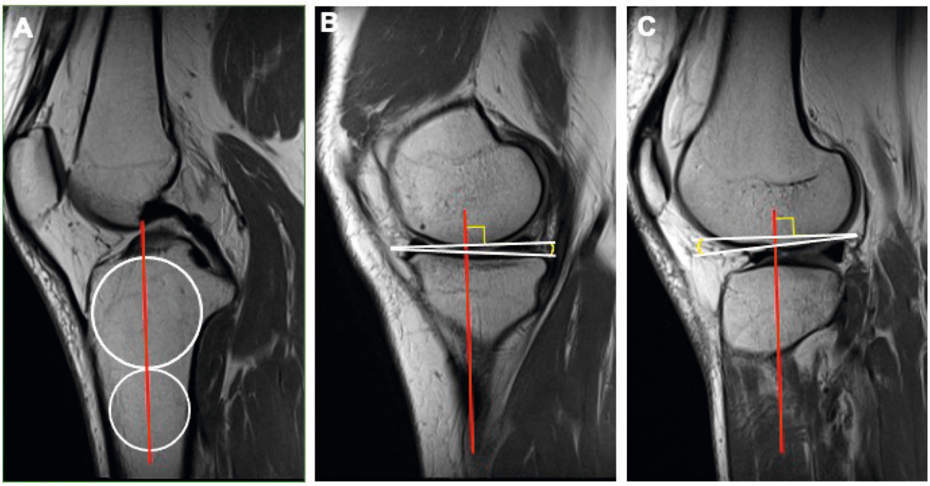
Two examples of remnant measurements on sagittal PD sequence MRI images are shown. (A) Example demonstrating the ACL torn proximally. (B) Example demonstrating the ACL torn in the midsubstance.

Figure 2.



Multiple measurement methods for different anatomical risk factors in the axial plane are shown. (A) NWI is the ratio of the intercondylar notch (red line) to the bicondylar width (white and red line) at the level of the popliteal groove. The angle between the notch apex to inferior margins of medial and lateral side of the notch represents the notch angle (yellow line). (B) A type A intercondylar notch shape is shown.

Figure 3.



Measurement method of the posterior tibial slopes and meniscal slopes in the sagittal plane is shown. (A) A central image is first used for the measurement of the longitudinal axis of the tibia. (B) The MTS is the angle between the line drawn tangent to MTP center and line orthogonal to the tibial longitudinal axis (the same method was used for the LTS). (C) The LMS is the angle between the line drawn tangent to center of medial meniscosynovial border and the line orthogonal to the tibial longitudinal axis (the same method was used for the MMS).

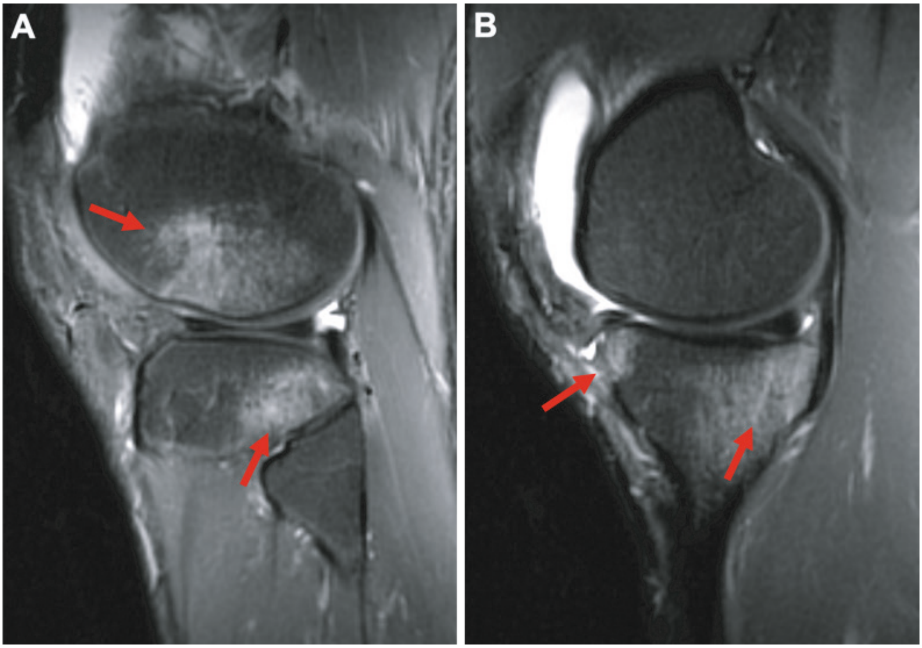
Table 1. Magnetic Resonance Sequences and measurement techniques for anatomical risk factors

Variables	Sequence	Measurement technique
NWI	Axial PD	Ratio between the NW and BCW at the level of the PG[11]
Notch angle	Axial PD	Angle between notch apex to inferior margins of medial and lateral side of the notch[11]
Notch morphology	Axial PD	A-shaped notches are narrower at apex than at base; U-shaped notches do not taper from base to apex; W-shaped notches have 2 apices[12]
Alpha angle	Sagittal PD	Angle between LAF and BL[13]
MTS	Sagittal PD	Angle between line drawn tangent to MTP center and line orthogonal to the tibial longitudinal axis[14]
LTS	Sagittal PD	Angle between line drawn tangent to LTP center and line orthogonal to the tibial longitudinal axis[14]
MMS	Sagittal PD	Angle between line drawn tangent to center of medial meniscosynovial border and line orthogonal to the tibial longitudinal axis[15]
LMS	Sagittal PD	Angle between line drawn tangent to center of lateral meniscosynovial border and line orthogonal to the tibial longitudinal axis[15]
LFCI	Sagittal PD	Ratio of the best-fitting flexion and extension circles of the femoral diaphysis[7]

NWI indicates notch width index; MTS, medial tibial slope; LTS, lateral tibial slope; MMS, medial meniscal slope; LMS, lateral meniscal slope; LFC, lateral femoral condyle index; TE, time to echo; NW, notch width; PG, polities groove; BCW, bicondylar width; LAF, longitudinal axis of femur; BL, Blumensaat line; MTP, medial tibial plateau; LTP, lateral tibial plateau; PD indicates proton density weighted.

To determine injury mechanisms, all concomitant ligament (such as the medial or lateral collateral ligament) and meniscal injuries were recorded for each study patient. Only grade II and III ligament injuries were considered ligament tears for analysis purposes. Sagittal images of the LFC, LTP, medial femoral condyle (MFC), and medial aspect of the tibial plateau (MTP) were then reviewed to assess bone bruise patterns in the lateral-medial and anterior-posterior directions (Figure 4). These contusions were defined as a traumatically involved increased signal intensity on the IR sequence and decreased signal intensity on the PD sequence.[17] Relative severity of bone contusions was further classified according to the International Cartilage Repair Society (ICRS) knee cartilage lesion mapping system as none, minimal (just beneath the subchondral bone), moderate (extends from the articular surface but not beyond the physeal scar), and severe (extends beyond the physeal scar).[18] A compartment was considered injured if at least one injury element existed (if a bone bruise or meniscal tear was present).[10]

Figure 4.



Images of bone bruise patterns on sagittal IR sequence MRI images are shown. (A) A lateral compartment injury with a moderate centrally located LFC contusion and a moderate posteriorly located LTP contusion is seen. (B) Minimal anterior and a severe posteriorly located MTP contusion is demonstrated.

For final analysis, proximal ACL tears were defined as tears within the proximal 25% of the ACL (leaving ≥ 75% of the distal ACL intact) as these are often candidates for primary ACL repair.[19] Furthermore, ACL tear location outcomes were stratified by age, growth plate status, gender, all injury mechanism groups (with minimum of 25 patients), associated lesions, anatomical risk factors, and bone bruise patterns.

Statistical analysis

All statistical analyses were performed using SPSS Version 25 (SPSS Inc., Armonk, NY, USA). Independent samples t-tests were used to evaluate continuous variables and reported in mean ± standard deviation (SD). Pearson's Chi-square test or Fisher exact test was used to compare discrete variables and reported in frequency and percentage. One-Way ANOVA with post hoc Bonferroni test was used for inter-group comparisons. The Pearson's or Spearman (non-parametric variables) correlation coefficient was determined to identify any correlations between anatomical factors and tear location. Finally, a multivariable enter logistic regression analysis was performed to identify risk factors associated with tear location. A prior power calculation for linear regression analyses was used to determine the number of required patients to achieve an adequately powered study (80%).[20] A total of 139 patients were needed to detect a 15% difference, with 15 variables evaluated for potential predictive value and type I error probability α of 0.05. All comparative analyses were two-sided, and $p < 0.05$ was used as the threshold for statistical significance.

Results

Study demographics

A total of 354 knee MRIs with confirmed ACL tears were identified. After applying the exclusion criteria, 254 patients were ultimately included in this study. Mean age was 34 ± 13 (range 9 – 74) years, 44% were male, mean BMI was 24.6 ± 4.2 kg/m^2, and 44% sustained an ACL tear in their right knee. Mean time from injury to MRI was 7 ± 8 days. The most common injury mechanisms was skiing (42%), followed by soccer (17%), and basketball (10%). Eight-six patients (34%) had associated MCL injury. Descriptive data are detailed in Table 2.

Table 2. Patient demographics of all patients at time of injury

Variables	All patients (n = 254)
Age (years); mean ± SD (range)	34 ± 13 (9 – 74)
Male gender; n (%)	114 (45%)
BMI (kg/m2); mean ± SD (range)	24.6 ± 4.2 (21.8 – 26.6)
Right side; n (%)	113 (45%)
Days from Injury to MRI mean ± SD (range)	7 ± 8 (0 – 31)
Injury mechanism; n (%)	
Skiing	106 (42%)
Soccer	42 (17%)
Basketball	26 (10%)
Football/rugby	6 (2%)
Other	75 (29%)
Any additional ligamentous injury; n (%)a	111 (44%)
PCL	0 (0%)
MCL	86 (34%)
FCL	33 (13%)
PT	6 (2%)
PFL	32 (12%)
Any meniscus injury; n (%)	124 (49%)
Medial	79 (31%)
Lateral	72 (28%)

[a] Only grade 2 or 3 tears were used for analysis; N indicates number of patients; SD, standard deviation; MRI, magnetic resonance imaging; PCL, posterior cruciate ligament; MCL, medial collateral ligament; LCL, lateral collateral ligament; PT, popliteus tendon; PFL, popliteofibular ligament.

ACL tear location

The overall mean total length of the ACL on MRI was 38.0 ± 3.5 mm (range 26.1 – 48.7 mm), of which the mean distal remnant length was 25.5 ± 4.9 mm (range 0.0 – 39.8 mm), and the mean proximal remnant was 12.5 ± 4.9 mm (range 0.0 – 37.5 mm). As a result, the mean tear location was 67 ± 12% (range 0 – 100%), and 60 (24%) patients had a tear within the proximal 25% of the ACL.

Univariate analysis

When analyzing age as a continuous variable, patients with a proximal ACL tear were significantly older than those with a midsubstance tear (39 ± 12 vs. 33 ± 12 years, $p < 0.001$). On the other hand, patients with open growth plates had significantly less proximal tear location (i.e. distal remnant length as a percentage of the total ACL length; 57 ± 22% vs. 68 ± 12%, $p = 0.003$), respectively. No differences in tear location between gender, concomitant ligament, and meniscal injuries were found (all $p > 0.100$; Table 3). A stenotic type-A notch was present in 42% of all patients, while type-U and type-W were present in 51% and 7%, respectively. Further analyses did not reveal statistical differences in tear location as a percentage of the entire ACL length between notch types (Type-A: 68% vs. Type-U: 67% vs. Type-W: 63%, $p = 0.254$). Other anatomical risk factors similarly did not correlate with ACL tear location (all $p > 0.1$; Table 4).

Table 3. Univariate analyses of potential injury factors for predictors of ACL tear location[a]

Variables	N	Mean tear location ± SD	P-value
Gender			
Male	114	68 ± 12%	0.777
Female	140	67 ± 13%	
BMI (kg/m2)			
<25	229	67 ± 12%	0.494
>25	22	66 ± 19%	
Growth plate status			
Open	13	57 ± 22%	0.003
Closed	241	68 ± 12%	
Injury mechanism			
Skiing	105	67 ± 13%	
Soccer	42	67 ± 7%	0.898
Basketball	26	66 ± 10%	
Any ligamentous injury			
Yes	111	67 ± 13%	0.884
No	143	67 ± 12%	
MCL injury			
Yes	86	69 ± 11%	0.193
No	168	67 ± 13%	
PLC injury			
Yes	54	65 ± 13%	0.118
No	200	68 ± 12%	

Table 3. Univariate analyses of potential injury factors for predictors of ACL tear location[a] *(Continued)*

Variables	N	Mean tear location ± SD	P-value
Any meniscal injury			
Yes	124	68 ± 13%	0.503
No	130	67 ± 12%	
Medial meniscus			
Yes	79	68 ± 13%	0.487
No	175	67 ± 12%	
Lateral meniscus			
Yes	72	69 ± 13%	0.283
No	182	67 ± 12%	

[a] Tear location indicates the length of distal remnant as percentage of aggregate; [b] Only grade 2 or 3 tears were used for analysis; MCL, medial collateral ligament; LCL, lateral collateral ligament; PLC, posterolateral corner; MM, medial meniscus; LM, lateral meniscus: Significant differences are displaced in bold.

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Table 4. Univariate analyses of potential anatomical risk factors for predictors of ACL tear location[a]

Variables	Mean ± SD	Correlation coefficient	P-value
NWI	0.293 ± 0.029	0.015	0.809
Notch angle (deg)	43.1 ± 6.1	0.046	0.469
Alpha angle (deg)	38.8 ± 3.7	-0.042	0.502
MTS (deg)	5.6 ± 2.6	0.048	0.444
LTS (deg)	6.0 ± 2.8	0.047	0.454
MMS (deg)	3.1 ± 2.7	-0.006	0.930
LMS (deg)	2.2 ± 3.5	0.053	0.402
LFCI	0.706 ± 0.058	-0.078	0.218

[a] Tear location indicates the length of distal remnant as percentage of aggregate distal and proximal length; NSI, notch shape index; NWI, notch width index; MTS, medial posterior tibial slope; LTS, lateral posterior tibial slope; MMS, medial meniscal slope; LMS, lateral meniscal slope; LFCI, lateral femoral condyle index

Bone bruising was observed in 251 (99%) patients. The prevalence of bone bruises was 65% on the LFC, 96% on the LTP, 13% on the MFC, and 55% on the MTP. Of all patients with bone contusions on the lateral compartment, 94% of LFC bruises were centered on the central third, while 98% of LTP bruises were on the posterior third. On the medial side, 75% of contusions were in the central third of the MFC and 93% were in the posterior third of the MTP.

When comparing bone bruise patterns between patients with and without proximal tears, presence of bone bruises in the lateral compartment only was significantly associated with proximal ACL tears (58% vs. 36%, respectively, $p = 0.002$), while contusions in both compartments were significantly more common in patients with midsubstance tears (61% vs. 37%, respectively, $p = 0.001$; Table 5). Bone bruising at the LFC (25% versus 39%, $p = 0.045$) and MTP (10% versus 22%, $p = 0.045$) were significantly less severe (none/minimal vs. moderate/severe) in patients with proximal tears compared to non-proximal tears. No differences were found in edema severity for other injury sites (both $p > 0.1$)

Table 5. Bone bruise patterns between patients with proximal versus non-proximal tears[a]

Variables	Proximal ACL tear (> 75%)		P-value
	Yes (n = 60)	No (n = 192)	
Lateral compartment only	35 (58%)	70 (36%)	**0.002**
LTP	16 (27%)	26 (13%)	**0.016**
LTP + LFC	17 (28%)	45 (23%)	0.418
Other	2 (3%)	0 (0%)	0.055
Medial compartment only	2 (3%)	4 (2%)	0.629
Various	2 (3%)	4 (2%)	0.868
Both compartments	22 (37%)	118 (61%)	**0.001**
LTP + MTP	5 (8%)	29(15%)	0.188
LTP + MTP + LFC	15 (25%)	62 (32%)	0.305
LTP + MTP + LFC + MFC	1 (2%)	20 (10%)	**0.032**
Various	1 (2%)	7 (3%)	0.798
No bone bruise	1 (2%)	2 (1%)	0.556

[a] Values are presented as No. (%); MTP, medial tibia plateau; LTP, lateral tibia plateau; MFC, medial femoral condyle; LFC, lateral femoral condyle; Significant differences are displaced in bold.

Multivariate analysis

Six independent variables with the lowest p-values were entered in the multivariate enter logistic regression model to find the best predictors for tear location ($R^2 = 0.121$, $F\,(5.66)$, $p < 0.001$). Multivariate analyses showed that patients more often had a proximal tear if they were older ($p = 0.008$), whereas open physis ($p = 0.025$), both compartment injury ($p = 0.005$), and PLC injury ($p = 0.017$) were independent predictors of decreased likelihood of a proximal ACL tear (Table 6).

Table 6. Multivariate enter logistic regression analysis for predictors of ACL tear location[a]

Variables	B	SE	β	P-value	95% CI
Age: continue	0.16	0.06	0.18	**0.008**	0.05 to 0.30
Both compartment injury: yes vs. no	– 4.28	1.52	– 0.17	**0.005**	– 7.28 to – 1.28
PLC injury: yes vs. no	– 4.48	1.87	– 0.15	**0.017**	– 8.17 to – 0.78
Growth plate status: closed vs. open	– 8.30	3.69	– 0.15	**0.025**	– 15.58 to -1.04
MCL injury: yes vs. no	1.53	1.62	0.06	0.345	– 1.66 to – 4.72
LFCI: continue	– 10.48	12.93	– 0.05	0.419	0.05 to 0.30

[a] Tear location indicates length of distal remnant as percentage of aggregate distal and proximal length; B, unstandardized beta-coefficient; Beta, standardized beta-coefficient; 95% CI (LB–UB), 95% confidence interval lower bound–upper bound; PLC, posterior lateral corner; MCL, medial collateral ligament; LFCI, lateral femoral condyle index; Significant differences are displaced in bold.

Discussion

The main findings of the present study were that proximal tears were associated with older age, while the presence of open physes, both compartment injuries, and PLC injury significantly decreased the likelihood of a proximal ACL tear. Interestingly, no anatomical risk factors were identified that were associated with ACL tear location. These findings may help orthopaedic surgeons to predict which patients might be eligible for ACL preservation techniques, such as selective arthroscopic primary ACL repair.

In this study, an important predictive role was observed for age on ACL tear location. It was noted that proximal tears were found more commonly older patients ($p < 0.001$). These findings are consistent with a recent study reporting a higher incidence of proximal ACL tears in older patients,[19] but the exact reason remains unknown. It can be hypothesized that some form of mucoid degeneration, due to the decreasing blood supply that comes with age, is the likely etiology of the strong correlation between older age and proximal tear location. Although older patients seem to be excellent candidates for ACL repair, further studies assessing and comparing the outcomes of this procedure with the gold standard of ACL reconstruction are needed. In addition, it might also be possible that the tear location may also be related to mechanisms of injury. The rationale for this hypothesis is that older patients generally participate less frequently in knee-strenuous and pivoting sports,[21] which might alter motion patterns and could therefore influence ACL tear patterns. Further study in this area, however, are also warranted.

A recent case-control study assessed predictive factors for the possibility of arthroscopic primary ACL repair and showed that older age, lower BMI, and surgery within four weeks of injury were associated with increased likelihood of repair, while lateral meniscus tears decreased the likelihood of repair [22] This study confirms some of their findings as older age was, as previously mentioned, indeed associated with a higher tear location. On the contrary, however, no association was found between BMI or lateral meniscus tear and tear location. As the present study did not assess tissue quality, one of the hypotheses for this difference could be that these factors are associated with better or lower tissue quality and that, therefore, these patients might had a higher or lower likelihood of primary repair.

When reviewing mechanisms of injuries, it was noted that bone bruise patterns significantly differed between patients with proximal tears compared to patients with other tear locations. Based on a thorough assessment of these results, all lateral bone contusions were present along the central portion of the LFC and along the posterior third of the LTP and appeared more prevalent and severely contused than those along the medial compartment. These findings are suggestive that a substantial anterior translation of the lateral aspect of the tibia relative to the femur with a valgus component occurred in the majority of our patients with acute ACL injuries.[23] Nevertheless, although ACL injuries may exhibit the same net loading, motion patterns might differ significantly between different ACL tear patterns,[24] while it has also been suggested that degree of bone bruising may progressively increase when the level of energy imparted on the knee increases during injury.[25] Given these findings, it seems that when a mild pivot shift occurs, there is some IR and mild anterior tibial translation (ATT), resulting in a lateral tibial plateau subluxation only, which is associated with bone edema in the lateral compartment. On the contrary, a more severe pivot shift can occur with further tibial plateau anterior subluxation, eventually reaching a point where the medial plateau is contused.[10,26] Future biomechanical studies should further elucidate and potentially confirm these findings.

When reviewing other risk factors and taking these considerations into account, it is surprising that none of the studied tibial and femoral bony morphology measurements were associated with ACL tear location, given that the surface geometry of the tibial articular cartilage and underlying subchondral bone has a significant influence on transmitting loads across the knee joint.[27] In particular, a steeper LTS has been associated with increased ATT in the ACL-injured knees, although the results widely vary.[15,28] As the ACL is the primary passive restraint against ATT, increased translation has been shown to induce greater ACL loading stress subsequently.[29] Similarly, a decreased lateral femoral condyle index (LFCI) has been suggested to be associated with increased gliding of the LFCI over the LTP, thereby resulting in a greater pivoting mechanism and increased ACL loading stress.[7] Although these risk factors may increase ACL loading, this study demonstrated that the specific injury mechanism is the most important contributory factor in ACL tear location. Nevertheless, ACL injury, and especially tear location, likely has a multifactorial etiology in which the studied factors may all be contributory.

Besides femorotibial biomechanics, the anatomical variance of the femoral intercondylar notch has also been a topic of interest.[30] Some studies suggest that patients with a reduced notch index or intercondylar notch stenosis (A-shaped notch) may have a higher predisposition for ACL injury.[6] Both ACL impingement and correspondingly smaller ACL size have been reported as the reason for this potentially increased incidence of ACL injury.[31] Therefore, one may expect that narrow intercondylar notch dimensions may also influence ACL tear patterns, but this study, however, did not find any correlation between intercondylar notch dimensions and ACL tear locations.

Over the last decades, numerous studies have described series with proximal, midsubstance, and other tear type patterns.[32] It remains challenging, however, to distinguish among different tear types as clear definitions are currently suboptimal. Furthermore, many tears may be classified as a proximal third tear, since a large portion of ACL tears rupture near the proximal and middle third junction (22%).[33] As a result, this may have previously led to misclassification of certain tear types, given the high and wide-ranging reported rate of proximal ACL tears in the orthopaedic literature (range 43% – 71%).[19,33,34] In recent years, several studies have suggested that tear within the proximal quarter of the ligament may be eligible for primary repair, as these tear types have sufficient length for reapproximation to the femoral insertion site.[2,3] Therefore, we have used this threshold to define proximal tears. This study indicates that only 24% of all ACL tears are within this quarter of the ligament and can thus be classified as a proximal ACL tear.

Limitations

There are limitations to the present study. First, although the total number of enrolled patients was high (n = 254), only a small group of patients presented with proximal ACL tears (24%). However, this most likely reflects an accurate representation of the incidence of tears within the proximal quarter. Secondly, although the sensitivity of MRI for diagnosis ACL injuries is high, the present study lacks an intra-operative assessment to confirm ACL tear location, and no control group with intact ACLs was present. In addition, other factors, such as neuromuscular or injuries to the anterolateral ligament (ALL), may have a confounding effect on ACL tear location but were not considered in the current study. Thirdly, the most common mechanism of injury was a skiing, which could have influenced the outcomes in this study. Furthermore, it is important to note that there was an increased risk for type II errors as post-hoc power analysis showed that for some parameters, such as the posterior slopes, more than 100 patients per group were needed to determine a statistical difference between both groups. Nevertheless, it remains unclear if that would also lead to a clinically relevant difference since the differences between both groups were very small in certain parameters. Finally, although bone contusions are thought to be a static representation of the injury mechanism, this assumption has not been thoroughly validated.

The clinical relevance of the present findings is that this study helps to understand orthopedic surgeons which patients are eligible for remnant preservation, including ACL repair. Furthermore, this study adds to the literature in understanding how and where ACLs commonly tear. Lastly, this study confirms previously reported findings in the scarce literature regarding primary ACL repair.[19]

Conclusion

No anatomical risk factors were identified to play a role on tear location. Although most patients have midsubstance tears, proximal ACL tears were more commonly found in older patients. Bone contusions involving the medial compartment are associated with midsubstance tears may indicate that different injury mechanisms play a role in the location where the ACL tears.

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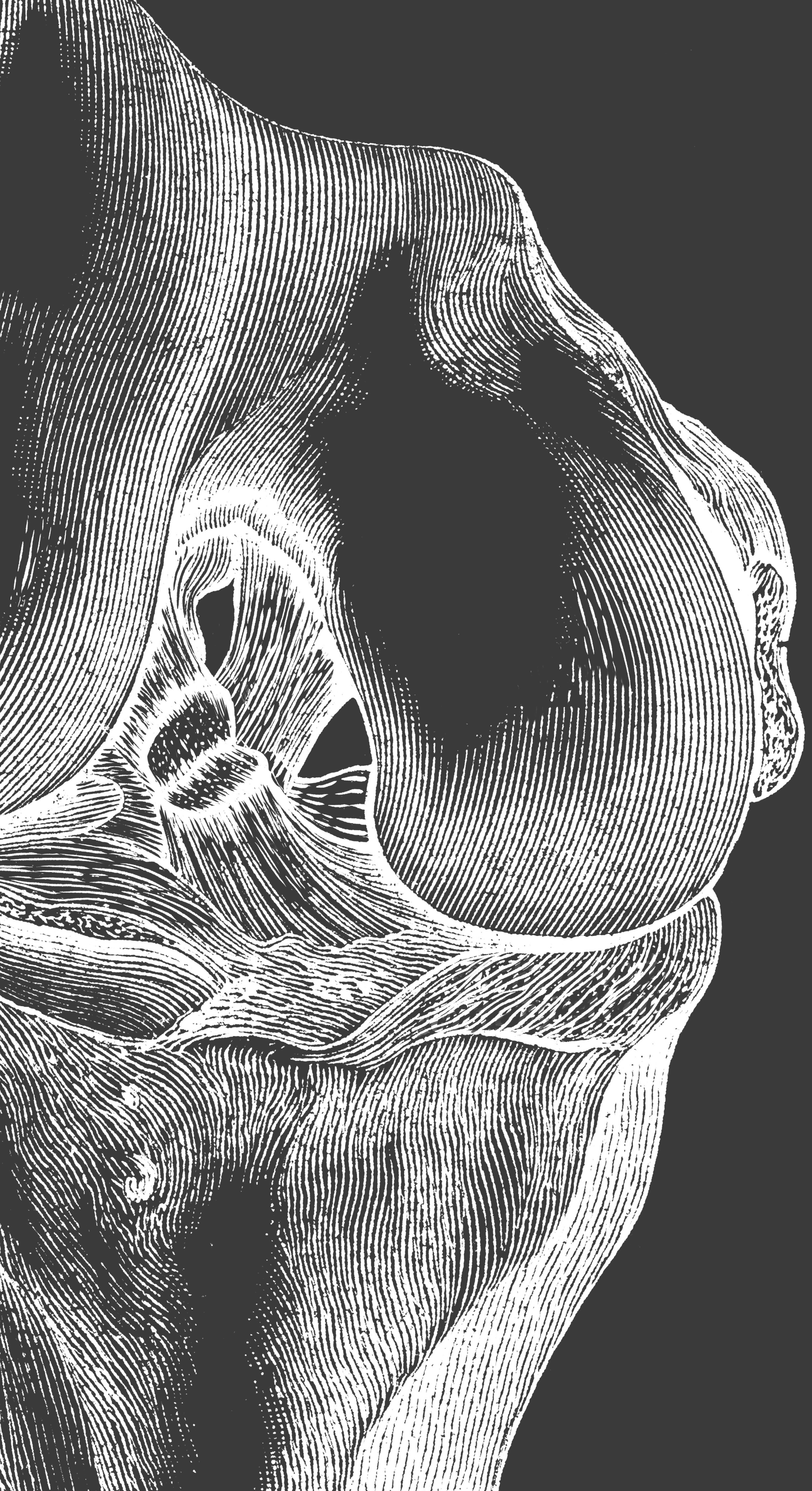

Chapter 6

Distal remnant length can be measured reliably and predicts primary repair of proximal anterior cruciate ligament tears

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Abstract

Purpose

To assess the reliability and predictive value of quantifying anterior cruciate ligament (ACL) tear location on magnetic resonance imaging (MRI) and assess the predictive value of tear location on the eligibility for arthroscopic primary repair of proximal ACL tears.

Methods

In this case-control study, all adult patients undergoing acute ACL surgery between 2008-2020 were retrospectively reviewed. All patients were treated with the treatment algorithm of undergoing primary repair when proximal tears with sufficient tissue quality were present intraoperatively, and otherwise underwent single-bundle ACL reconstruction. Sagittal MRI images were reviewed to measure proximal and distal remnant lengths along the anterior aspect of the torn ligament, and tear location was calculated as distal remnant divided by total remnant length. Interobserver and intraobserver reliability for remnant measurements were calculated. Then, receiver operating curve analysis (ROC) was performed to calculate the optimal cut-off for the possibility of primary repair with the different measurements.

Results

Two hundred and forty-eight patients were included, of which 151 underwent repair (61%). Inter- and intraobserver reliability ranged between 0.92 to 0.96 (95% confidence interval [CI] 0.55 – 0.98) and 0.91 to 0.97 (95% CI 0.78 – 0.98, respectively). All patients with a tear location of ≥80% on MRI could undergo repair, whereas all patients with tear location of <60% required reconstruction. The positive predictive value of a proximal quarter tear (≥75%) on primary repair was 94%. Older age was correlated with more proximal tear location ($p<0.001$), but there was no correlation between tear location and gender, BMI, or timing of surgery (all n.s).

Conclusion

This study showed that tear location could reliably be quantified on MRI by assessing distal and proximal remnant lengths. Tear location in the proximal quarter of the ACL was found to have a positive predictive value for repairability of 94%. These findings may assist orthopaedic surgeons in evaluating which patients are eligible for primary ACL repair preoperatively.

Introduction

Rupture of the anterior cruciate ligament (ACL) is a common injury in the active population, with an overall incidence of more than 200.000 injuries in the United States annually.[1] In the early days, surgical intervention of ACL injuries consisted of performing open primary repair in the acute setting.[2] Although initial short-term outcomes were encouraging, the long-term results were not satisfactory.[3] Due to this unpredictable nature, the concept of primary suture repair was abandoned, and with a shift towards ACL reconstruction.[4]

Although ACL reconstruction has evolved into a reliable procedure for restoration of knee stability, prevention of further injury, and to improve activity levels, there remains some concern regarding higher failure rates in younger patients with resultant revision procedures and significant numbers of patients not returning to sports.[5,6] In recent years, several surgeons and researchers have once again pursued the concept of primarily repairing ACL tears, encouraged by the potential advantage of preserving native tissue without the need for graft harvesting.[7–10] From a clinical perspective, improved outcomes can be expected by applying modern-day advancements to selected groups of patients presenting with proximal ACL tears.[11] However, the precise role of this treatment remains controversial as the current data is limited.[12]

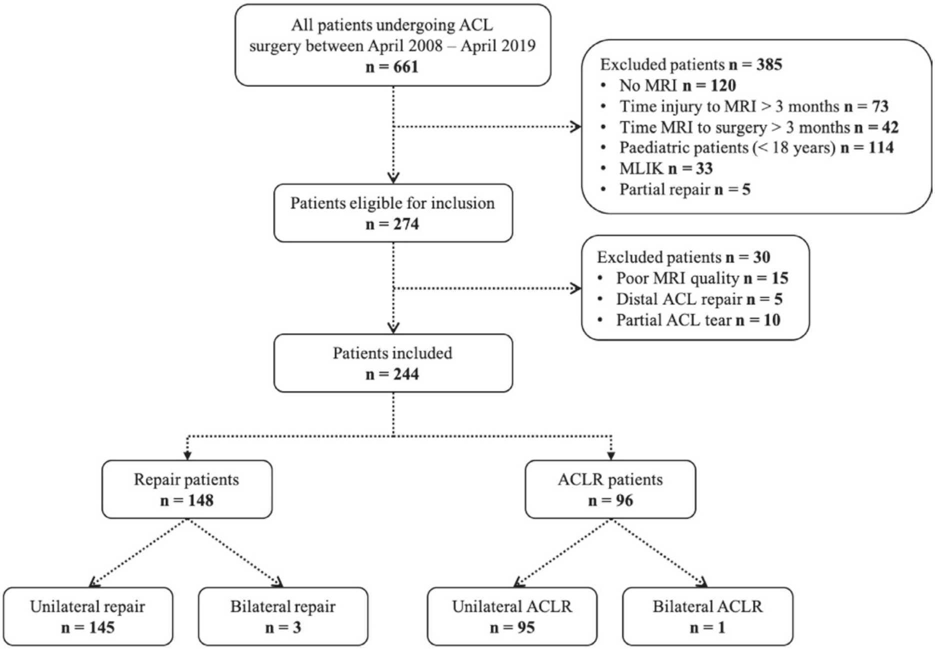
A key component for successful outcomes of primary ACL repair is patient selection[13,14], specifically the length of tissue must be sufficient for re-tensioning to the femoral insertion, and the quality of tissue must be sufficient to withhold sutures. With this recognized role of tear location, recent studies have advocated using magnetic resonance imaging (MRI) to predict eligibility for primary repair.[11] However, knowledge regarding the threshold of minimum distal remnant length on preoperative MRI as a predictor for eligibility of surgical repair is currently unknown, as has been recently determined for PCL reinsertion repair.[15]

The purpose of the present study was to quantify tear location on preoperative MRI by measuring proximal and distal remnant length, to assess the reliability of this measurement, and to assess the positive predictive value of this tear location on the eligibility of primary repair of proximal ACL tears. The hypothesis was that these measurements are more reliable than our previous proposed tear-type classification[16], and that distal remnants were greater in length in patients eligible versus not eligible for primary repair.

Materials and methods

The study protocol was approved by the hospital's institutional review board (IRB number 2020–0001). A prospectively maintained database was retrospectively reviewed to identify all patients surgically treated for ACL injuries between April 2008 and April 2020. Surgical treatment of ACL injuries was performed according to a tissue preservation algorithm in which reinsertion of the ligament was performed when repairable ligaments were present (i.e. proximal tear and sufficient tissue quality), while single-bundle ACL reconstruction was performed if primary repair was not possible (midsubstance tears with insufficient length to be reapproximated to the femoral wall or poor tissue quality to withhold suture passage). All surgeries were performed by the senior author (GSD). A total of 665 patients underwent ACL surgery within this timeframe. After applying exclusion criteria (Figure 1), a total of 251 patients were included in this study, including 150 patients treated with primary repair and 100 treated with ACL reconstruction. Although this study demonstrates a unique analysis, it should be noted that data from 50% of patients have been reported on clinically in previous studies.[16]

Figure 1.



Flowchart of the studied population. ACLR indicates ACL reconstruction.

Surgical procedure and treatment algorithm

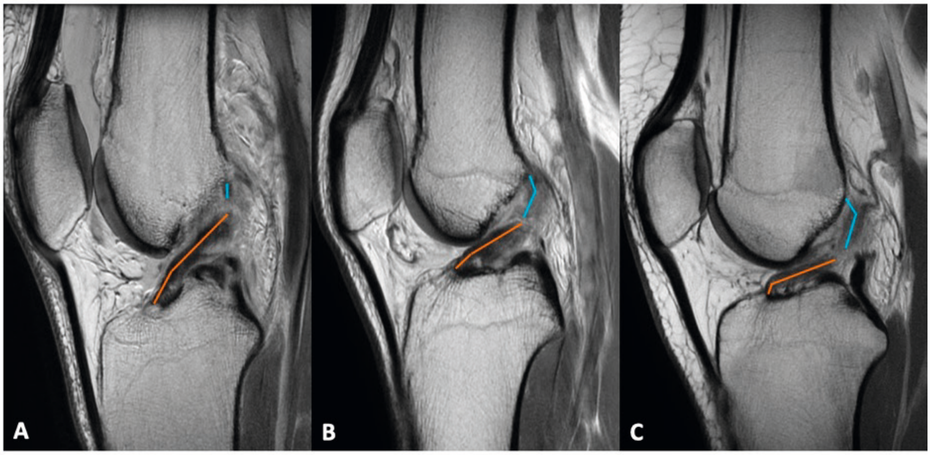
All patients were placed in supine position and prepped and draped in the normal sterile fashion as for knee arthroscopy. Standard anterolateral and anteromedial portals were created, and a general assessment of the knee was performed for tear type, tissue quality, and eligibility for ACL repair. Primary repair was considered in all cases when proximal tears were present (i.e. if the distal ACL remnant was of sufficient length for re-tensioning to the femoral insertion) and sufficient tissue quality was present (i.e. if the distal remnant was of sufficient tissue quality to withhold intrasubstance suturing and re-tensioning towards the anatomical footprint of the ACL). Once the ACL was deemed repairable, primary repair using suture anchor fixation was performed, which has been previously described in more detail.[17,18] When non-repairable tears were present, standard single-bundle ACL reconstruction with an anteromedial portal drilling technique was performed, utilizing either hamstring autografts (32%), quadriceps autografts (13%), bone-patellar tendon-bone autografts (10%), allografts (43%), or hybrid grafts (1%).

Data collection

For all patients, patient demographics such as gender, age at time of surgery, body mass index (BMI), side of injury, delay from injury to MRI, and delay from injury to surgery were collected.

Preoperative MRIs were then retrospectively reviewed to assess the exact tear location by reviewing the sagittal, coronal, and axial planes. Since MRIs were performed at different institutions, scanning technique varied. Using a digital ruler, the distal and proximal remnant lengths were measured along the anterior aspect of the torn ACL on sagittal short TE MR images with an accuracy of 0.01 mm for linear measurements. Specifically, the sagittal image that most clearly showed the anterior tibial insertion was selected. The distal remnant was then measured from this point to the mid-section of the proximal part of the distal fibers of the torn ligament using multiple measurements on a single slice to correct for the wavy contour of the ligament (Figure 2). Similarly, the starting point for the proximal remnant was the most superior point of the femoral attachment onto the lateral femoral condyle, and the end was the mid-section of the distal part of the proximal fibers of the torn ligament. If needed, measurements were performed over multiple slices to establish maximum length. If the ACL was torn obliquely, the mid-section of the remnant was identified as the tear location. Tear location was defined as the length of distal remnant as percentage of the aggregate length of the distal and proximal remnant. Finally, these findings were correlated with operative reports to assess ultimate treatment (repair or reconstruction).

Figure 2.



Three examples of sagittal proton density-weighted (short TE) MRI images of different patients with ACL tears. (A) The ACL is torn proximally; distal remnant was measured to be 38 mm, proximal remnant 6 mm. The ACL was repaired. (B) The ACL is torn at the junction of the proximal and middle thirds; distal remnant was measured to be 26 mm, and the proximal remnant 12 mm, The ACL was reconstructed. (C) The ACL is torn at the midsubstance; distal remnant was measured to be 24 mm, and proximal remnant 16 mm. The ACL was reconstructed.

Subgroups were defined based upon age (18 – 24, 25 – 34, 35 – 44, and ≥45 years), gender, BMI (< 25 and ≥ 25 kg/m²), and surgical delay (< 4 and ≥ 4 weeks following injury). Subsequently, tear locations were reviewed and compared between subgroups.

Reliability analysis

Twenty MRI studies were first randomly obtained for reliability assessment from our electronic radiology patient archiving and communication system (PACS) (Sectra AB, Linköping, Sweden). These studies were reviewed by an experienced musculoskeletal magnetic resonance radiologist (DNM), a musculoskeletal radiologist post-doc fellow (BC), and an orthopedic research fellow (HDV) using the aforementioned measurement method to assess the interobserver reliability. The radiologist post-doc fellow and the orthopedic research fellow then repeated their measurements three weeks after the initial assessment to assess the intra-observer reliability. All MRI studies were reviewed in blinded fashion by the radiologist fellow and the orthopedic research fellow. Any disagreement between both reviewers was resolved in consensus fashion, and the senior radiologist was consulted if no agreement was reached.

Statistical analyses

All statistical analyses were performed using SPSS Version 25 (SPSS Inc., Armonk, NY, USA). First, intra- and inter-observer agreement was tested using the interclass correlation coefficient (ICC). Descriptive data were then assessed for normality using the Shapiro–Wilks test. A sample-size power analysis was performed and suggested that 34 patients in both groups were needed to show a 20% difference in ACL tear location with a power of 80%. Independent samples t-tests were used when comparing normally distributed data and reported in mean ± standard deviation (SD). Whitney U test was applied when comparing non-normally distributed data and reported in median with interquartile ranges (IQR). Chi-square test or Fisher exact test was used when comparing discrete variables and reported in frequency and percentage. One-Way ANOVA with post hoc Bonferroni test was performed to compare three or more groups of continuous variables. Finally, Pearson's correlation coefficient was performed to identify any correlations between tear location and age for the entire cohort. All comparative analyses were two-sided, and a difference of $p < 0.05$ was considered statistically significant.

Results

Patient demographics

A total of 248 patients were enrolled, which included 151 (61%) treated with primary repair and 97 (39%) with ACL reconstruction (Figure 1). Median age was 36 years (IQR 26 – 44 years), median BMI was 25 kg/m² (IQR 23 – 27 kg/m²), 57% were males, and 54% sustained an ACL tear in their right knee. Median time from injury to MRI was 6 days (IQR 3 – 15 days), and time from MRI to surgery was 24 days (IQR 13 – 41 days). Most common injury mechanisms were skiing (30%), followed by soccer (14%), and basketball (14%). Four patients underwent bilateral ACL surgery (2%), including three bilateral repairs and one bilateral reconstruction. Descriptive data are shown in Table 1.

Table 1. Patient demographics of all patients in the study cohort stratified by treatment.

	All patients (n = 248)	Repair (n = 151)	Reconstruction (n = 97)	P-value*
Age (years); median (IQR)	36 (26 – 44)	40 (33 – 47)	29 (21 – 39)	<0.001
Male gender; n (%)	141 (57%)	77 (51%)	64 (66%)	0.020
Right side; n (%)	132 (54%)	79 (52%)	53(53%)	0.968
BMI (kg/m²); median (IQR)*	25 (23 – 27)	25 (23 – 27)	25 (23 – 27)	0.208
Injury to surgery (days); median (IQR)	32 (20 – 59)	31 (19 – 50)	34 (25 – 78)	0.011
Meniscal injury; n (%)	141 (57%)	83 (55%)	58 (60%)	0.454
Medial meniscus	65 (26%)	43 (28%)	22 (23%)	0.311
Lateral meniscus	108 (44%)	60 (40%)	48 (50%)	0.131
Chondral injury; n (%)	58 (23%)	41 (27%)	17 (18%)	0.057
Injury mechanism; n (%)				0.158
Skiing	75 (30%)	58 (38%)	17 (18%)	
Soccer	35 (14%)	15 (10%)	20 (21%)	
Basketball	34 (14%)	18 (12%)	16 (16%)	
Jump from height / traumatic fall	14 (6%)	11 (7%)	3 (3%)	
Football / Rugby	13 (5%)	4 (2%)	9 (9%)	
Volleyball	11 (4%)	6 (4%)	5 (5%)	
Tennis	7 (3%)	5 (3%)	2 (2%)	
Motor vehicle accident	6 (2%)	2 (1%)	4 (4%)	
Other / unspecified	53 (21%)	32 (21%)	21 (22%)	

Asterisk Mann-Whitney U test was used to compare continuous variables, while Chi-square tests or Fisher exact test (in case one of the numbers is < 5) was used to compare nominal data; SD, standard deviation; N, number of patients; BMI, body mass index; Asterisk, BMI was missing in seven patients.

Interobserver and intraobserver reliability

Interobserver reliability was found to be excellent between all three observers for the distal remnant (ICC = 0.92, 95% confidence interval [CI] 0.78 to 0.97), as well as for the proximal remnant (ICC = 0.94, 95% CI 0.87 to 0.97), and tear location (ICC = 0.96, 95% CI 0.91 to 0.98). Similarly, intra-observer reliability was also noted to be excellent for both the radiology post-doc fellow and orthopaedic research fellow (range ICC 0.91 to 0.97, 95% CI 0.55 to 0.98). No differences in both interobserver and intraobserver reliability were found between the different measurements (range ICC 0.91 to 0.97; Table 2).

Table 2. Intraobserver and Interobserver agreement of ACL remnant length measurements (n = 20).

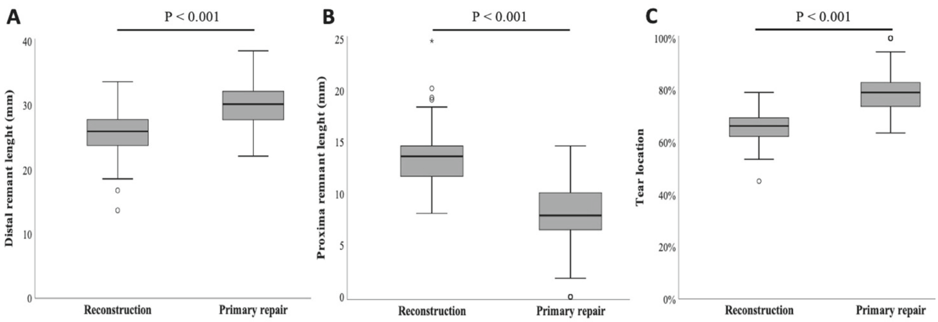
	Distal remnant ICC	Proximal remnant ICC	Tear location ICC
Intra-observer 1	0.92 (0.79 to 0.97)	0.91 (0.55 to 0.97)	0.95 (0.81 to 0.98)
Intra-observer 2	0.97 (0.92 to 0.99)	0.94 (0.85 to 0.98)	0.96 (0.89 to 0.98)
Interobserver	0.92 (0.78 to 0.97)	0.94 (0.87 to 0.97)	0.96 (0.91 to 0.98)

ICC, intraclass correlation coefficient; Intra-observer 1 represent orthopaedic research fellow; Intra-observer 2 represent radiology post-doc fellow.

Remnant lengths on preoperative MRI

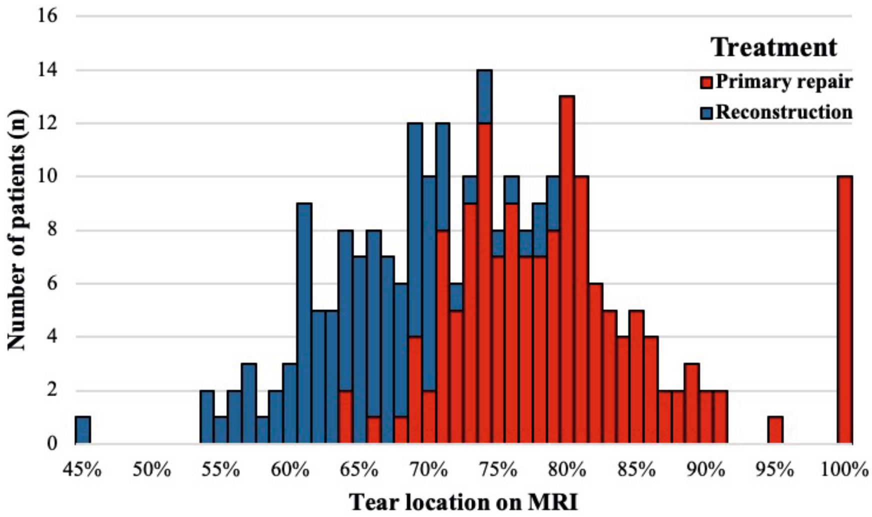
When comparing patients who ultimately underwent repair to those who underwent reconstruction, patients treated with repair had significantly greater distal remnant length (mean 30 ± 3 mm vs. 26 ± 3 mm, $p < 0.001$; Figure 3), and significantly shorter proximal remnant length (8 ± 3 mm vs. 13 ± 3 mm, $p < 0.001$), respectively. As a result, the mean tear location was significantly more proximal in the repair group (80 ± 8% vs. 66 ± 6%, respectively, $p < 0.001$; Figure 3 and 4). It was noted that all patients with a tear location at ≥ 80% on MRI ultimately underwent repair, whereas all patients with a tear location < 60% were reconstructed (Table 4). When taking 75% as the cutoff value for tear location, the sensitivity was 71%, with a specificity of 93%, positive predictive value of 94%, negative predictive value of 68%, and accuracy of 79%.

Figure 3.



Box plot distribution of (A) distal remnant length, (B) proximal remnant length, (C) tear location between those patients treated with ACL reconstruction as compared to those treated with repair. In each box-plot, values are presented as median (line), interquartile range (box), and minimum (lower whisker) and maximum (upper whisker).

Figure 4.



Scatterplot shows the correlation between tear location and age.

Subgroup analyses

When comparing age-specific outcomes, a significantly more proximal tear location was found in patients older than 35 years, as compared to those younger than 35 years (77 ± 9% vs. 71 ± 10%, $p < 0.001$; Table 3). Pearson's correlation analyses revealed a significant correlation between older age and more proximal tear location (correlation coefficient 0.305; $p < 0.001$).

Table 3. Remnant lengths on preoperative MRI in this cohort stratified by age[a]

	18 – 24 years (n = 51)	25 – 34 years (n = 63)	35 – 44 years (n = 75)	≥ 45 years (n = 59)	ANOVA
Distal	27 (17 – 36 mm)	28 (20 – 37 mm)	29 (19 – 36 mm)	29 (14 – 39 mm)	0.084
Proximal	12 (0 – 20 mm)	11 (0 – 25 mm)	9 (0 – 18 mm)	8 (0 – 17 mm)	<0.001b
Tear location	69 (54 – 100%)	72 (54 – 100%)	76 (60 – 100%)	78 (45 – 100%)	<0.001c

[a] Values are presented in mean with range; [b] Significant difference, using One-Way ANOVA with Bonferroni correction, between age group 35–44 years vs. 18–24 years ($p < 0.001$), between ≥45 years vs. 18–24 years ($p < 0.001$), between age group 25–34 years vs. 35–44 years ($p = 0.028$), and between age group 25–34 years vs. ≥45 years ($p = 0.001$);
[b] Significant differences between age group 35–44 years vs. 18–24 years ($p = 0.001$), between ≥45 years vs. 18–24 years ($p < 0.001$), and between age group 25–34 years vs. ≥45 years ($p = 0.009$).

When comparing other subgroups, there was no significant difference in tear location between male and female patients (74 ± 10% vs. 75 ± 10%, respectively, n.s.), nor in BMI < 25 and ≥ 25 kg/m² (75 ± 10% vs. 74 ± 10%, respectively, n.s.). Similarly, no difference was found in tear location between patients undergoing ACL surgery in the acute (< 4 weeks) and subacute setting (4 weeks – 3 months) (75 ± 10% vs. 74 ± 10%, respectively, n.s.).

Table 4. Diagnostic parameters of remnants lengths and their predictive values in reparability of the ACL.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Distal remnant					
≥ 34 mm	12%	100%	100%	38%	43%
≥ 32 mm	30%	96%	92%	48%	56%
≥ 30 mm	52%	89%	88%	54%	67%
≥ 22 mm	100%	6%	61%	100%	62%
Proximal remnant					
< 8 mm	54%	100%	100%	58%	72%
< 10 mm	72%	87%	91%	67%	79%
< 12 mm	91%	73%	84%	85%	84%
< 16 mm	100%	15%	65%	100%	67%
Tear location					
≥ 80%	46%	100%	100%	54%	67%
≥ 75%	71%	93%	94%	68%	79%
≥ 70%	95%	75%	86%	90%	87%
≥ 60%	100%	10%	64%	100%	65%

PPV indicates positive predictive value; NPV, negative predictive value.

Discussion

The main finding of this study was that remnant lengths of the torn ACL that were measured on preoperative MRIs were highly reliable with all ICC above 0.9, and that these measurements may help orthopaedic surgeons in their preoperative assessment to assess which patients are eligible for primary ACL repair. It was noted that all patients with tear location of ≥ 80% on MRI could be repaired, while those with < 60% required ACL reconstruction.

In the senior author's practice, all patients are treated according to the same surgical treatment algorithm. With this algorithm, patients with sufficient remnant length and good tissue quality that can be approximated to the femoral wall, and that can withhold intraligamentary suturing intraoperatively, undergo primary repair, and patients are otherwise reconstructed. This concept of ligament preservation has recently been subject to a resurgence of interest as multiple new selective arthroscopic ACL repair techniques have been reported on.[12] While primary repair yields promising early results, it has been recognized that strict indications are paramount as outcomes may vary for different tear patterns.[11,19] In general, improved outcomes after ACL repair can be expected in patients with acute, proximal ACL tears since these tend to have better vascularity and increased intrinsic healing capacity as compared to midsubstance tears.[20,21] Besides the limited ligament-to-ligament healing response, repair of shorter distal remnants are also less likely to be successfully repaired due to insufficient tissue length for retensioning to the femoral wall.[22,23]

With this in mind, it is important to make a comprehensive preoperative assessment as to whether to ACL can be preserved. Previously, our group have suggested using the modified Sherman classification to correlate different tear patterns with several ligament preservation techniques based upon tear location.[24] With this classification system, ACL tears can be classified as type I tear (proximal avulsion tear), type II tear (proximal tear), type III tear (midsubstance tear), type IV tear (distal tear), or type V tear (distal avulsion tear). This classification system has shown substantial interobserver reliability (Kappa 0.670) and substantial to nearly perfect intraobserver reliability (Kappa 0.741 to 0.934). Although ACL tears in the proximal quarter may be eligible for femoral reattachment, it remains challenging to differentiate between different types since clear definitions are currently lacking. For example, some ACL tears may be defined as proximal by some and as midsubstance tears by others, displayed by the kappa coefficient of 0.670 in our previous tear type reliability study. In addition, the threshold lengths for the ability to perform primary repair remain unknown when using this classification system. Therefore, the present study has validated a straightforward measurement protocol that has shown both excellent inter- and intraobserver reliability, and which more accurately predicts eligibility for primary repair, as compared to the tear type classification.

When only analyzing preoperative MRIs, the present study suggests that all patients with tear location ≥ 80% were eligible and ultimately treated with primary repair, whereas those with a tear location < 60% all underwent ACL reconstruction. Furthermore, it was noted that a tear location of ≥ 75% was highly predictive for the possibility of primary repair. In the literature, no other cutoff values for eligibility for proximal ACL repair have been identified. When reviewing other knee ligaments, Goiney et al. performed a similar analysis for repair versus reconstruction of PCL tears and recently noted that knees with a distal PCL remnant length on MRI of ≥41 mm were eligible for proximal repair, whereas those with a distal length of ≤32 mm were reconstructed due to insufficient tissue length.[15] Nevertheless, it should be noted that they did not express distal remnant length as a percentage of the total PCL length, since this could differ among individuals.

When comparing subgroups, this study revealed a correlation between remnant length and higher age. Previously, a recent MRI-based study also showed a significantly higher incidence of type I tears in patients aged 35 years and older as compared to those younger than 35 years (23% vs. 8%)[25], confirming the findings in this current study. When reviewing mean reported ages in recent systematic reviews, repair patients indeed appear to be older than historical controls undergoing ACL reconstruction.[11] We can only speculate on the reason for this finding. One of the reasons may be related due to different injury mechanism that may lead to higher incidence of proximal tears in the older patient population, while also an age-related decrease in vascularity in the proximal section of the ligament may play a role.[26]

In this study, no differences were found between ACL tear location on MRI within the acute and subacute setting. On the contrary, it has been shown that better tissue quality can be expected within the early phase after injury as the ligament remnant can potentially retract after the first several weeks.[27] Despite this, torn ACLs have been shown to occasionally reattach to the roof of the intercondylar notch or posterior cruciate ligament (PCL), after which the length and quality of the remnant can be maintained.[28] Therefore, some tears may even be repaired in the chronic setting.[29] Nevertheless, this might explain why this study did not find any differences between both groups' tear locations, although future studies are needed to confirm these findings and to determine the optimal time frame to repair a torn ACL.

When reviewing clinical outcomes of primary ACL repair, a recent meta-analysis showed that all primary repair techniques seemed safe with a mean failure rate of 11%, reoperation rate of 9%, and subjective outcomes of >85% of the maximum scores.[11] However, it should be noted that although these results may be promising, it seems that younger patients are at increased risk for failure after treatment, including primary ACL repair and Ligamys repair.[13,30] Furthermore, the overall current reported level of evidence is still low and therefore there is a need for higher-quality, comparative studies in which outcomes of larger patient groups are compared to the current gold standard of ACL reconstruction.

There are limitations to this study. First, potential selection bias has occurred as eligibility for primary repair is surgeon dependent. Nonetheless, all patients were repaired if the distal remnant length was felt to be of sufficient length for reinsertion. Future studies with different cohorts and surgeons are therefore needed to confirm these findings. Secondly, tissue quality is also important for achieving successful outcomes, and this was not addressed further. Thirdly, given the retrospective nature, no intraoperative assessment could be performed. A comparable prospective study is therefore needed to confirm these findings. In addition, it was noted that in some cases, the tear locations of both bundles varied. This may have influenced outcomes in this study since the current measurement protocol cannot correct for these tear patterns. Nevertheless, this influence is expected to be low since these tear patterns are infrequently seen.[25] Finally, the primary goal of this study was to assess the correlation between remnant lengths and eligibility of repair; further studies are needed to assess if there is a correlation between tear location and the long-term outcomes of primary repair. Despite these limitations, outcomes of this study are valuable as the proposed measurements protocol enables orthopaedic surgeons to accurately predicts which patients are eligible for primary ACL repair.

Conclusion

This study showed that tear location could reliably be quantified on MRI by assessing distal and proximal remnant lengths. Tear location in the proximal quarter of the ACL was found to have a positive predictive value for repairability of 94%. These findings may assist orthopaedic surgeons in evaluating which patients are eligible for primary ACL repair preoperatively.

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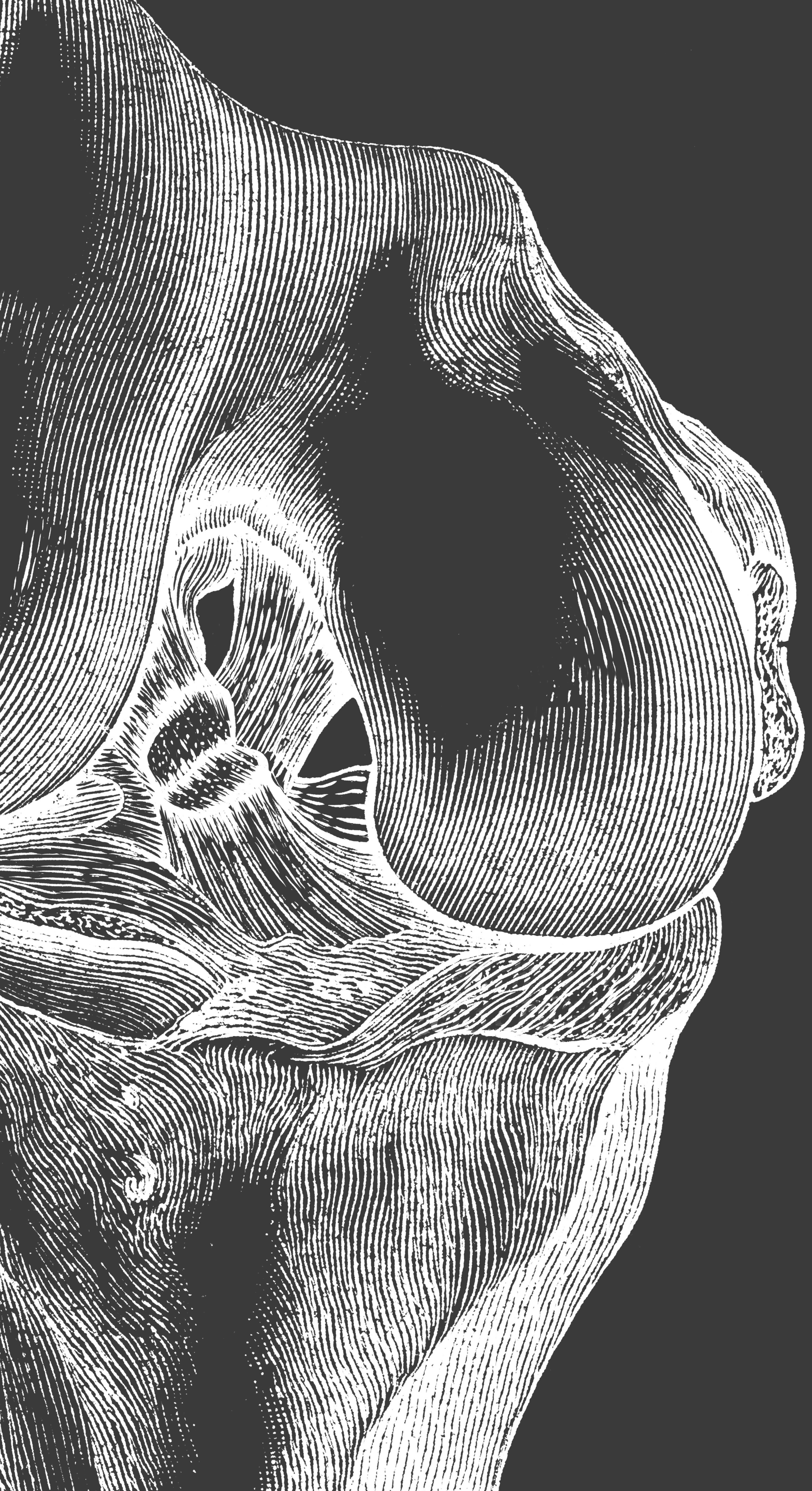
Part 4

Outcomes of ACL repair



Chapter 7

Primary repair with suture augmentation for proximal anterior cruciate ligament tears: a systematic review with meta-analysis

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Abstract

Purpose
To assess the outcomes of arthroscopic primary repair of proximal anterior cruciate ligament (ACL) tears with suture augmentation in the literature.

Methods
A systematic search was performed using PubMed, EMBASE, and Cochrane for studies reporting on outcomes of primary repair of proximal ACL tears with suture augmentation between 2015-2021. Primary outcomes included failure and reoperation rates, whereas secondary outcomes consisted of functional outcomes. Proportion meta-analysis was performed to assess the overall incidence of failure rates. Outcomes of adults and adolescent were reported separately.

Results
Thirteen studies with 418 patients were included in this study (mean age 32 years, mean follow-up 2.0 years, 49% male). There were no randomized studies and overall grade of recommendation was weak. Overall failure rate for primary repair with suture augmentation was 8% (95% CI 3.9–14.4), but this was higher for younger patients (17%; 95% CI 2.5 – 63.9) than for older patients (6%; 95% CI 3.8–8.9). The risk for additional reoperations, complications, or hardware removal was low (all <2%), while functional outcomes were good to excellent (all >80% of maximum score).

Conclusion
Current literature shows that primary repair with suture augmentation is a reliable treatment option for proximal ACL tears with a failure rate of 8% and good functional outcome scores at short-term follow-up. Although functional outcomes were good irrespective of age, failure rates were higher in young patients (17% vs. 6%, respectively). There is a need for high-quality comparative studies with large group of patients to compare these outcomes with ACL reconstruction.

Introduction

Historically, open anterior cruciate ligament (ACL) repair was associated with high complication and failure rates.[1] Over the last decade, however, several investigators have advocated performing primary anterior cruciate ligament (ACL) repair using an arthroscopic approach and only on selected patients with proximal tears.[2,3] Clinically, the outcomes of ACL repair with advanced arthroscopic techniques and modern rehabilitation protocols have shown improvement and encouraging results with higher potential for early healing and better functional outcomes as compared with reconstruction surgery.[4,5]

Due to this renewed interest in ACL repair, several novel repair techniques have recently emerged, including suture repair alone and repair with either static or dynamic augmentation.[2] Of all the described procedures, it has been shown that primary repair with static augmentation has both the lowest failures and least complications of these techniques.[4] With this technique, the repaired ligament is augmented with a braided suture tape to increase construct strength and overall stiffness.[6] Although multiple systematic reviews on this topic have been published in recent years[2–4,7], it should be noted that several have combined the outcomes of different surgical techniques (open vs. arthroscopic) and different tear locations (proximal vs. midsubstance), thereby resulting in significant heterogeneity.[2] Furthermore, many new studies have recently been published that have not yet been included in these reviews.[8–10] Therefore, it is important to assess the latest outcomes of the most promising repair technique (i.e. repair with static augmentation for proximal ACL tears only).

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The aim of this systematic review with meta-analysis is therefore to assess the clinical and functional outcomes of recent studies performing primary repair with suture augmentation of proximal ACL tears. The second aim of this study is to stratify these results by age. It was hypothesized that the overall level of evidence for repair is low, but that the results are uniform and promising. Furthermore, it was hypothesized that older age is correlated with improved outcomes.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed to perform this systematic review with meta-analysis.[11]

Literature search

On June 22, 2022, a systematic search was performed using the electronic search engines PubMed, Cochrane Library, and Embase with the search algorithm *"Anterior Cruciate Ligament AND (repair OR reinsertion OR reattachment OR healing OR suture) AND ('suture augmentation' OR 'internal brace')"* for studies reporting on outcomes of primary ACL repair with suture augmentation. Since this technique was first described in 2015,[12] the search was limited to recent studies published since then. After duplicates were excluded, two reviewers (HDV and JPL) both independently reviewed all studies for titles and abstracts. Subsequently, full-texts of eligible studies were reviewed by the same two reviewers to assess study eligibility. Furthermore, references of the included studies were screened for any missing studies. This was also performed independently by both reviewers. Finally, both literature searches were compared and consensus was ultimately reached on the inclusion and exclusion of all studies.

Studies were included when they reported on (i) outcomes of primary repair with suture augmentation, (ii) treating proximal tears, (iii) minimum 1-year follow-up, (iv) minimum level IV studies, and (v) minimum cohort of 10 patients. Studies were excluded when they reported on (i) treating multiligamentous knee injuries or knee dislocations, (ii) treating distal (bony) avulsion tears, (iii) abstract only, or (iv) reported on the same but smaller patient cohort.

Methodological quality of studies

The adjusted Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence was used to assess the level of evidence of the included studies.[11] In addition, the Methodological Index for Non-Randomized Studies (MINORS) instrument was used to assess the methodological quality of the included studies.[13] Although this instrument is designed to evaluate the methodological quality of both non-comparative and comparative studies, only the non-comparative factors of the MINORS instrument were used since only the repair cohorts were included in this meta-analysis.

Data extraction

All data were collected in Excel 2017 (Microsoft Corp., Redmond, WA, USA). First, study demographics were collected including author names, year of publication, number of patients, and study design. Then, patient demographics were collected including age at time of surgery, gender, length of follow-up, and delay from injury to surgery. To assess clinical outcomes, treatment failure (defined as rerupture or symptomatic instability), (expected) reoperations (defined as surgical intervention besides revision surgery), and any complication besides failure and reoperations (defined as any undesirable and unexpected result of surgery) were collected. Furthermore, removal of hardware rates (ROH; without performing any other surgical procedure) due to irritation were collected, while those removed routinely were reported separately (defined as 'expected ROH'). In addition, clinical stability, either using KT-1000 measurements or Rolimeter arthrometer, was collected. Finally, collected functional outcomes included preinjury and postoperative Tegner score,[14] Lysholm score,[14] International Knee Documentation Committee (IKDC) objective and subjective score,[15,16] Knee injury and Osteoarthritis Outcome Score (KOOS), Single Assessment Numeric Score (SANE) on knee function,[17] Marx activity rating scale,[18] and visual analog scale (VAS) for pain[19].

Statistical analysis

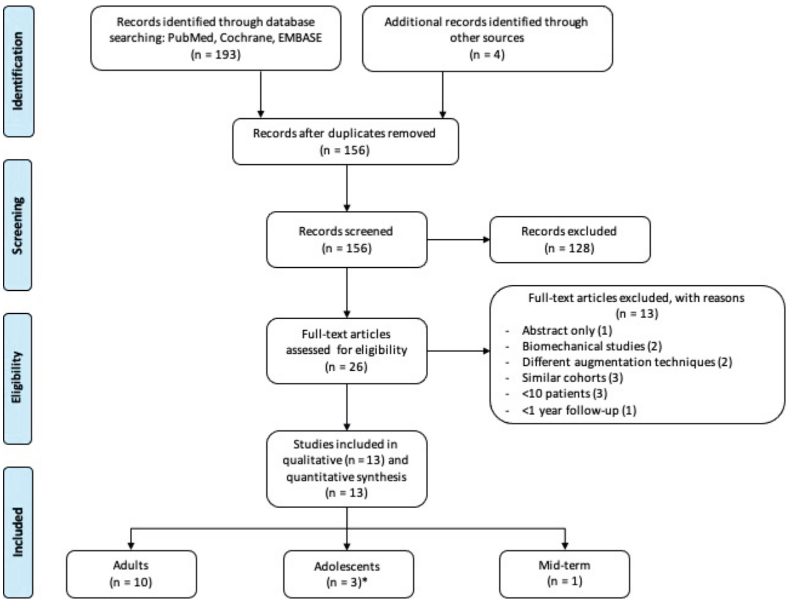
R version 4.0.0 (R Foundation for Statistical Computing, Vienna, Austria) and Excel 2017 were used for statistical analysis. For categorical outcomes, overall incidence was calculated using proportion meta-analysis.[20] This tool allows calculating a pooled proportion from studies reporting a single proportion. A subgroup analysis was performed based upon age at time of surgery (< 18 and ≥ 18 years). Using a random-effects model by the back-transformation of the weighted mean of the logit-transformed proportions with Dersimonian weights, effect sizes and 95% Confidence Intervals (CI) were calculated. For continuous outcomes, effect sizes and pooled outcomes were calculated by calculating a weighted average and these were reported in mean ± standard deviation (SD). Previously defined methods were used in case results were presented in alternative fashion. In case multiple studies reporting on identical patient cohorts but with different length of follow-up, only studies reporting the two-year results were used for overall outcomes, while the mid-term results were reported separately. All tests were two-sided, significance of statistical differences was attributed to p-value of < 0.05.

Results

Study selection

One-hundred thirty-five studies were screened for eligibility on title and abstract and 26 articles were subsequently reviewed on their full text for inclusion. A total of 13 studies were included[9,10,21–31] of which eight assessed the outcomes of adult cohorts[9,10,21,23,24,27,28,31,32], two of adolescent cohorts[25,26], one of both adult and adolescent cohorts[22], and one mid-term outcomes[30] (Fig. 1).

Figure 1.



A PRISMA flowchart is shown.

Quality of studies

No level I or II studies were identified. There were four level III studies (25%)[21–23,26], and there were nine level IV studies (75%)[9,10,24,25,27–32]. Using the GRADE system, overall recommendation for using primary repair with suture augmentation for proximal ACL tears was weak based on the fact that most studies were retrospective level IV studies. In addition, the mean methodological quality of studies scores was 10.8 out of 16 points (68% of maximum), according to the MINORS criteria (Table 1).

Table 1. Quality assessment of the included studies using the Methodological Index for NonRandomized Studies (MINORS) criteria

Authors	Year	Journal/Meeting	Evidence	Study design	1	2	3	4	5	6	7	8	Total
Batista et al.[32]	2020	J ISAKOS	IV	Case Series	1	2	1	0	0	1	2	0	7
Burton et al.[21]	2020	Arthroscopy	IV	Case Series	2	2	2	1	0	2	1	0	10
Dabis et al.[22]	2020	KSSTA	IV	Case Series	2	2	2	2	0	2	2	0	12
Douoguih et al.[41]	2020	ASMAR	IV	Case Series	2	2	1	2	0	2	2	0	11
Gagliardi et al.[42]	2019	AJSM	III	Retrospective	2	2	1	2	0	2	1	0	10
Heusdens et al.[24]	2019	KSSTA	IV	Case Series	2	2	2	1	0	2	21	1	12
Heusdens et al.[25]	2020	KSSTA	IV	Case Series	2	2	2	2	0	2	2	0	12
Hopper et al.[27]	2021	KSSTA	IV	Case Series	2	2	2	1	0	2	1	1	11
Kalina et al.[43]	2019	Acta Chir Orthop Tr	IV	Case Series	2	2	1	2	0	1	1	0	9
Mattiassich et al.[29]	2020	Sports. Sportschaden Sportschaden	III	Retrospective	2	2	2	2	1	1	2	2	14
Schneider et al.[10]	2020	J. Clic. Med.	IV	Case Series	2	2	1	2	0	1	22	0	10
Szwedowski et al.[31]	2021	J. Clic. Med.	III	Cohort	2	2	2	2	0	1	1	0	10
Vermeijden et al. [30]	2020	Arthroscopy	III	Retrospective	2	2	2	2	1	2	2	0	13

Only the non-comparative part of the MINORS criteria was used (i.e., first 8 questions).

The criteria of MINORS with 0 points when not reported, 1 when reported but not adequate, and 2 when reported and adequate. Maximum score is 16.

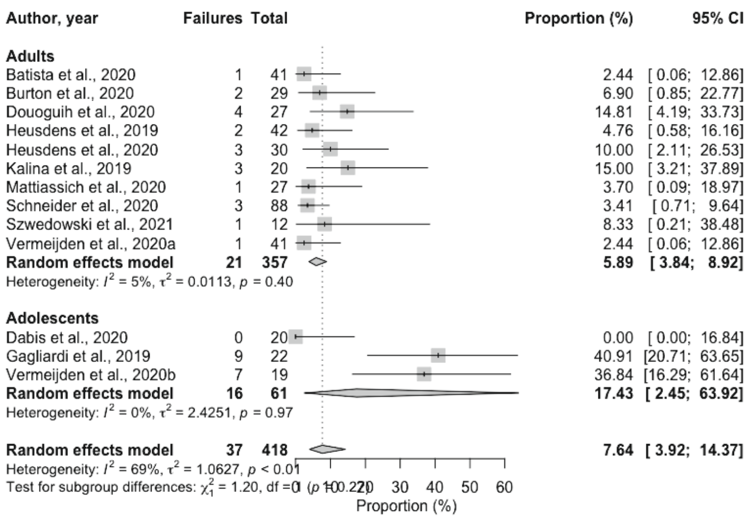
1. A clearly stated aim: the question addressed should be precise and relevant in the light of available literature.
2. Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion).
3. Prospective collection of data: data were collected according to a protocol established before the beginning of the study.
4. End points appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome which should be in accordance with the question addressed by the study. In addition, the end points should be assessed on an intention-to-treat basis.
5. Unbiased assessment of the study end point: blind evaluation of objective end points and double-blind evaluation of subjective end points. Otherwise, the reasons for not blinding should be stated.
6. Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events.
7. Loss to follow-up less than 5%: all patients should be included in the follow-up. Otherwise, the proportion lost to follow-up should not exceed the proportion experiencing the major end point.
8. Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% CI, according to the expected incidence of the outcome event, and information about the level for statistical.

Overall outcomes

A total of 418 patients in 12 studies were included with a mean age 32 ± 10.6 years, mean follow-up of 2.0 years (range 0.4 – 4.5 years), mean surgical delay of 32 days (range 0 – 336 days), and 49% were male gender. All patients were treated for proximal ACL tears (100%; Table 2). Most studies performed primary ACL repair using transosseous tunnel fixation (85%)[9,10,21,23–31]; two study performed primary repair using dual suture anchor fixation (15%)[22,32]. It should be noted, that the study assessing mid-term outcomes of ACL repair was excluded here.

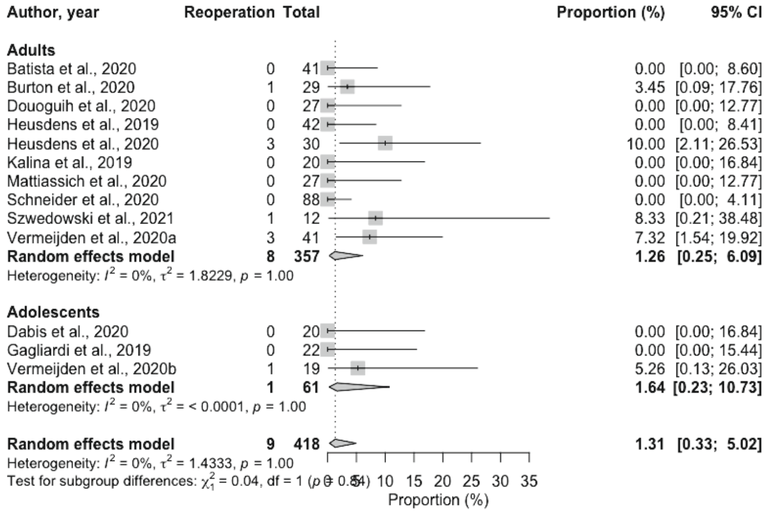
The overall failure was 8% (95% CI 3.9% – 14.4%; Fig. 2), reoperation rate was 1% (95% CI 0.3% – 5.0%; Fig. 3), complication rate was <1% (95% CI 0.1% – 4.4%; Fig. 4), and ROH rate was <1% (95% CI 0.2% – 2.2%; Fig. 5). Objective laxity assessment, either performed using the KT-1000 arthrometer or Rolimeter, showed a mean side-to-side difference of 1.1 ± 2.3 mm in 201 patients. Regarding functional outcomes, the mean Tegner score decreased 0.6 points (95% CI -1.1 – -0.1; Fig. 7) from preinjury to postoperatively, while the Lysholm score was 91 ± 10, the IKDC subjective was 88 ± 13, KOOS was 84 ± 9, SANE was 84 ± 15, Marx activity was 8.4 ± 2.6, and VAS pain score was 0.9 ± 1.5 (Table 3).

Figure 2.



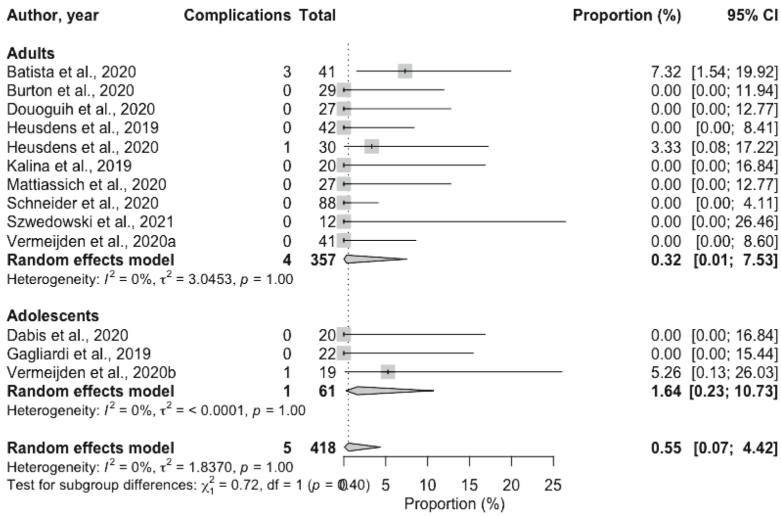
Proportion meta-analysis to estimate the incidence of failures following primary ACL repair with suture augmentation.

Figure 3.



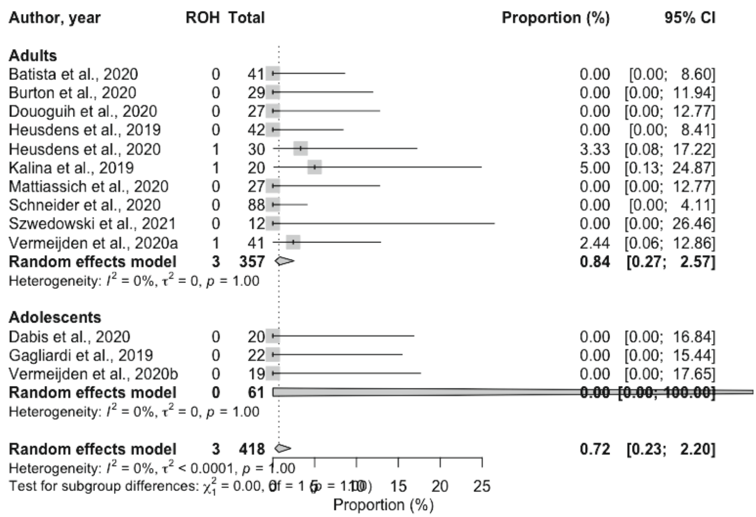
Proportion meta-analysis to estimate the incidence of reoperations following primary ACL repair with suture augmentation.

Figure 4.



Proportion meta-analysis to estimate the incidence of complications following primary ACL repair with suture augmentation.

Figure 5.



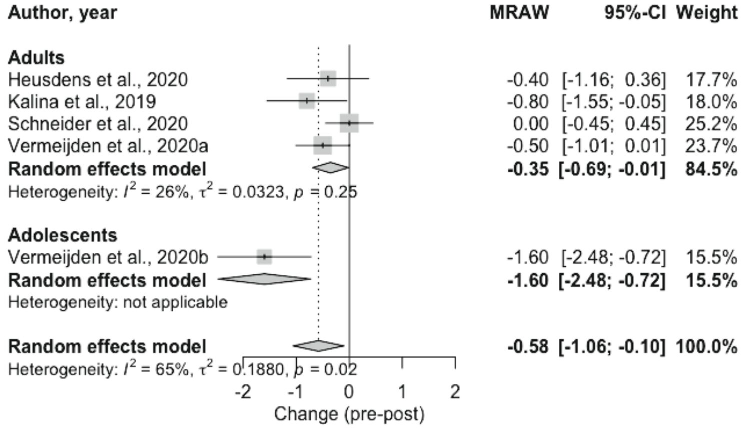
Proportion meta-analysis to estimate the incidence of removal of hardware following primary ACL repair with suture augmentation.

Adult patients

Ten studies assessed the outcomes of adult patients. A total 357 patients were identified with a mean age of 35 ± 11.2 years, mean follow-up of 1.9 years (range 0.4 – 4.5 years), mean surgical delay of 32 days (range 0 – 336 days), and 48% was male gender (Table 2).

The failure rate was 6% (95% CI 3.8% – 8.9%; Fig. 2), reoperation rate was 1% (95% CI 0.3% – 6.1%; Fig. 3), complication rate was <1% (95% CI 0.0% – 7.5%; Fig. 4), and ROH rate was <1% (95% CI 0.3% – 2.6%; Fig. 5). Among 191 patients undergoing objective laxity assessment, mean side-to-side difference was 1.1 ± 2.3 mm. Mean Tegner score decreased 0.4 points (95% CI 0.7 – 0.0; Fig. 6) from preinjury to postoperatively, whereas the Lysholm score was 90 ± 11, the IKDC subjective was 87 ± 11, KOOS was 84 ± 9, SANE was 84 ± 11, Marx activity was 8.4 ± 2.6, and VAS pain score was 1.0 ± 1.6 (Table 3).

Figure 6.



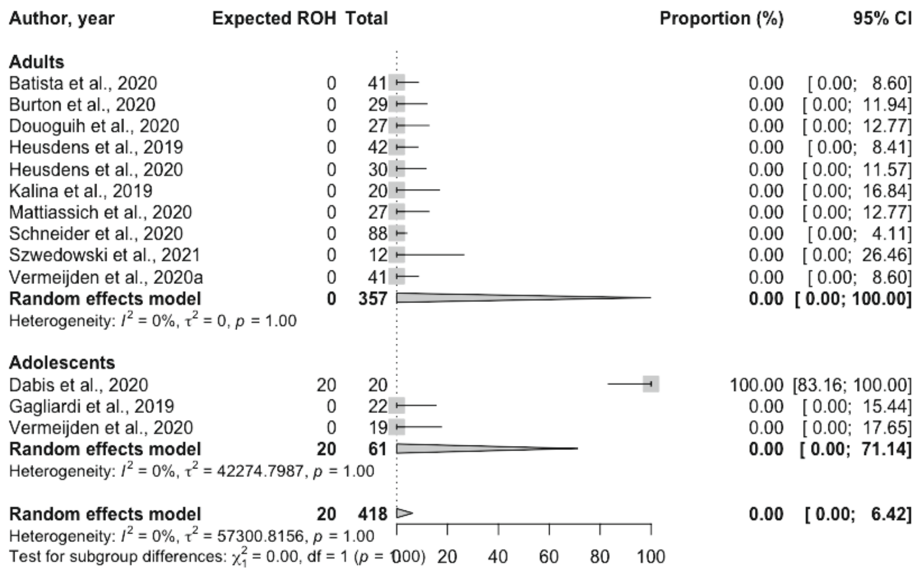
Mean change in pre- and postoperative Tegner scores following primary ACL repair with suture augmentation.

Adolescent patients

Three studies assessed the outcomes of adolescent patients. In total, 61 patients were identified with a mean age of 15 ± 4.0 years, mean follow-up of 2.2 years (range 1.8 – 4.5 years), mean surgical delay of 32 days (range 10 – 78 days), and 39% was male gender (Table 2).

The failure rate was 17% (95% CI 2.5% – 63.9%; Fig. 2), reoperation rate was 2% (95% CI 0.2% – 10.7%; Fig. 3), complication rate was 2% (95% CI 0.2% – 10.7%; Fig. 4), and ROH rate was 0% (95% CI 0.0% – 100%; Fig. 5). The suture augmentation was routinely removed in all patients in one study with 20 patients (Fig. 7). Objective laxity assessment in 20 patients using the KiRA dynamic accelerometer showed a mean side-to-side difference of 1.2 mm. Mean Tegner score decreased 1.6 points (95% CI 0.7 – 0.0; Fig. 6) from preinjury to postoperatively, the Lysholm score was 95 ± 9, the IKDC subjective was 89 ± 21, SANE was 86 ± 27, and VAS pain score was 0.3 ± 0.5 (Table 3).

Figure 7.



Proportion meta-analysis to estimate the incidence of expected removal of hardware following primary ACL repair with suture augmentation.

Mid-term outcomes

One study assessed the mid-term outcomes of 34 patients treated with ACL repair. Mean age of this cohort was 38 ± 15.5 years, mean follow-up was 5.7 years (range 5.0 – 7.4 years), 53% was male gender, and all patients were treated within three months after injury (Table 2).

The failure rate at mid-term follow-up was 18%, the reoperation rate was 9%, the complication rate was 0%, and the ROH rate was 0%. No objective laxity assessment was performed in any of the included patients. Among these patients, the mean Marx activity score was 7.3 ± 5.2, and VAS pain score was 1.0 ± 1.5 (Table 3).

Table 2. Patient characteristics of studies reporting outcomes of arthroscopic primary ACL repair with suture augmentation

Authors	Year	SA device	No. pts	FU (years)		Age (years)		Delay (days)		Male (%)	Prox (%)
				Mn	Range	Mn	SD	Mn	Range		
Adult patients											
Batista et al. [b][32]	2021	Smith & Nephew	41	1.0		27.6	10.0	64	21 – 336	68%	100%
Burton et al.[21]	2020	Arthrex	29	2.8	2.0 – 4.5	32.2	7.2			72%	100%
Douoguih et al.[41]	2020	Arthrex	27	2.8	2.0 – 3.8	27.4	8.6			67%	100%
Heusdens et al.[24]	2019	Arthrex	42	2.0		33.0	14.5		<3mnd[a]	57%	100%
Heusdens et al. [b][25]	2020	Arthrex	30	2.0		31.1	9.1	46	28 – 84	50%	100%
Kalina et al.[43]	2019	Arthrex	20	1.0				28	14 – 42		100%
Mattiassich et al.[29]	2020	Arthrex	27	>1	1.0 – 1.5	35.4	11.8		<6wks[a]	37%	100%
Schneider et al.[10]	2020	Arthrex	88	1.8	1.0 – 3.3	42.0	13.0	1.5	0 – 18	24%	100%
Szwedowski et al.[31]	2021	Arthrex	12	1.2	0.4 – 2.0	35			<2mnd[a]	50%	100%
Vermeijden et al.[b][30]	2020	Arthrex	41	2.4	1.6 – 4.4	35.1	8.5	45[c]	22 – 114	66%	100%
Adolescent patients											
Dabis et al.[22]	2020	Arthrex	20	2.7	2.4 – 4.3	12.9		45	14 – 78	40%	100%
Gagliardi et al.[42]	2019	Arthrex	22	3.2	2.2 – 3.4	13.9	3.2	34	18 – 70	55%	100%
Vermeijden et al. [b][30]	2020	Arthrex	19	2.2	1.8 – 2.6	17.1	4.8	17[c]	10 – 20	21%	100%
Mid-term outcomes											
Hopper et al.[27]	2021	Arthrex	34	5.7	5.0 – 7.4	37.8	15.5		<3mnd[a]	53%	100%
Adult patients			357	1.9	0.4 – 4.5	34.6	11.2	32	0 – 336	48%	100%
Adolescent patients			61	2.2	1.8 – 4.5	14.6	4.0	32	10 – 78	39%	100%
Mid-term outcomes			34	5.7	5.0 – 7.4	37.8	15.5		<3mnd[a]	53%	100%

Table 2. Patient characteristics of studies reporting outcomes of arthroscopic primary ACL repair with suture augmentation *(Continued)*

Authors	Year	SA device	No. pts	FU (years)		Age (years)		Delay (days)		Male (%)	Prox (%)
				Mn	Range	Mn	SD	Mn	Range		
Total[c]			418	2.0	0.4 – 4.5	31.5	10.6	32	0 – 336	49%	100%

SA device indicates suture augmentation device; No. pts. number of patients; FU, follow-up in years; wks, weeks; Mn, mean; prox., percentage of patients with proximal tears; [a] These studies only reported criteria such as operation within certain number of weeks; [b] The authors were contacted for data regarding this study; [c] Totals were only based upon adult and adolescent studies; mid-term outcomes were excluded.

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Table 3. Functional and patient-reported outcomes of studies reporting outcomes of arthroscopic primary ACL repair with suture augmentation

Authors	Year	No. pts	KT-1000	Tegner		Lys-holm	IKDC Subj	KOOS	SANE	Marx	VAS Pain
				Pre	Post						
Adult patients											
Batista et al.[32]	2021	41			9.3±0.6						
Burton et al.[21]	2020	29							78		
Douoguih et al.[41]	2020	27						84±13	83±13	8.6±4.0	1.1±1.8
Heusdens et al.[24]	2019	42						85±3		8.3±1.0	1.3±1.9
Heusdens et al. b,[25]	2020	30	0.8±1.1	6.2±1.9	5.8±2.0	86±10	85±10				
Kalina et al.[43]	2019	20		8.2±1.4	7.4±1.7	91.0±7	89±10				
Mattiassich et al.[29]	2020	27	1.4±1.7			87±11	82±14	83±12			
Schneider et al.[10]	2020	88	1.0±3.0	6.0±2.0	6.0±2.0	92±11	87±11				
Szwedowski et al.[31]	2021	12	1.9±3.5			89					
Vermeijden et al. b,[30]	2020	41	1.9±1.2	6.7±1.4	6.2±1.6	92±11	90±9		89±13		0.6±1.1
Adolescent patients											
Dabis et al.[22]	2020	20	1.2		8.0±3.0				86±27		
Gagliardi et al.[42]	2019	22				97±8	91±10				
Vermeijden et al. b,[30]	2020	19		8.4±1.2	6.8±2.1	93±10	86±29				0.3±0.5
Mid-term outcomes											
Hopper et al.[27]	2021	34								7.3±5.2	1.0±1.5
Adult patients		304	1.3±2.4	6.6±3.0	6.7±1.3	90±11	87±11	84±9	84±11	8.4±2.6	1.0±1.6
Adolescent patients		61	1.2	8.4±1.2	7.2±2.6	95±9	89±21		86±27		0.3±0.5
Mid-term outcomes		34								7.3±5.2	1.0±1.5

Table 3. Functional and patient-reported outcomes of studies reporting outcomes of arthroscopic primary ACL repair with suture augmentation *(Continued)*

Authors	Year	No. pts	KT-1000	Tegner		Lys-holm	IKDC Subj	KOOS	SANE	Marx	VAS Pain
				Pre	Post						
Total*		365	1.3±2.4	6.6±1.8	6.8±1.9	91±10	88±13	84±9	84±15	8.4±2.6	0.9±1.5

No. of pts indicates number of patients; IKDC, International Knee Documentation Committee score; KOOS, Knee injury and Osteoarthritis Outcome Score; SANE, Single Assessment Numeric Evaluation; Marx, Marx Activity Scale; VAS, visual analog score; Mn, mean; SD, standard deviation; Asterisk, totals were only based upon adult and adolescent studies; mid-term outcomes were excluded.

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Discussion

The main finding of this systematic review with meta-analyses was that primary repair with suture augmentations seems to be a reliable and safe treatment option in selected patients with proximal ACL tears at short-term follow-up. In 418 patients treated with this procedure, the overall failure was 8%, while reoperation, complication, and ROH rates were low. Although good functional outcomes were found in all patients, higher failure rates were found in those younger than 18 years, respectively. Furthermore, the failure rate at mid-term follow-up was higher than those at short-term follow-up. Finally, it should be noted the overall level of evidence for ACL repair with suture augmentation was low and that there was a high risk for bias. However, it should also be noted that, in general, reporting on novel procedures tends to be retrospective in nature.

When reviewing the literature regarding primary ACL repair, most recent studies have advocated to augment the repaired ligament using suture tape augmentation. The rationale for augmenting the repair construct is that the suture tape acts as a protective primary stabilizer throughout the early healing phase, which allows for early mobilization.[6] Recent preclinical studies using nonabsorbable high-strength sutures have shown increased strength of the ACL repair construct, thereby reducing peak loads and restricting the gap formation.[33] This may lead to lower failure rates, as Massey et al. found an higher mean load to failure when adding suture augmentation to a repaired ACL (279N to 693N).[34] Furthermore, it has been suggested that ACL repair with suture augmentation might completely restore the native ACL function, while non-augmented repair techniques have shown increased lengthening at low loads.[33] It should be noted, however, that other studies have advocated to augment the repaired ligament with a dynamic intraligamentary stabilization (DIS) technique rather than a static augmentation technique to further improve the clinical outcomes of these procedures.[2]

When reviewing the clinical outcomes, this systematic review with meta-analysis showed low overall failure rates and good to excellent functional outcomes scores. It is difficult to compare these failure rates with failure rates of other repair techniques, as the current literature remains scarce.[2] Nevertheless, a recent systematic review indeed reported lower failure rates following static augmentation as compared to non-augmented repair and dynamic augmented repair (7% vs. 10% vs. 11%).[4] In addition, the overall failure rate in the present study is also lower that the failure rate following non-augmented ACL repair (8% vs. 10%). reported in the above mentioned systematic review.[4] Given these findings, implementation of static augmentation seems safe and might reduce failure rates in patients undergoing ACL repair. Therefore, it could be argued to include suture augmentation on all repairs considering the low reported complication rate although this does not factor in surgical costs. It should be noted, however, that this technique should only be performed in patients with proximal tears, as a systematic review on historical outcomes of open primary repair showed improved outcomes in patients with proximal tears as compared to those with midsubstance tears.[35] Although the failure rate in adult patients was low, it is also important to note that the mean age was relatively high (35 years). Since this procedure is most commonly performed in the slightly older patient population, it is therefore also difficult to directly compare these failure rates with those reported in the ACL reconstruction literature.

When reviewing the outcomes between younger and older patients treated with augmented ACL repair, this study showed higher failure in those patients younger than 18 years (17.4% vs. 6.3%, respectively). Although it is well known that failure rates for ACL reconstruction in young patients are high (up to 15%)[36–38], there is much controversy regarding ACL repair in young athletes. As a result, some authors have suggested to utilize these techniques cautiously in the young patients, as it could be possible that the healed ACL after primary repair might not be strong enough in this patient cohort.[22] Based on the current literature, however, it is difficult to identify the place that primary ACL repair holds in the treatment algorithm in this patient group due to the limited evidence and widely varied failure rates (0% to 41%). Nonetheless, some theoretical advantages of primary ACL repair certainly exist in young patients as growth deficits can be avoided, while potentially reducing the risk of osteoarthritis.[39] Therefore, this study shows that there is a need for more and higher-level evidence studies assessing outcomes in this young patient population.

Although short-term outcomes of ACL repair with suture augmentation seems to be promising, only one study was identified reporting the outcomes at 5-year follow-up.[30] In this study by Hopper et al., the failure rate in 28 patients was 18% at latest follow-up. Although these outcomes are clearly better than historically reported disappointing mid-term outcomes following open ACL repair[1], the reported midterm outcomes are inferior to those reported at short-term follow-up (5% failure rate), especially those reported after dynamic augmentation[40]. Therefore, more studies with extended follow-up are needed to assess if outcomes of primary repair surgery will indeed deteriorate with longer follow-up.

There are limitations to this study. First of all, most included studies were retrospective in nature and were also lacking a control group. Therefore, potential selection and treatment bias could have influenced the outcomes in each included study. In addition, although the literature search was conducted carefully by two independent reviewers, there is always an increased risk for selection bias. Thirdly, since suture tape augmentation is a relatively new procedure in the treatment of ACL injuries, the overall number of included patients was low. As a result, no correction for potential confounders other than age, such as timing of surgery, concomitant injuries or gender could be performed. Finally, the mean follow-up was relatively short (2.0 years, range 0.4 – 4.5 years), and more patients need to be follow-up until at least the mid-term. Nevertheless, based on the present findings, we recommend clinicians to perform primary ACL repair in selected patients with acute proximal ACL tears.

Conclusion

Current literature shows that primary repair with suture augmentation is a reliable and safe treatment option for proximal ACL tears with a failure rate of 8% and good functional outcome scores at short-term follow-up. Although patient-reported outcomes were good irrespective of age, failure rates were higher in young patients (17% vs. 6%, respectively). There is a need for high-quality comparative studies with large group of patients to assess the outcomes with ACL reconstruction.

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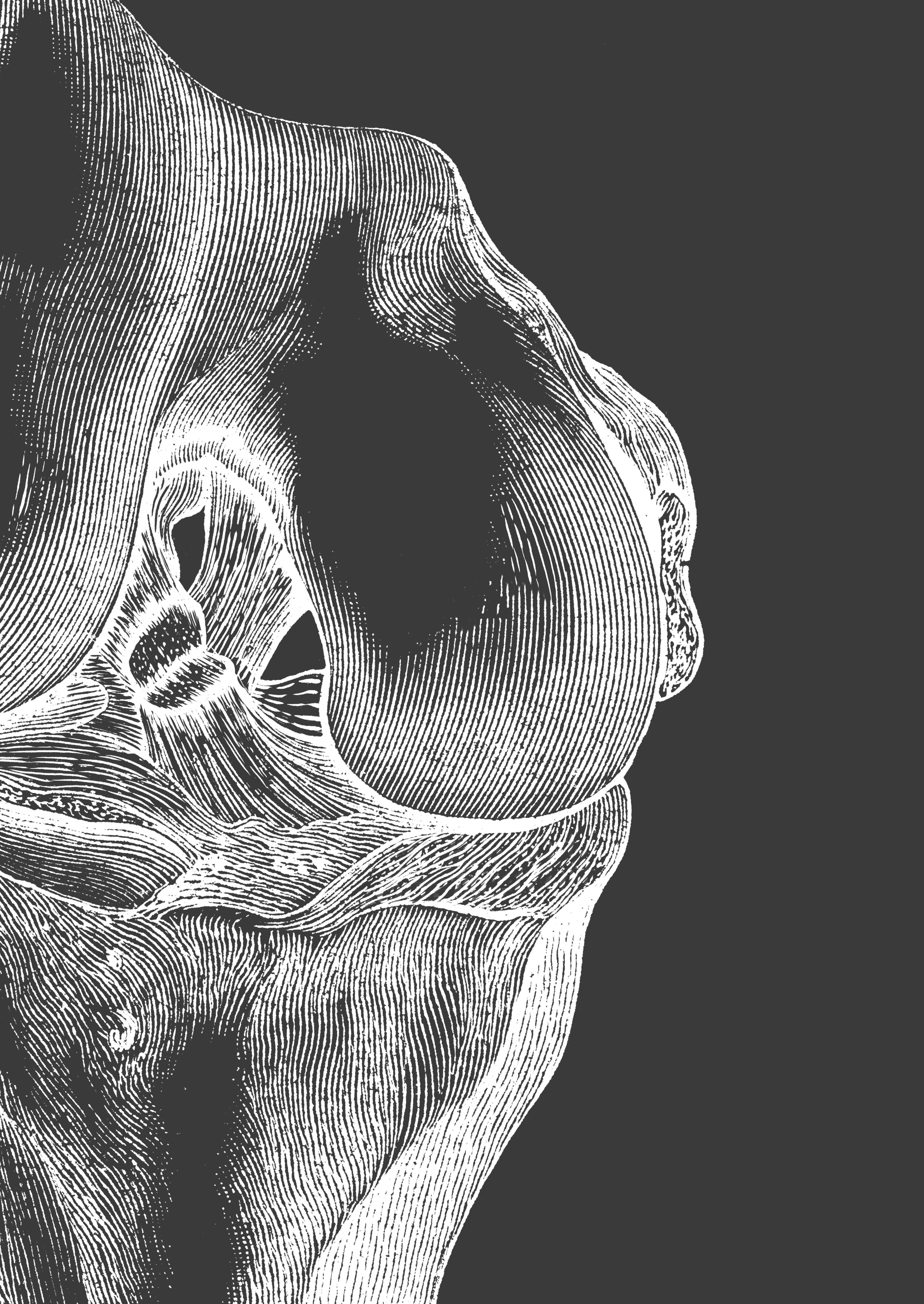

Chapter 8

Role of age on success of arthroscopic primary repair of proximal anterior cruciate ligament tears

Vermeijden HD, van der List JP, DiFelice GS

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Abstract

Purpose

To assess failure rates and patient-reported outcomes measures (PROMs) following arthroscopic primary ACL repair of proximal tears in different age groups.

Methods

Between 2008 and 2017, the first 113 consecutive patients treated with repair were retrospectively reviewed at minimum of 2-years. Patients were stratified into three age groups: ≤21, 22–35, and >35 years. Primary outcomes were ipsilateral reinjury or reoperation, and contralateral injury rates, and secondary outcomes consisted of Lysholm, modified Cincinnati, Single Assessment Numeric Evaluation (SANE), International Knee Documentation Committee (IKDC) subjective, pain, and satisfaction scores. Group differences were compared using chi-square tests and Mann-Whitney U tests.

Results

Follow-up was obtained in 113 patients (100%). Median age was 35 years (IQR 23–43) and median follow-up was 2.2 years (IQR 2.0–2.8). Overall, ACL reinjury occurred in 13 patients (11.5%), reoperation in seven patients (6.2%), complications in two patients (1.8%) and contralateral ACL injury in four patients (3.5%). Overall, median Lysholm was 95 (IQR 89–100) and IKDC subjective 92 (IQR 84–99).

Treatment failure was significantly higher in the youngest age group (37.0%) as compared to the middle and older groups (4.2% and 3.2%, both $p<0.005$). No significant differences were seen in reoperation, complication, or contralateral injury rates between groups (all $p>0.2$), nor in PROMs between the groups (all $p>0.1$).

Conclusion

The failure rate of primary repair of proximal ACL tears is high in patients aged 21 or younger (37.0%), and this should be taken into account when discussing repair in this patient group. In patients older than 21, repair may be an excellent treatment with low failure (3.5%) and complication rates (1.2%) and good subjective scores.

Introduction

Anterior cruciate ligament (ACL) reconstruction has been the gold standard for surgical management of ACL injuries for the last three decades.[1] Although this technique is reliable in restoring knee stability and has acceptable failure rates between 3% and 7%,[2–4] a subset of patients complain of donor-site morbidity,[5] there are proprioceptive deficits,[6] and not all patients return to their pre-injury sports level.[7] As a result of these disadvantages, researchers have continued to seek for other options in the treatment algorithm for ACL injuries.

One of these options has been selective arthroscopic primary repair for patients with proximal ACL tears.[8] Historically, the reported outcomes of open ACL repair were rather disappointing with high failure rates at longer follow-up,[9] but recent studies have focused on improving patient selection by only performing primary repair for proximal tears,[10] as there is better vascularity at the proximal end of the ligament and subsequently better healing capacity when compared to that of midsubstance tears.[11,12] An important reason for the renewed attention paid to primary repair is the potential benefit of the surgery as the native ligament is preserved along with its proprioceptive function, and donor-site morbidity can be avoided.[13–15]

Recent meta-analyses reported that primary repair is a safe procedure with overall acceptable failure rates in adult patients, but also identified that the current studies are small cohort studies with limited level of evidence.[8,16] Furthermore, a recent study by Gagliardi et al. reported a high failure rate following primary repair in adolescent patients, but these findings have not been confirmed in other cohorts.[17,18]

The purpose of this study was therefore to assess failure rates and patient-reported outcomes measures (PROMs) following arthroscopic primary ACL repair of proximal tears in different age groups. We hypothesized that failure rates in patients 21 years and younger would be higher when compared to patients older than 21 years, while subjective outcomes would be good regardless of age following surgical repair.

Materials and methods

Patient selection

This study is an expansion of a previously reported cohort of patients (n = 56).[19] Following Institutional Review Board approval (IRB number: 2017-0404-CR2), a retrospective case series study was conducted between April 2008 and September 2017. All included patients underwent arthroscopic primary repair for proximal complete isolated ACL injuries (no partial tears and no injury of additional ligaments). The same surgical intra-operative treatment algorithm was applied to all patients with ACL injuries where patients with good tissue quality (i.e. sufficient tissue quality to withhold intrasubstance suturing and re-tensioning towards the femoral footprint) and proximal tears (i.e. sufficient tissue length for re-tensioning towards the anatomical footprint of the ACL with a visual gap of less than 1 mm using a grasper) were treated with primary repair, while standard reconstruction was performed in cases involving non-repairable tears (i.e. midsubstance tears or ligaments with poor tissue quality). During this period, 339 patients were surgically treated for ACL tears and all surgical procedures were performed by the senior author (GSD). Patients were considered for inclusion if a minimum of two-year follow-up was present and were excluded when treated with ACL reconstruction (n = 127), treated with augmented repair (n = 48), treated for multiligamentous injuries (defined as an injury of ≥ 2 knee ligaments; n = 46), and when treated with primary repair for distal tears (n = 5). One hundred-thirteen patients (39% of all patients) had a proximal tear with sufficient tissue quality and underwent primary ACL repair and were followed for a minimum of two years. To determine clinical outcomes between different age groups, all patients were subdivided into three groups based upon age at time of surgery: 21 years and younger, between 22 and 35, and older than 35 years. These age groups were determined based upon a preliminary analysis that showed high failure rates in patients aged 21 years and younger, which was confirmed using receiver operating curve analysis (ROC; see results section), and on a recent study which showed a higher incidence of proximal ACL tears in patients older than 35 years.[20]

Surgical technique

The procedure of primary arthroscopic ACL repair using dual suture anchor fixation was performed as previously described.[21] In brief, both bundles were first sutured individually from distal to proximal in a horizontal Bunnell-type suture pattern using a Scorpion suture passer (Arthrex, Naples, FL). Each bundle was then reapproximated to its femoral footprint using a 4.75-mm BioComposite SwiveLock suture anchor (Arthrex). It should be noted that in the more recent patients, an internal suture augmentation, consisting of an InternalBrace (Arthrex, Naples, FL), became clinically available and was, in the early stage, added in the majority of cases, especially in those patients with higher risk for re-injury (i.e. younger patients, patients with visually assessed valgus alignment, suboptimal tissue quality, and/or patients performing sports at high activity levels). Currently, and for the past several years, ACL repair with suture augmentation is the standard of care in all of our patients. Following the same technique of suturing the ligament, the AM suture anchor is preloaded with an internal suture tape augmentation. After the anchor is deployed in the femoral cortex, the suture tape augmentation is channeled through a small 2.5 mm tunnel, which is drilled from the anteromedial cortex of the tibia to the anterior side of the tibial footprint. The suture augmentation is tensioned in full extension and then fixed using a single suture anchor that is placed into the anteromedial cortex of the tibia.[14]

Post-operative management

All patients followed similar postoperative rehabilitation protocols focusing on early mobilization combined with a knee-brace worn for the first four weeks. Within the first days following surgery, passive ROM exercises and swelling control are initiated. At four weeks, physical therapy is continued as per guidance of their own sports' physical therapist but focused on milestones rather than timing. Return to pivoting sports is allowed six to twelve months postoperatively when ROM and muscle strength are sufficient (≥ 90% isokinetic strength).

Data collection

All patients were closely followed and seen in clinic at one week, one-, three-, and six months, and one- and two-, and five years postoperatively. Patients underwent physical examination in clinic performed by the clinical team of the senior author (GSD), and were asked to complete outcomes surveys to assess patient-reported outcomes. If patients did not follow-up in clinic they were contacted to assess if failure of treatment (symptomatic instability, re-injury, or revision surgery) had occurred and were also asked to complete the set of questionnaires.

Outcomes

The primary outcome measure was clinical failure, which was defined as objective laxity (i.e. side-to-side difference ≥3 mm, grade ≥2 Lachman, and/or grade ≥2 pivot shift test), or symptomatic subjective feeling of instability. Recently, patients have been tested using either KT-1000 measurements (MEDmetric Corp, San Diego, CA, USA), or Rolimeter arthrometer (Aircast, Germany). In case of suspected failure, MRI was performed to confirm re-rupturing of the ACL. Furthermore, reoperation rates were assessed, which were defined as any surgical intervention besides revision surgery (e.g. meniscus injury). Additionally, complications other than failure or reoperations, and contralateral injuries were assessed.

Secondary outcomes were PROMs. Therefore, Lysholm Knee Score[22], modified Cincinnati Score[23], Single Assessment Numeric Evaluation (SANE)[24], Subjective International Knee Documentation Committee (IKDC)[25], Tegner Activity Level[22], pain (using a visual analog scale ranging from 'no pain' to 'unbearable pain' from 0 to 10)[26], and satisfaction scores, which were assessed on a Likert-scale (very satisfied – satisfied – neutral – unsatisfied – very unsatisfied) were collected as well. Satisfaction scores were reported as the percentage of satisfied patients.

Statistical analysis

SPSS Version 25 (SPSS Inc., Armonk, NY) was used for all statistical analysis. Data was tested for normal distribution using Shapiro-Wilk tests. As data was not normally distributed, continuous variables were presented as median with interquartile ranges (IQR), and nominal variables were presented as number (n) with percentage (%). The Kruskal-Wallis one-way ANOVA was used to compare multiple groups with continuous variables and the Mann-Whitney U test was used to compare two groups of continuous variables, while Chi-square tests or Fisher exact tests (in case one of the numbers is < 5) were used to compare nominal data between groups. Bonferroni correction was used to adjust for multiple pairwise comparisons. ROC analysis was performed to assess or confirm the optimal age cutoff for high vs. low failure rates. Significance of statistical differences was attributed to p-value of < 0.05.

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Results

Patient demographics

Follow-up was available for all 113 consecutive patients (100% follow-up), of which 78% were seen in clinic and 22% completed online questionnaires and assessment of failure by telephone (Table 1). Overall, median age was 35 years (mean 34 years; interquartile range (IQR) 23 – 43 years), 55% were male, median time from injury to surgery was 38 days (IQR 18 days – 92 days), and median follow-up was 2.2 years (IQR 2.0 – 2.8 years). Fifty-one patients (45.1%) had meniscal injury, and 28 (24.7%) chondral injuries. The most frequent trauma mechanism was skiing (20.4%), followed by soccer (16.8%), and basketball (10.6%). In 60 patients (53.1%), a suture augmentation was added to the repair. Baseline information is shown in Table 2.

There were 27 patients in the youngest group (24%), 24 patients in the middle group (21%), and 61 patients in the oldest group (54%). Patients in the youngest group were more often female compared to older patients (youngest: 70.1% vs. middle: 45.8% vs. oldest: 33.9%, p = 0.006), and had a lower BMI compared to the oldest group (23.4 vs. 25.6, p = 0.003). The oldest patients had lower preinjury Tegner score compared to younger patients (oldest:

median 6 vs. middle: 7 vs. youngest: 9, $p < 0.001$), while a higher incidence of chondral injury was found in the oldest group (oldest: 41.9% vs. middle: 3.7% vs. youngest: 4.2%, $p < 0.001$). Suture augmentation was significantly more frequently added to the repair in the youngest and middle patient group as compared to the oldest group (youngest: 77.8%, vs. middle: 62.5%, vs. oldest: 38.7%, $p = 0.002$). There were no differences in time from injury to surgery, follow-up time, or meniscal injury between all three age groups (all $p > 0.05$; Table 2).

Table 1. Clinical evaluation methods used for all patients*

	All patients (n = 113)
In-person evaluation	88 (77.9%)
Online + telephone evaluation	18 (15.9%)
Telephone evaluation	7 (6.2%)
PROMs	89 (78.8%)
Laxity assessment	16 (14.2%)

Asterisk indicated reported in number (%); PROMs, patient-reported outcomes measurements.

Table 2. Patient demographics following primary ACL repair in all patients and the different age-subgroups

	All patients (n = 113)	≤ 21 years (n = 27)	22 - 35 years (n = 24)	≥ 35 years (n = 62)	P-value
Age (years); median (IQR)	35 (23 – 43)	16 (16 – 18)	28 (26 – 31)	42 (38 – 49)	<0.001
Male gender; n (%)	62 (54.9%)	8 (29.6%)	13 (54.2%)	41 (66.1%)	0.006
Delay (days injury-surgery); median (IQR)	38 (18 – 93)	20 (14 – 82)	39 (25 – 96)	40 (18 – 92)	0.216
BMI (kg/m^2); median (IQR)	24.4 (22.8 – 28.3)	23.4 (19.8 – 24.8)	24.2 (22.3 – 27.4)	25.6 (23.4 – 27.7)	0.004
FU (years); median (IQR)	2.2 (2.0 – 2.8)	2.1 (1.9 – 2.7)	2.4 (2.1 – 3.3)	2.2 (2.0 – 2.6)	0.254
Preinjury Tegner score; median (IQR)	6 (6 – 8)	9 (6.5 – 9)	7 (6 – 9)	6 (5 – 7)	<0.001
Meniscal injury	51 (45.1%)	14 (51.9%)	11 (45.8%)	26 (41.9%)	0.686
Medial meniscus; n (%)	25 (22.1%)	8 (29.6%)	4 (16.7%)	13 (21.0%)	0.510
Lateral meniscus; n (%)	38 (33.6%)	9 (33.3%)	10 (41.7%)	19 (30.6%)	0.624
Meniscal treatment					
Repair; n (%)	10 (8.8%)	3 (11.1%)	3 (12.5%)	4 (6.5%)	0.068
Meniscectomy; n (%)	26 (25.7%)	4 (14.8%)	6 (25.0%)	19 (30.6%)	
Repair + meniscectomy; n (%)	5 (4.4%)	2 (7.4%)	2 (8.3%)	1 (1.6%)	
Conservative; n (%)	7 (6.2%)	5 (18.5%)	0 (0.0%)	2 (3.2%)	
Chondral injury; n (%)	28 (24.8%)	1 (3.7%)	1 (4.2%)	26 (41.9%)	<0.001
Chondral treatment					
Chondroplasty; n (%)	26 (23.0%)	1 (3.7%)	1 (4.2%)	24 (38.7%)	0.001
Conservative; n (%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	2 (3.2%)	
ACL repair + SA; n (%)	60 (53.1%)	21 (77.8%)	15 (62.5%)	24 (38.7%)	0.002

SD, standard deviation; N, number of patients; BMI, body mass index; FU, follow-up; SA, suture augmentation.

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Failures

At latest follow-up, 13 (11.5%) failures occurred at a median time after surgery of 1.1 years (IQR 0.8 – 1.7 years). No statistically significant difference in failure rate was found between patients treated with suture augmentation as compared to those patients without suture augmentation (13.3% vs. 9.4%, p = 0.517; Table 4). Eleven re-injuries (84.6%) were traumatic, while two (15.4%) were atraumatic. Of these 13 patients, nine patients underwent uncomplicated reconstructive surgery similar to primary reconstruction. Of the remaining patients, two patients were treated conservatively, and two are scheduled for revision surgery.

Table 3. Outcomes among different age groups following arthroscopic primary ACL repair*

	All patients (n = 113)	≤ 21 years (n = 27)	22 - 35 year (n = 24)	≥ 35 years (n = 62)	P-value
Failure	13 (11.5%)	10 (37.0%)	1 (4.2%)	2 (3.2%)	<0.001
Reoperation	7 (6.2%)	2 (7.4%)	3 (12.5%)	2 (3.2%)	0.260
Complication	2 (1.8%)	1 (3.7%)	0 (0.0%)	1 (1.6%)	0.600
Contralateral failure	4 (3.5%)	2 (7.4%)	1 (4.2%)	1 (1.6%)	0.390

Asterisk indicated reported in number (%)

Risk of subsequent re-injury was significantly higher for the youngest group (37.0%) as compared to the middle and oldest (4.2%, p = 0.004 and 3.2%, p < 0.001, respectively). Failure rates were significantly higher in patients younger than 18 years as compared to those older than 18 years (38.1% versus 5.4%, p < 0.001). Using ROC analysis, age of 21 years was confirmed as the threshold for high versus low failure rates with an area under the curve of 0.830 (95% CI, 0.719 – 0.942) with a sensitivity 0.769 and specificity of 0.850. In the youngest group, no difference was noted in failure rates between patients treated with and without suture augmentation (38.1% versus 33.3%, p > 0.999).

Table 4. Failure rates between patients with and without suture augmentation stratified per age group*

	ACL repair	ACL repair + SA	P-value
≤ 21 years	2 / 6 (33.3%)	8 / 21 (38.1%)	>0.999
22 - 35 years	1 / 9 (11.1%)	0 / 15 (0.0%)	0.375
≥ 35 years	2 / 38 (5.3%)	0 / 24 (0.0%)	0.518

Asterisk indicated reported in number (%); SA, suture augmentation

Reoperation, complication and contralateral failures

No significant differences were seen in reoperation, complication, or contralateral failure rate between all groups (all p > 0.05; Table 2). Regarding reoperations, in two patients (18 and 32 years of age) the tibial suture anchor was removed due to irritation, one patient underwent chondroplasty (35 years of age), and four patients had secondary meniscus lesions of which three underwent partial meniscectomy (21, 29, and 41 years of age) and one meniscal repair (25 years of age).

Concerning complications, one patient (aged 18 years) experienced hyperesthesia of the leg following a nerve block complication, while in another patient (35 years of age) the tip of the self-retrieving suture passer broke off during surgery and was lost within the ligament fibers. Both cases were successfully treated non-operatively. No infections or arthrofibrosis were reported.

Regarding contralateral injuries, four patients (3.5%) sustained a contralateral injury at a median follow-up of 1.3 years. Of those, two patients were aged 16 years, one 32 years, and one 38 years at time of secondary injury.

Clinical assessment

At median follow-up of 2.3 years (range 1.6 – 10.4 years; IQR 2.1 – 3.2 years), in all patients without re-injuries and that returned for clinical follow-up full ROM was achieved (n = 75), and no extension deficits were noted. Of these patients, 63 patients (84.0%) had negative Lachman examination while 12 (16.0) had a grade 1 with firm endpoint (1A). Additionally, 65 patients (86.7%) had negative pivot shift test, whereas 10 (13.3%) had a grade 1 finding. Laxity assessment was available in 16 patients seen in clinic, of which one sustained a traumatic re-injury and had a side-to-side difference of 6 mm. Median side-to-side difference in the 15 patients without failure was 1.2 mm (IQR 1.0 – 2.4 mm) with no patients showing a difference of >3 mm.

Patient-reported outcomes measures

In 89 patients without failures and who completed outcomes surveys (79%), median patient-reported outcomes were a Lysholm of 95 (IQR 89 – 100), modified Cincinnati 96 (IQR 88 – 100), SANE 90 (IQR 85 – 99), subjective IKDC 92 (IQR 84 – 99), pain score 0 (IQR 0 – 1), and 91% of patients were very satisfied or satisfied with their repaired ACL. No significant differences were found in any of the PROMs between groups (all p > 0.05) (Table 5).

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Table 5. Patient-reported outcomes among different age groups following arthroscopic primary ACL repair*

	All patients (n = 89)	≤ 21 years (n = 16)	22 - 35 years (n = 18)	≥ 35 years (n = 55)	P-value
Lysholm; median (IQR)	95 (89 – 100)	100 (91 – 100)	95 (82 – 100)	95 (90 – 100)	0.422
Modified Cincinnati; median (IQR)	96 (88 – 100)	100 (96 – 100)	99 (86 – 100)	92 (88 – 100)	0.119
SANE; median (IQR)	90 (85 – 99)	95 (90 – 100)	90 (75 – 95)	90 (85 – 99)	0.122
Subjective IKDC; median (IQR)	92 (84 – 99)	98 (89 – 100)	94 (82 – 99)	92 (82 – 99)	0.359
Pain score; median (IQR)	0 (0 – 1)[a]	0 (0 – 1)[b]	1 (0 – 2)[c]	0 (0 – 1)[d]	0.188
Satisfied; n (%)	69 (91%)[e]	15 (94%)	13 (92%)[f]	41 (91%)[g]	0.787

* PROMs of those patients without revision surgery or completed surgical evaluation before re-injury; SANE, Single Assessment Numeric Evaluation; IKDC, International Knee Documentation Committee; [a] Reported in 68 patients; [b] Reported in 13 patients; [c] Reported in 15 patients; [d] Reported in 45 patients; [e] Reported in 75 patients; [f] Reported in 15 patients; [g] Reported in 45 patients.

Discussion

The main finding of this study was that the failure rate of selective arthroscopic primary ACL repair in patients 21 years and younger was significantly higher (37.0%) as compared to patients older than 21 years (3.5%). Furthermore, it was noted that patient-reported outcomes measures were good regardless of age with excellent scores in all groups. Low complication rates were also noted following the procedure in all age groups with high patient satisfaction among those patients without failure (91%).

An overall failure rate of 11.5% was found in patients treated with primary repair, which is similar to failure rates found in the literature.[16] In addition, no statistical difference was noted in failure rates in patients treated with and without suture augmentation (13.3% vs. 9.4%), although it is important to note that high-risk patients were more frequently treated with these augmented repairs. When comparing age groups, the risk of re-injury was significantly higher in patients 21 years and younger as compared to patients older than 21 years of age. Interestingly, the additional suture augmentation did not decrease the failure rate in this high-risk patient group (38.1% versus 33.3%). Although it is known from ACL reconstruction literature that failure rates in young patients are high (up to 28%),[3,27–29] there are certainly other factors contributing to this finding. First of all, it is possible that the repaired ACL might not be strong enough in this highly demanding patient cohort. Another factor may be that some patients may have returned to sports too-early since rehabilitation protocols for ACL repair have not yet been established.[30] As younger patients are more likely to have greater exposure to high-risk for ACL (re)injury activities, a shorter rehabilitation timeline has been shown to result in higher failure rates, especially in this age group with ACL reconstruction.[31] Furthermore, it might be possible that due to less knee joint awareness (more 'normal' feeling of the knee), as indicated by higher Forgotten Joint Scores,[32] young patients felt fine about their knee quite early after surgery, and some returned to sports prior to 6 months after surgery on their own initiative. Certainly, as with ACL reconstruction failure rates in this younger cohort, the etiology of the higher failure rates with ACL repair is likely to be multifactorial.

Previously published studies in younger patients have shown contradictory results following primary repair. Recently, Dabis et al. reported 0% failures in their cohort of 20 patients aged 12.9 treated with primary repair with internal bracing at two years follow-up.[18] Furthermore, objective laxity assessment in their study did not show any significant side-to-side difference. Gagliardi et al., on the other hand, noted that 13 of 22 patients (41%) failed following primary repair compared to 6 of 151 (4%) patients following ACL reconstruction using quadriceps tendon grafts.[17] When looking closely at these results, it is notable that a different technique was used with only a single repair suture placed and fixed proximally on the femoral cortex, while a separate femoral tunnel was used for the suture augmentation. At the current time, it is difficult to differentiate between the best application of ACL repair in the younger age groups as there is simply a limited amount of series from which to draw conclusions. Based on the current series, we recommend that practitioners utilize these techniques cautiously in the younger age groups.

Over the last decade, large cohort and ACL registry studies that are focused on ACL reconstruction have consistently shown that higher failure rates occur in younger patients.[3,27–29] It seems, however, that the failure rates of primary repair in these patients may be higher as compared to ACL reconstruction. Despite this higher risk of failure, there are certainly potential advantages of primary repair over reconstruction in selected patients. There are several (potential) advantages of repairing a torn ACL. With primary repair, the ligament is preserved, no grafts are harvested, thereby avoiding graft-site morbidity and allowing a more rapid clinical recovery. In addition, it has been suggested that ROM returns earlier following repair compared to reconstruction.[13] Finally, in a previous study by our group we suggested that patients undergoing primary repair had less knee joint awareness compared to those treated with reconstruction.[32]

On the contrary, primary repair also has some disadvantages, since the majority of ligaments can only be repaired in the (sub)acute setting. Therefore, with acute surgery some patients may undergo unnecessary surgery, as there is a subset of (particularly older) patients that could potentially be treated conservatively and simply adjust their activity level and undergo physical therapy rather than requiring ACL reconstruction.[33–35] Additionally, in case of failure of the repair, which is higher in younger patients, patients undergoing revision surgery have to undergo a second rehabilitation program, while there is also increased risk for concomitant cartilage and meniscal damage during re-injury. Therefore, the potential benefits of primary repair should be weighed critically against the risks, especially in the younger patient population.

In patients aged 22 – 35 years, the failure rate was low (4.2%), and similar findings have been reported in previous ACL reconstruction studies.[36] In the literature, the highest prevalence of primary ACL tears is reported between ages 17 and 35 years (65%), with 32.2% of injuries between ages 26 and 35 years.[36] Given the low failure rates and satisfying subjective PROMs, primary repair may therefore be a good treatment option in this patient group.

The majority of patients undergoing repair were older than 35 years of age (55%). In this group, all patients desired to return to their usual sports activities and were given both conservative and surgical treatment options (physical therapy versus repair versus reconstruction). Before surgery, all patients consented for both surgical procedures in which an intraoperative decision, based upon tear type and tissue quality, was made to determine the ultimate treatment. When reviewing the failure rates in this group, failure rates were low (3.2%) and consistent with reconstruction literature.[37,38] In recent years, excellent outcomes of ACL reconstruction in older patients have been reported.[38–40] As recreational athletes older than 35 years of age are increasingly participating in physically demanding and knee-strenuous sports, primary repair may be an excellent treatment option in this age group given the minimally invasive nature of the surgery, although comparative studies with ACL reconstruction need to be performed.

When looking at subjective outcomes, this study showed good to excellent overall PROMs. This is consistent with data from the aforementioned systematic review with meta-analysis on primary repair outcomes, that showed mean Lysholm score of 94±8, modified Cincinnati of 93±12, subjective IKDC of 91±9, and SANE of 90±13 in 1101 patients.[16] When stratified by age, no significant differences in PROMs between age groups were found in the present study in those patients without failure. Few studies have evaluated patient-reported outcomes of primary repair in younger patients; Dabis et al. showed similar good patient-reported outcomes scores.[18] Given these findings, good subjective outcomes following primary repair may be expected in all patients, although longer follow-up studies are needed.

This study assessed the failure rate and patient-reported outcomes of primary repair, and recently we have begun obtaining objective stability tests on all patients. Despite some controversy in the literature as to the best method of laxity assessment, laxity assessment remains undoubtedly important to assess and compare clinical outcomes following ACL surgery. Although measurements were only performed in a small subset of patients in this study, the objective stability testing revealed small side-to-side differences in those patients without failures. Finally, it should be noted that other repair studies have shown similar KT-1000 results at two-year follow-up.[18,41–43]

Limitations

There are limitations to this study. First of all, other differences in baseline characteristics besides age were noted, which could have influenced the outcomes between groups. Secondly, unequal group sizes were present in this study which could have influenced the outcomes. Thirdly, only a small subset of patients had objective stability testing, and more patients need to undergo these measurements. Furthermore, no preinjury PROM's were available and, therefore, no proportion of patients exceeding the MCID could be determined. In addition, although no differences in clinical outcomes were found between those patients treated with or without suture augmentation, the different surgical techniques may have influenced outcomes in this study. Moreover, assessment of tissue quality and tissue length are by definition surgeon dependent and difficult to objectify. Finally, follow-up was relatively short (median 2.2, IQR 2.0 – 2.8 years), and these patients are being be followed up to mid-term (minimum 5 years) follow-up in order to assess if deterioration of outcomes occurs in this larger group, as was historically reported for open repairs.[9]

Conclusion

The failure rate of primary repair of proximal ACL tears is high in patients aged 21 or younger (37.0%), and this should be taken into account when discussing repair in this patient group. In patients older than 21, repair may be an excellent treatment with low failure (3.5%) and complication rates (1.2%) and good subjective scores.

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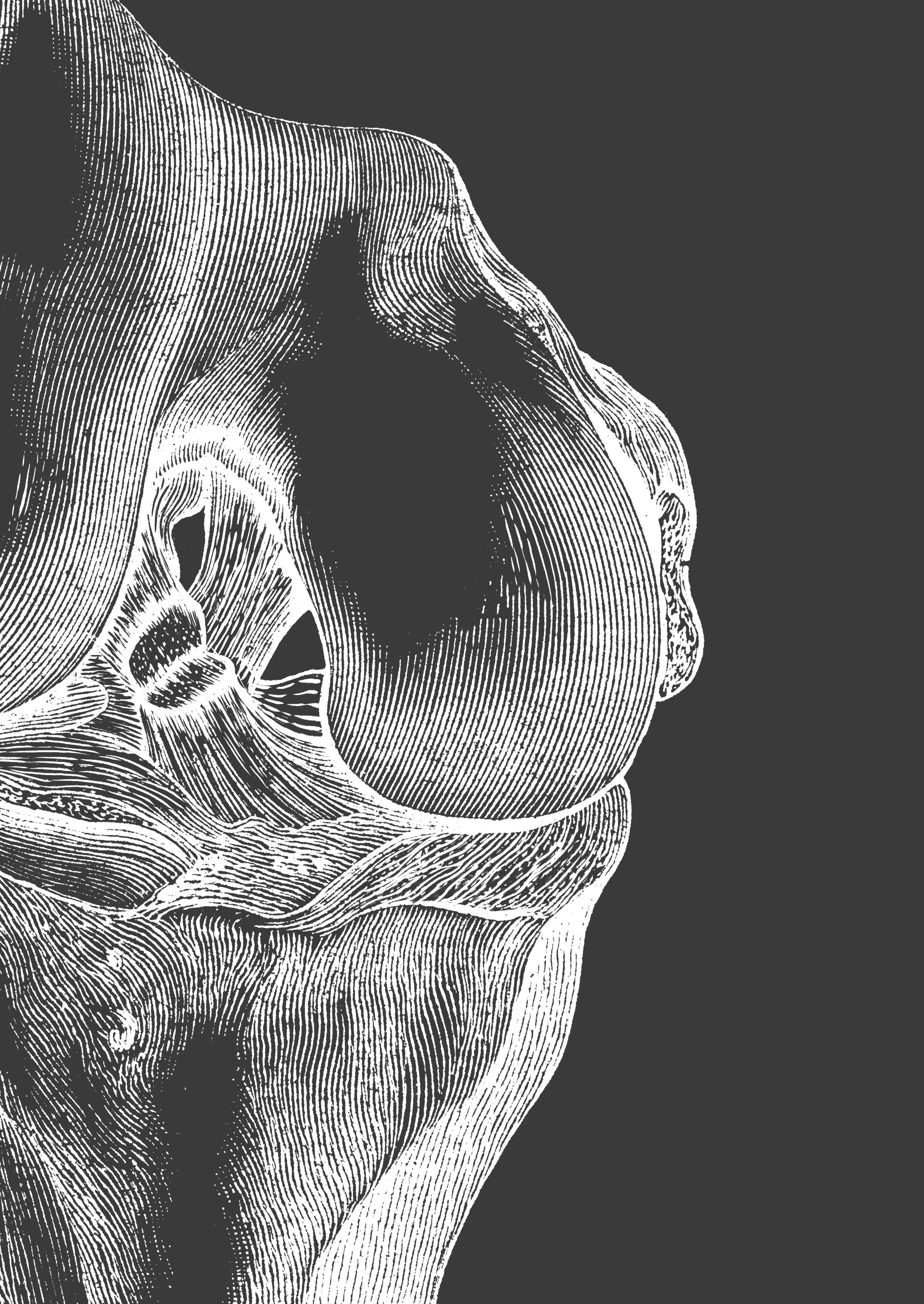


Chapter 9

Return to sports following arthroscopic primary repair of the anterior cruciate ligament in the adult population

Vermeijden HD, van der List JP, O'Brien R, DiFelice GS

Knee. 2020 Jun;27(3):906-914

Abstract

Purpose
To assess return to sport (RTS) rates and evaluate the timeline of rehabilitation milestones following arthroscopic primary anterior cruciate ligament (ACL) repair.

Methods
A retrospective review of all patients treated with primary repair between 2008 and 2018 was conducted. All adult patients with preoperative Tegner of ≥6 and minimum follow-up of 2-years were included. Patients were seen in clinic or contacted to complete the postoperative Tegner, and report their time to return to work, time to running, and time to RTS. Additionally, they were asked to complete the ACL-Return to Sport After Injury (ACL-RSI). Outcomes were compared using Mann-Whitney U tests and chi-square tests.

Results
Sixty patients treated with repair were included, of which 85% returned to any sports, 70% returned to knee-strenuous sports, and 60% returned to preinjury level. Patients returned to work in 7 days (IQR 5–14 days), running in 90 days (IQR 57–120 days), and sports in 180 days (IQR 116–270 days). Overall, ACL-RSI score was 80.0 (IQR 53.0–95.0). Higher return to preinjury rates was found in patients with older age and lower fear of reinjury (all $p<0.05$).

Conclusion
Following primary ACL repair, 70% of adult patients returned to knee-strenuous sports and 60% to preinjury levels by 180 days postoperatively. Positive predictors for return to preinjury levels included older age and low fear of reinjury.

Introduction

Anterior cruciate ligament (ACL) injuries are commonly sustained during sports activities[1,2], and ability to return to sport (RTS) is considered an important indication for operative treatment.[3] In young and active patients, the current surgical standard for these injuries is reconstruction of the ligament to restore knee stability thereby facilitating return to play.[4] Over the last decade, several studies have reported good outcomes following ACL reconstruction with acceptable rates of sports participation, especially in competitive athletes.[1]

Successful RTS is thought to be an important indicator of success after ACL surgery.[5,6] Although the majority of patients are cleared for sports between 6 and 12 months postoperatively, between 35% and 45% of patients do not return to their pre-injury sports level.[5,7] Over the years, multiple factors have been identified to be associated with ability to RTS.[8] Due to recent increased interest on psychological factors, there has been enhanced focus on how they may influence successful RTS, as higher levels of psychological readiness are associated with RTS.[9]

Over the last decade, there has been a resurgence of interest in primary repair of proximal ACL tears[10,11], due to the tissue preserving nature of the surgery, and elimination of potential donor site complications[12]. Therefore, the surgery is considered less invasive, and in at least one series, full range of motion (ROM) was noted to return earlier compared to reconstruction [13]. Acceptable failure rates (average 11%) with good short-term outcomes have been reported in small case-series[10], although concerns persist regarding both clinical outcomes in young patients and longer term patient outcomes[12,14]. To date, only one study assessed RTS rates following primary repair; however, it should be noted that the sample size was small (24 patients) and follow-up was short (1 year).[15]

Therefore, the study purpose was to assess RTS rates and evaluate the timeline of rehabilitation milestones following selective arthroscopic primary ACL repair. We hypothesized the majority of patients would return to their pre-injury sports levels (similar to ACL reconstruction) and achievement of rehabilitation milestones would occur in a shorter timeframe as compared to historical controls of patients undergoing ACL reconstruction.

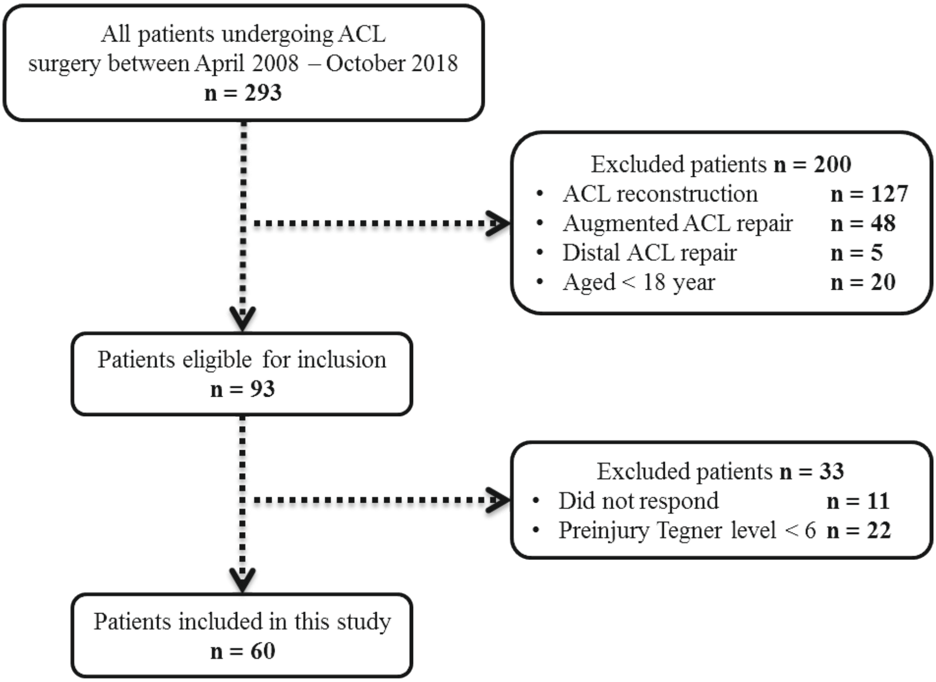
Materials and methods

Patient selection

Following Institutional Review Board approval (IRB# 2017-0404), all patients who underwent ACL surgery performed by the senior author (GSD) between April 2008 and October 2017 were retrospectively identified from a prospectively collected database. During this timeframe, 293 patients underwent ACL surgery, and following inclusion and exclusion criteria (Figure 1), 93 patients treated with primary repair for proximal tears were deemed eligible for inclusion and were asked to complete the same set of surveys in clinic or online. For this study, only patients with a preinjury self-reported level of activity ≥6 (i.e. participation in knee-strenuous sports) were included. Eighty-two patients (85% of eligible patients) completed at least one survey at a minimum of 2-year follow-up. Of these patients, 22 reported an activity level <6. Therefore, 60 patients treated with primary repair ultimately were included in this study.

Although this study demonstrates a unique analysis, data on other outcome measures of some patients have been published previously.[16,17]

Figure 1.



Flowchart of the studied population following primary repair.

Indications

The same surgical treatment algorithm was applied for all patients consisting of arthroscopic primary repair for those presenting with proximal tears (i.e. sufficient remnant length and good tissue quality to withhold intraligamentary suturing), while standard ACL reconstruction was performed in the setting of non-repairable tears (i.e. mid-substance tear or insufficient tissue quality). Primary repair was preferably performed in the acute setting (within 4 weeks). However, some tears were repaired in the chronic setting, as the final decision was ultimately made during arthroscopy in which the treatment depended on tissue length and quality. In addition, primary repair was considered in all age groups, while concomitant injuries (i.e. meniscal damage or chondral injury) were not considered as contra-indications.

Surgical technique

The surgical technique of arthroscopic primary ACL repair for proximal tears has been described previously in more detail.[18] In brief, the anteromedial (AM) and the posterolateral (PL) bundles are sutured using a self-retrieving suture passer in alternating and interlocking Bunnel-type patterns towards the avulsed ends using #2 FiberWire and #2 TigerWire (Arthrex, Naples, FL). Then, 4.5x20mm holes are tapped, drilled, or punched depending on bone density. The PL bundle is reattached in anatomical fashion using suture anchor fixation with the knee at 115° of flexion, followed by the AM bundle that is reattached with the knee at 90°.

More recently, an InternalBrace, consisting of a Fibertape (Arthrex, Naples, FL), became clinically available and was added to the majority of cases.[19] Ligament augmentation is thought to protect the repaired ACL from accidental overtensioning, especially during the healing phase. In the early stages, augmented repairs were performed specifically in patients at increased re-injury risk, while in a later phase; implementation of the InternalBrace had become standard of care for all. Following the same procedure of ligament suturing, the suture anchor of the AM bundle is preloaded with Fibertape. After deploying the suture anchor, Fibertape is channeled along the anterior third of the repaired ACL, and placed through a small (2.5mm) drill hole in the tibia using a suture passer. The Fibertape is then tensioned with the knee in full extension and fixed to the the anteromedial tibial cortex using suture anchor fixation.

Postoperative management

All patients followed the same rehabilitation protocol. To avoid unexpected buckling of the limb and provide general support during the early recuperative phase, patients wore a hinged brace for the first four weeks postoperatively. Rehabilitation started immediately following surgery, and focused on weight-bearing, early ROM, and regaining quadriceps muscle control. Weight-bearing as tolerated was initially allowed with the brace locked in extension. Patients with concurrent meniscal repair were kept partial weight-bearing for the first four to six weeks, while patients were weight-bearing as tolerated following partial meniscectomy. Formal physical therapy and closed-chain hamstring exercises were advanced as per standardized ACL reconstruction protocols and generally initiated within four to six weeks postoperatively. The decision for clearance of RTS, usually after a six to nine-month recovery period, was based upon ROM, knee stability, and quadriceps muscle strength (>90% isokinetic strength compared to the contralateral side).

Data collection

As part of routine clinical care, all patients were thoroughly reviewed in clinic at one week, one, three, and six months, and one, two, and five years. Patients underwent physical examination and were asked to complete the same set of follow-up sports surveys. When patients were unable to return for clinical visits, they were contacted, via phone or email, and asked to complete the same questionnaires in an online format.

Outcomes

Primary outcome in this study was return to knee-strenuous sport; assessed using the Tegner Activity Scale.[20] This validated scale is graded from 0-10, with each ascending value representing more knee-strenuous activities.[20] A Tegner score of 10 indicates ability to participate in competitive sports at elite levels and a score of 6 is equivalent to participation in knee-strenuous sports at recreational levels. Sports participation was based on patients' self-reported preinjury and current activity levels. Successful return to knee-strenuous sports were defined as returning to Tegner level ≥6.[5] Furthermore, ability to RTS at the lowest recreational level (Tegner ≥5) and return to the same preinjury or higher activity level were also assessed.[1] If failure of treatment occurred, this was classified as no return to sports (if no postoperative Tegner level was available).

Secondary outcomes included patient-reported time to return to work, time to discontinue brace usage, time to return to running, and time to return to sports participation. All patients were therefore asked to complete questions regarding time from surgery to return to these functional milestones.

Lastly, psychological readiness to RTS participation was assessed using the ACL-Return to Sport After Injury scale (ACL-RSI; short version).[21] This scale has been validated in prior studies and is scored on an 11-point Likert scale from 0-100.[21] Higher scores quantify greater psychological readiness to RTS. Additionally, association between psychological readiness and RTS was also assessed by determining ACL-RSI scores between subgroups (Tegner level ≤5, 6-7, and ≥8).[22]

Statistical analysis

SPSS Version 25 (SPSS Inc., Armonk, NY) was used for all statistical analyses. Distribution of variables was tested using Kolmogorov–Smirnov test. Due to non-normally distributed data, descriptive analysis of continuous variables included median with interquartile ranges (IQR), while discrete variables reported as frequencies with percentages. Univariate analysis was conducted using Mann–Whitney U test for continuous variables, and chi-square tests for discrete variables. Receiver operating curve analysis (ROC) was used to find optimal cutoff for association between ACL-RSI scores and RTS. A repeated ANOVA was used to assess differences between preinjury and postoperative activity levels. Kruskal-Wallis one-way ANOVA was used to compare multiple groups with continuous variables followed by Bonferroni correction to adjust for multiple pairwise comparisons. Correlation between Tegner scores and ACL-RSI scores was assessed using Spearman correlation coefficients as strong (r>0.5), good (0.5 < r < 0.3), or weak (0.3 < r < 0.1). A p-value of ≤0.05 was considered statistically significant.

Results

Patient demographics

Sixty patients were enrolled in this study. Median age at surgery was 36 years (range 18–60, IQR 27–43 years), 68% were males, median BMI was 25.5kg/m^2 (IQR 23.4–27.3kg/m^2), and median follow-up was 2.4 years (IQR 2.1–3.7 years). Twenty-eight patients (47%) had concurrent meniscal injury and 17 (27%) had chondral injury. Fifty-three patients (88%) sustained their ACL injury during sports activity, and the most common injury mechanism was skiing (25%), followed by soccer (17%), and basketball (13%). In 28 patients (47%), the repair was augmented with an internal suture augmentation. Baseline characteristics are displayed in Table 1.

Table 1. Patient demographics of patients treated with primary ACL repair

	All included (n = 60)
Age (years); median (IQR)	36 (27 – 43)
Male gender; freq. (%)	41 (68%)
Delay (days injury-surgery); median (IQR)	47 (22 – 103)
BMI (kg/m2); median (IQR)	25.5 (23.4 – 27.3)
Sports injury; freq. (%)	53 (88%)
High-risk sport; freq. (%)a	36 (60%)

Table 1. Patient demographics of patients treated with primary ACL repair *(Continued)*

	All included (n = 60)
Meniscal injury; freq. (%)	28 (47%)
Medial meniscus	12 (20%)
Lateral meniscus	23 (38%)
Meniscus treatment; freq. (%)	
Repair	6 (10%)
Meniscectomy	18 (30%)
Repair + Meniscectomy	2 (3%)
Conservative	2 (3%)
Chondral injury; freq. (%)	16 (27%)
Preinjury Tegner; freq. (%)	
Tegner 6	27 (45%)
Tegner 7	21 (35%)
Tegner 8	5 (8%)
Tegner 9	5 (8%)
Tegner 10	2 (4%)
Follow-up (years); median (IQR)	2.4 (2.1 – 3.7)

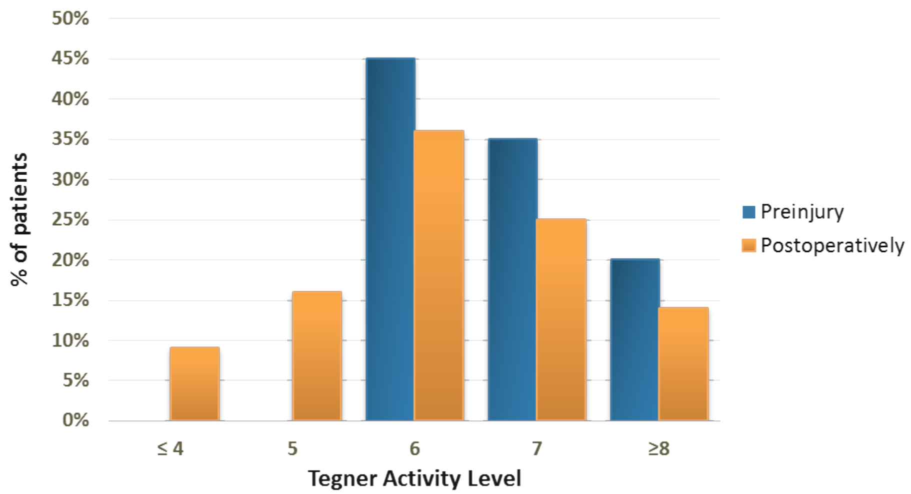
N, number of patients; *BMI*, body mass index; *Freq.*, frequencies; *SD*, standard deviation; [a] High-risk sports for ACL injury included basketball, soccer, football, lacrosse, skiing and volleyball.[58]

9

Return to sport

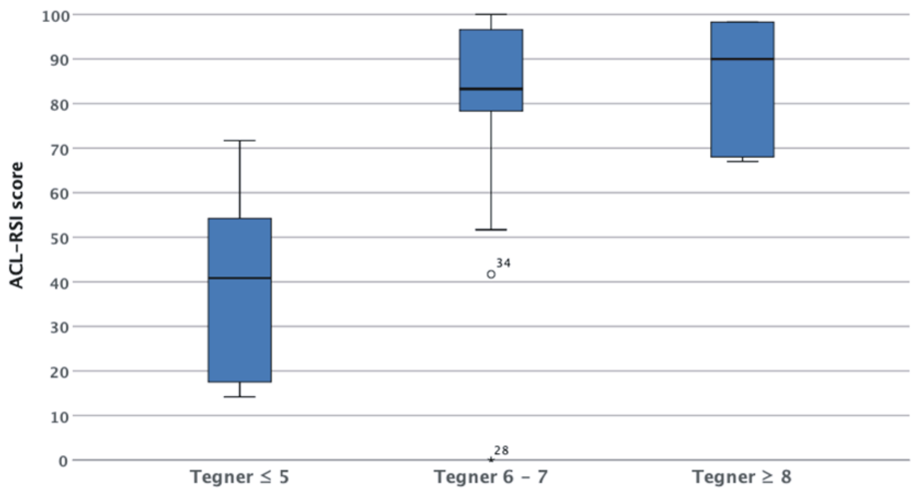
At latest follow-up, 51 patients (85%) returned to any sports participation (i.e. Tegner activity level ≥5), whereas 42 (70%) returned to knee-strenuous sports (i.e. Tegner level ≥6). Four patients (7%) substained a rerupture. Thirty-six patients (60%) were able to return to pre-injury sports level; 15 (25%) shifted to a lower activity level, while nine (15%) were unable to RTS (Figure 2). Of these patients, four were unable to RTS due to reinjury, while five were more generally unable. Median preinjury Tegner level was 7 (IQR 6–7) and median postoperative Tegner level was 6 (IQR 5–7; $p<0.001$). Data of 41 patients showed overall median ACL-RSI score of 80.0 (IQR 53.0–95.0; Figure 3). Spearman's correlation between ACL-RSI scores and Tegner levels was 0.534.

Figure 2.



Distribution of activity levels before injury and after primary repair

Figure 3.

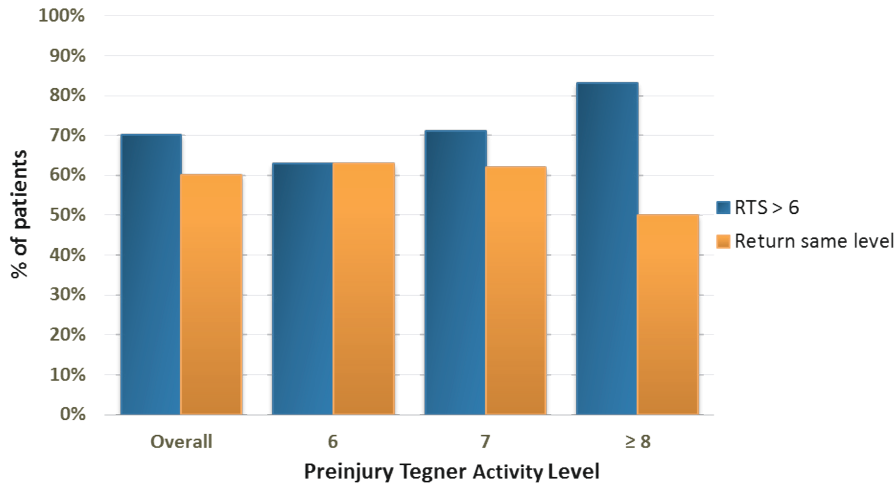


Associating between psychological readiness and postoperative Tegner Level. ACL-RSI scores were significantly higher in patients with levels ≥ 8 and levels 6 – 7 as compared to levels ≤5 ($p<0.001$, and $p=0.008$, respectively). No difference was found between patients with activity levels 6–7 and ≥8 ($p>0.999$; Table 5). Data was available in 41 patients.

Return to knee-strenuous sports

When comparing patients who returned to knee-strenuous sports (70%) to those who did not (30%), univariate analyses showed significantly higher median ACL-RSI scores were found in patients who returned to Tegner level ≥6 (median 85.0 versus 40.9, respectively, $p < 0.001$; Table 2A). Using ROC-curve analysis, an ACL-RSI score of 57.1 was identified as the threshold to return to knee-strenuous sports with an area under the curve (AUC) of 0.921 (95% CI, 0.837–1.000) and with sensitivity 0.903 and specificity 0.800. No significant differences were found in other independent variables (all n.s.) Return to knee-strenuous sports rates subdivided by preinjury Tegner activity levels is shown in Figure 4.

Figure 4.



Associating between preinjury Tegner levels versus return to knee-strenuous sports and return to preinjury sports participation

Table 2A. Patient demographics of those who RTS versus those who did not (NRTS)

	RTS (n = 42)	NRTS (n = 18)	P-value
Age (years); median (IQR)	36 (28 – 47)	34 (24 – 42)	0.183
Male gender; freq. (%)	31 (73%)	8 (55%)	0.164
Delay (days injury-surgery); median (IQR)	47 (24 – 99)	48 (21 – 110)	0.891
BMI (kg/m^2); median (IQR)	25.2 (23.4 – 27.7)	24.1 (21.6 – 25.7)	0.149
Sports injury; freq. (%)	88 (91%)	15 (83%)	0.419
High-risk sport; freq. (%)[a]	26 (62%)	10 (56%)	0.645
Meniscal injury; freq. (%)	20 (48%)	8 (44%)	0.821
Medial meniscus	9 (21%)	3 (17%)	>0.999
Lateral meniscus	16 (38%)	7 (39%)	0.954

Table 2A. Patient demographics of those who RTS versus those who did not (NRTS) *(Continued)*

	RTS (n = 42)	NRTS (n = 18)	P-value
Chondral injury; freq. (%)	11 (26%)	5 (28%)	0.899
InternalBrace; freq. (%)	20 (48%)	8 (44%)	0.821
Preinjury Tegner; freq. (%)	7 (6 – 7)	6 (6 – 7)	0.171
Postoperative Tegner	7 (6 – 7)	5 (4 – 5)	<0.001
ACL-RSI; median (IQR)[b]	85.0 (76.7 – 97.7)	40.9 (16.9 – 57.5)	<0.001

N, number of patients; *BMI*, body mass index; *Freq.*, frequencies; *SD*, standard deviation; [a] High-risk sports for ACL injury included basketball, soccer, football, lacrosse, skiing and volleyball;[58] [b] ACL-RSI of 48 patients.

Return to preinjury level

When comparing patients who returned to preinjury sports participation level (60%) to those who did not (40%), patients returning at the same level were significantly older (median 40 versus 31 years, p=0.005), and had higher ACL-RSI scores (89.2 versus 41.7, p<0.001; Table 2B). ROC-curve analysis showed an ACL-RSI score of 74.2 as the threshold to return to preinjury sports level with an AUC of 0.924 (95% CI, 0.833–1.000) and with a sensitivity 0.885 and specificity of 0.933. The association between preinjury Tegner levels and return to the same sports level is also demonstrated in Figure 4.

Table 2B. Patient demographics of those who returned to preinjury level (PRE) versus those who did not (NPRE)

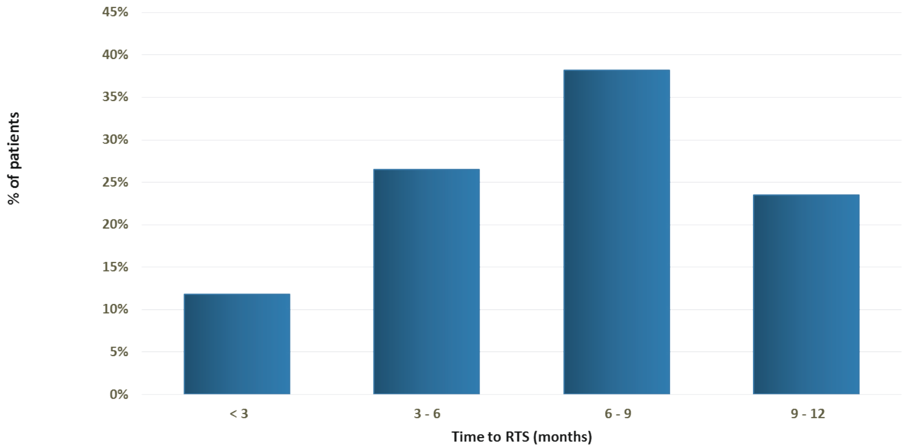
	PRE (n = 36)	NPRE (n = 24)	P-value
Age (years); median (IQR)	40 (35 – 48)	31 (24 – 37)	0.005
Male gender; freq. (%)	26 (72%)	15 (63%)	0.428
Delay (days injury-surgery); median (IQR)	47 (22 – 93)	48 (22 – 143)	0.689
BMI (kg/m^2); median (IQR)	25.2 (23.4 – 27.3)	24.2 (22.8 – 28.0)	0.419
Sports injury; freq. (%)	32 (89%)	21 (88%)	>0.999
High-risk sport; freq. (%)[a]	23 (64%)	13 (54%)	0.451
Meniscal injury; freq. (%)	14 (39%)	14 (58%)	0.139
Medial meniscus	7 (19%)	5 (21%)	0.895
Lateral meniscus	11 (31%)	12 (50%)	0.129
Chondral injury; freq. (%)	11 (31%)	5 (21%)	0.404
InternalBrace; freq. (%)	15 (42%)	13 (54%)	0.342
Preinjury Tegner; median (IQR)	7 (6 – 7)	7 (6 – 8)	0.465
Postoperative Tegner; median (IQR)	7 (6 – 7)	5 (4 – 6)	<0.001
ACL-RSI; median (IQR)[b]	89.2 (79.6 – 98.3)	41.7 (17.5 – 67.5)	<0.001

N, number of patients; *BMI*, body mass index; *Freq.*, frequencies; *SD*, standard deviation; [a] High-risk sports for ACL injury included basketball, soccer, football, lacrosse, skiing and volleyball;[58] [b] ACL-RSI of 41 patients.

Patient-reported milestones

In 42 patients who completed milestones questions, median time to return to work was 7 days (IQR 5–14 days). Time to discontinue knee brace use occurred at median 30 days postoperatively (IQR 21–39 days), time to return to running at 90 days (IQR 57–120 days), and time to return to sports activities at 180 days (IQR 116–270). Timing of RTS is shown in Figure 5.

Figure 5.



Timing of return to play. Data was available in 34 patients.

Discussion

The main study finding was 85% of patients returned to any sports participation, 70% to knee-strenuous sports, and 60% to preinjury levels of sports participation following primary ACL repair in the adult population. Furthermore, it was noted patients had high confidence in RTS, which was strongly associated with returning to sports participation.

In this study, the primary outcome was returning to knee-strenuous sports, and according to the Tegner Activity Scale, 70% treated with primary repair returned to knee-strenuous sports, while 60% returned to their pre-injury level. When reviewing previously published studies, the literature regarding RTS following primary repair is scarce, presumably due to the treatment being relatively new. Ortmaier et al. recently reported similar outcomes following 24 patients treated with repair compared to 25 treated with ACL reconstruction with an overall RTS rate of 91%[15], but only had a follow-up of 1 year. Furthermore, Hoffman et al. reported that 7 of 12 patients (58%) treated with primary repair returned to preinjury sports participation levels[23], which is similar to this study. When compared to both studies, the present study reported similar findings. From a recent meta-analysis, it is known 81% of patients return to any sports participation, while 65% return to their pre-injury level following ACL reconstruction [7], although moderate variability exists.[5] Although roughly similar results can be found in this study, it should be noted that no comparable age patterns were found between both studies (mean 25 versus median 36 years, respectively). Furthermore, no clearly defined definition of RTS exists, which makes it difficult to compare outcomes. Therefore, there is a need for prospective comparative studies with similar patient demographics to assess RTS between both treatment modalities.

This study demonstrates patients returning to preinjury levels were older as compared to those who did not (40 versus 31 years). On the contrary, several studies have consistently shown younger age associated with improved RTS outcomes in ACL reconstruction literature.[24] One explanation for this finding is that despite a majority of patients participating in competitive sports who returned to knee-strenuous sports (83%), 50% chose to return to less competitive sports. No association was found between preinjury Tegner levels and return to same sports levels, presumably as the group of patients involved in competitive sports was small (n=12). However, we hypothesize patients who returned to preinjury levels less often participated in sports requiring jumping, pivoting, and cutting maneuvers as compared to those who did not. As previous studies have shown older patients less often participate in knee-strenuous and pivoting sports at competitive levels[25], it can be expected higher return to preinjury rates will be found in older patients. However, it should be taken into account that as older patients are more likely to be treated with primary repair, since proximal tears are more frequently found in patients ≥ 35 years of age[26], the group of younger patients treated with repair is also exepected to be relatively small.

When looking closely at age, the majority of our patients were over 30 years of age. In this study, all patients performed knee-strenuous sports before injury and desired to return to play. Among older patients, excellent outcomes were found with high rates of return to both knee-strenuous and to preinjury sports level. It could be argued that a subset of older patients may be overtreated with surgery, as they could potentially be treated conservatively and still achieve successful outcomes.[27] Recent studies, however, have suggested that conservative treatment for these physically active patients leads to increased risk of residual instability and associated injuries, while poor knee function and debilitating symptoms encountered during daily activities have also been reported.[28] As a result, most patients abandon highly demanding sports activities.[29] Over the last decades, increasing numbers of older recreational athletes desire to maintain active lifestyles. Given the minimally invasive nature of the surgery, the low reported failure rates, and the good RTS outcomes, it is felt surgical repair may therefore be an excellent option in this progressively increasing group of patients.

When reviewing time to achieve rehabilitation milestones, time to return to work in this study was 7 days, while a prolonged interval is reported in ACL reconstruction literature (up to 78 days).[30] Similarly, time to return to running (90 days) and time to RTS (180 days) occurred in a shorter interval as compared to ACL reconstruction studies.[3] First, it should be noted rehabilitation and return-to-play protocols for repair have not yet been established, and functional milestone achievement may have occurred too rapidly.[31] However, the less-invasive nature of the repair surgery certainly contributes to these findings. Apropos to this concept Van der List and DiFelice previously demonstrated patients treated with repair have significantly more ROM as compared to those undergoing reconstruction at one week (89° versus 61°) and one month (125° versus 116°), and more patients treated with repair had full ROM at one month (57% versus 30%).[13] Given these findings, one may indeed expect that our patients also can return to work and attempt to start running in a shorter time frame compared to those treated with reconstruction. With regard to time to RTS, a subset of our patients elected to return earlier to sports activities, as they felt confident about their knee and their ability to participate in sports activities at an early stage despite the surgeons' recommendation to delay RTS until 6-9 months postoperatively. Further research is needed on optimization of rehabilitation protocols in this setting.

For all patients, as indicated by high ACL-RSI scores (80.0, IQR 53.0–95.0), fear of reinjury was low. Furthermore, psychological readiness was strongly associated with RTS; similar to previously published findings.[32] When looking at confidence in RTS following primary repair, only one preliminary study by Hennings et al. reported ACL-RSI scores.[33] Similar to the our findings, the authors reported excellent psychological readiness (94.5) in 13 patients at 1-year follow-up. Reviewing the ACL literature, various case-series noted similar ACL-RSI scores in patients undergoing reconstruction (range 65.2–74.3).[34,35] It is difficult to compare fear of reinjury between both treatments, as ACL-RSI scores are not commonly used as patient-reported outcomes measures in previous repair studies, while heterogeneity exists in reconstruction literature. Nevertheless, this study found a low fear of reinjury in patients treated with pimary repair. One explanation for this finding is that the knee feels nearly 'normal' following primary repair, as recently reported by another study of our group.[16] We speculate due to preservation of native ligament, and avoidance of tunnel drilling and graft site morbidity, patients are less aware of their affected knee, (it feels more 'normal'), and consequently more confident to return to sports participation.

There are study limitations. First, given the retrospective design of this study, potential selection bias could have been introduced, and individual changes in rehabilitation programs could not be eliminated. Secondly, possible recall bias may have significantly contributed to under- or over-estimation of patient-reported outcomes. However, this influence is expected to be low since passed milestones during rehabilitation are generally considered memorable events. Thirdly, patient-reported outcomes, besides Tegner levels, were missing in a subset of patients. Additionally, small sample sizes of subgroups prevented thorough statistical analysis. Finally, we could not identify reasons why patients were unable to return to their previous sports level because of non-knee related reasons, such as lack of time or loss of interest in sports activities.

Conclusion

Following primary ACL repair, 70% of adult patients returned to knee-strenuous sports and 60% to preinjury levels by 180 days postoperatively. Positive predictors for return to preinjury levels included older age and low fear of reinjury.

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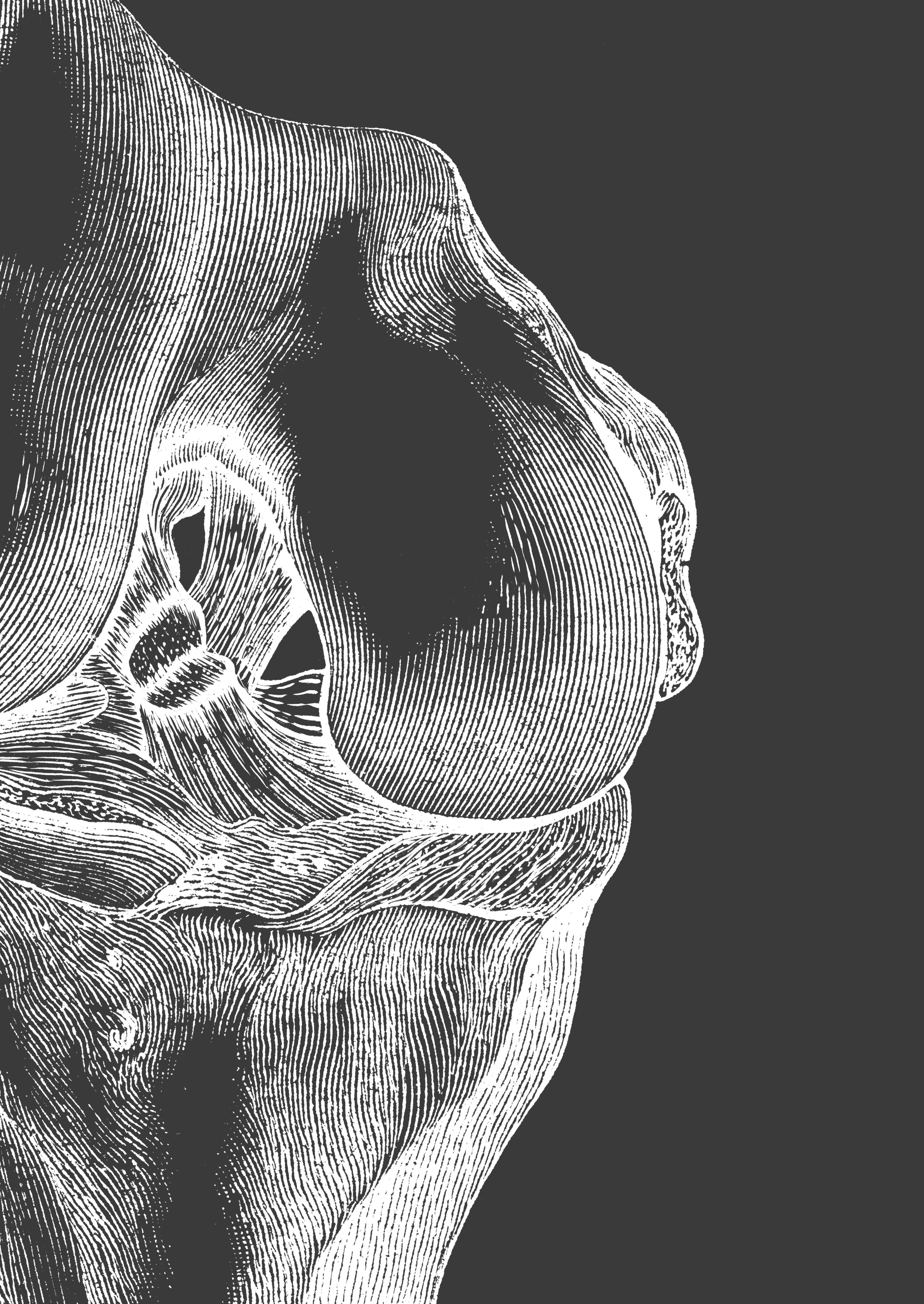

Chapter 10

Patients forget about their operated knee more following arthroscopic primary repair of the anterior cruciate ligament than following reconstruction

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Abstract

Purpose

To assess the extent to which patients forget their operative knee joint on a daily basis following arthroscopic primary repair as compared to reconstruction of the anterior cruciate ligament (ACL) at short-to-mid-term follow-up.

Methods

For this retrospective study, all patients undergoing ACL surgery between May 2012 and May 2017 were identified. All patients were treated with the algorithm of undergoing arthroscopic primary repair for proximal tears, and reconstruction for non-repairable tears. Patients were contacted to complete the Forgotten Joint Score (FJS-12) questionnaire between two- and five-years following surgery. A higher score represents a more favorable outcome indicating the patient's ability to 'forget' the joint in everyday life, whereas lower scores indicate a less favorable outcome. Data were analyzed using independent t-tests and chi-square tests, and multiple linear regression analysis was performed to correct for potential confounders.

Result

Eighty-three patients completed the questionnaire (57%). Patients who underwent primary repair thought about their operated knee less when compared to those patients who underwent reconstruction (85.3±14.2 vs. 74.3±23.3, *P*=0.022). These differences were significantly higher in patients older than 30 years (85.3±12.9 vs. 62.6±24.9, *P*=0.007), male patients (85.0±13.6 vs. 72.5±24.7, *P*=0.037), and patients with BMI above 25 kg/m^2 (85.9±14.5 vs. 64.7±25.6, *P*=0.009). After correcting for potential confounders, the overall difference remained significant (*P*=0.045).

Conclusion

Based on the data in this study, patients undergoing arthroscopic primary ACL repair can expect to have less daily awareness of their operated knee at short-to-mid-term follow-up as compared to patients undergoing ACL reconstruction.

Introduction

Currently, anterior cruciate ligament (ACL) reconstruction is considered the gold standard for the surgical treatment of ACL injuries.[1–3] This procedure has been shown to effectively restore knee stability and generally has a low failure rate, but there are also some disadvantages. With ACL reconstruction, surgery requires the harvesting of grafts and drilling of tunnels and some patients complain of persistent postoperative pain and/or complaints associated with graft site morbidity.[4–7] Over the last decade, there has been a renewed interest in arthroscopic primary repair of proximal ACL tears,[8–12] due to potential advantages over reconstruction that include not requiring tunnel drilling or graft harvesting and thereby preserving the native ligament and faster return of range of motion (ROM) postoperatively.[13–15]

In ACL surgery, various patient-reported outcomes measurements (PROMs) are used to evaluate and compare surgical outcomes.[16] The Forgotten Joint Score-12 (FJS-12) questionnaire is a relatively new PROM which assesses the awareness of a specific joint during daily activities.[17] A higher score is suggestive of a more favorable outcome indicating the ability to 'forget' the joint in everyday life, while lower scores indicate a less favorable outcome with the joint being on the patients mind more each day. Joint awareness not only reflects strong sensations such as pain and stiffness, but also includes more subtle sensations such as instability, weakness, or any other discomfort.[18] Furthermore, this questionnaire can discriminate minor differences not detected with the established PROMs.[17] The FJS-12 was initially developed and validated for arthroplasty surgery,[19,20]however; the current version allows use beyond joint arthroplasty.[18] Recently, the FJS-12 has therefore also been used in hip and knee joints pathology in general,[18,21,22] including ACL reconstruction surgery. Behrend et al. noted more knee joint awareness (i.e. less favorable outcome) following reconstruction of the ligament as compared to two similar healthy matched control groups at a minimum of one- and ten-years follow-up.[23]

The purpose of this study was therefore to assess daily to which extent patients forget their operated knee joint following arthroscopic primary repair compared to reconstruction of the ACL at short-to-mid-term follow-up. Due to preservation of native ligament, and avoidance of the morbidity associated with both tunnels and grafts, we hypothesized that there would be a decreased day-to-day awareness of the knee joint, indicated by higher FJS-12, following arthroscopic primary ACL repair as compared to ACL reconstruction.

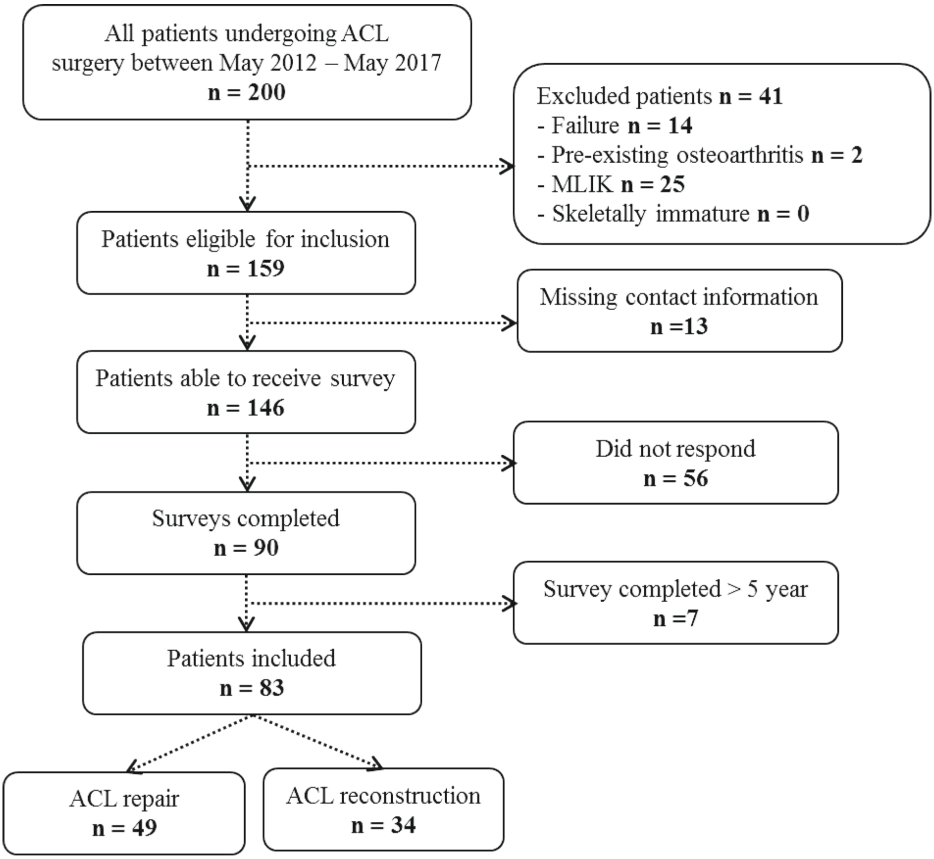
Methods

Patient selection

In this IRB approved retrospective study (IRB number 2017-0404), all patients from a prospective database from one surgeon (GSD) who underwent operative treatment for ACL injury were identified. All patients in this database were treated with the same surgical algorithm that was determined intraoperatively: arthroscopic primary ACL repair was performed in patients with proximal tears (i.e. when distal remnant length was sufficient to reattach the torn ligament back to the femoral footprint) and sufficient tissue quality to withhold suture passing. In patients with a higher risk of failure, an internal suture augmentation (InternalBrace; Arthrex, Naples, FL) was added to the repair which is thought to protect the ligament during the healing phase.[24] For patients with non-repairable tears (i.e. midsubstance tear or insufficient tissue quality to withhold sutures), standard ACL reconstruction was performed using autograft or allograft tissue.

All patients undergoing ACL surgery between May 2012 and May 2017 were screened for eligibilty for this study . Two-hundred patients were screened and following inclusion and exclusion criteria (Figure 1), a total of 146 patients were deemed eligible and were asked to complete the FJS-12 questionnaire either via mail or in the clinic. Seven patients were excluded for completing the questionnaire more than five-years following surgery, 13 patients had no contact information and 56 patients did not respond, resulting in a total of 83 patients completing the questionnaire (57%). Therefore, 49 patients undergoing primary repair, and 34 patients undergoing ACL reconstruction were included in this study that had completed FJS questionnaires at short- to mid-term follow-up .

Figure 1.



Flowchart of the studied population following primary ACL repair and reconstruction.

Surgical technique

The surgical technique of primary ACL repair has been previously described more extensively.[14] The repair was started by suturing the anteromedial (AM) in a Bunnell-type pattern from distal to proximal using a No. 2 FiberWire (Arthrex, Naples, FL, USA). A 4.5mm x 20mm holes is then tapped, drilled or punched depending on the density of the bone. The AM bundle is then reapproximated to its femoral footprint and the suture anchor deployed in the anteromedial origin with the knee in 90° of flexion. The same procedure was then repeated for the posterolateral (PL) bundle which was reapproximated with the knee in 115 degrees of flexion. The repair is completed after cutting the sutures and tested intraoperatively for tension, and stiffness of the repair, and range of motion (ROM) of the knee.

During more recent surgeries, an internal suture augmentation was added to the repaired ligament in order to protect the repair in those patients deemed to have a higher risk for re-rupture, such as young patients, patients with valgus leg deformity, and/or patients performing sports at high activity levels.[25] The internal suture was loaded into the AM suture anchor prior to its deployment, and was then channeled along the repaired ACL to the tibial footprint. A small drill hole was then drilled from the anteromedial cortex of the tibia to the anterior half of the tibial footprint and a passing wire is used to retrieve the suture augmentation through the tibia to the anteromedial cortex where it is fixed, with the knee in extension, using a suture anchor.

ACL reconstruction was performed in standard fashion using a variety of grafts: soft tissue allograft (n = 14), bone-patellar tendon-bone (BPTB) autograft (n = 9), hamstring autograft (n = 4) or hybrid graft (n= 3). Following anteromedial, either antegrade or retrograde, drilling of the femoral tunnel, interference screws were used to fix the BPTB block; soft tissue grafts were fixed proximally with interference screws, or with a ligament button, and both were fixed distally with an interference screw.

Post-operative management

Postoperative rehabilitation was similar for both groups and focused on early mobilization. All patients received a hinged brace in the operation room, and initially, weight-bearing was allowed with the brace locked in extension. In general, physical therapy was initiated early after the first week and focused on swelling control, range of motion and quadriceps activation. The brace was generally unlocked during ambulation once protective quadriceps function returned. In general, physical therapy was advanced at four to five weeks post-operatively when the brace was discontinued and gentle strengthening was begun. Patients were seen in the clinic at one week, one month and three, six and twelve months postoperatively to assess the progression of rehabilitation. Return to sports was allowed which was based both on patients' confidence, quadriceps muscle strength (90% of contralateral leg) and functional testing.

Forgotten Joint Score-12

The primary outcome in this study was joint awareness that was measured with the FJS-12 questionnaire consisting of 12 questions with a five-point Likert response format and is scored between 0-100. The questionnaire assesses how much patients think about or are bothered by their affected knee during daily life following ACL surgery and can differentiate even amongst highly active patients.[23] It should be noted, that even patients with healthy and well-functioning joints are sometimes aware of their knee, therefore, a 'forgotten joint' is hard to achieve.[23]

The FJS-12 score has been validated in a preliminary study to assess joint awareness after ACL reconstruction and showed high internal consistency and less ceiling effect compared to most KOOS and all WOMAC scales.[22] The minimal clinically important difference (MCID) reflects the smallest change in the FJS considered being clinically relevant. Although the MCID is normally used as a patient-level metric, this parameter was used as an approximation of a clinically relevant difference between both cohorts in the present study. To date, the MCID has not yet been validated for the FJS in ACL surgery and therefore half of the standard deviation (SD) was used to estimate the MCID.[26,27] Based on the SD of the entire cohort in this study (19.4), the MCID was determined to be 9.7-points.

Statistical analysis

All analyses were conducted with SPSS, version 25.0 (IBM Corp., Armonk, NY). A sample-size power analysis was performed (estimated mean of 85 and estimated SD of 15) and suggested that 21 patients in both groups were needed to reach 80% power. Outcomes between primary repair and reconstruction surgery were compared using independent t-tests for continuous variables, and chi-square tests or Fisher exact tests to compare nominal data (in case one of the numbers was <5). A post-hoc power analysis was performed to confirm adequate power was obtained to support these conclusions. A multiple linear regression method was applied to correct the FJS for possible confounding based on age, BMI, concomitant damage and duration of follow-up. All tests were two-sided and a *P* value <0.05 was considered statistically significant.

Results

Baseline characteristics

Eighty-three patients completed the FJS-12 questionnaire between two- and five-years (56%) following ACL surgery of which 49 underwent primary ACL repair and 34 underwent ACL reconstruction. In 30 repair patients (61%), an internal suture augmentation was added to the repair (Table 1). Mean age was 32.2 years (range 16 – 55 years), mean BMI 25.3 kg/m^2 (range 18.8 – 35 kg/m^2), 56% were male, and mean follow-up was 2.7 years (range 1.6 – 4.8 years). There was no significant difference in gender, BMI, concomitant damage and surgical delay between both groups. Patients treated with primary ACL repair were older (34.2 vs. 29.4 years, *P* = 0.047) and had shorter follow-up (2.5 vs. 3.0 years, *P* = 0.012). In the repair group, one technical complication occurred when the tip of the self-retrieving suture passer broke off during surgery and was lost in the ACL fibers. In the reconstruction group, one patient with a BPTB graft sustained a patella fracture during physical therapy. Both cases were treated conservatively with successful outcomes.

Table 1. Patient characteristics following primary ACL repair and ACL reconstruction

	Primary repair (n = 49)		Reconstruction (n = 34)		
	Mean ± SD	Range	Mean ± SD	Range	P-value
Age (years)	34.4 ± 10.7	15.5 – 55.0	29.4 ± 11.1	15.5 – 51.6	0.047
Male gender; N (%)	24 (51%)		20 (59%)		0.510
Delay (days injury-surgery)[a]	36	17 – 86[b]	74	34 – 186[b]	0.202
BMI (kg/m^2)	25.0 ± 3.8	18.8 – 35.9	25.6 ± 4.5	19.5 – 35.9	0.528
FU (years)	2.5 ± 0.8	1.6 – 4.8	3.0 ± 1.1	1.7 – 4.8	0.012
Concomitant damage					
Meniscus injury N (%)	24 (49%)		23 (68%)		0.092
Chondral injury N (%)	10 (20%)		8 (24%)		0.790

N: number of patients; M: males; F: females; BMI: body mass index; FU: follow-up.

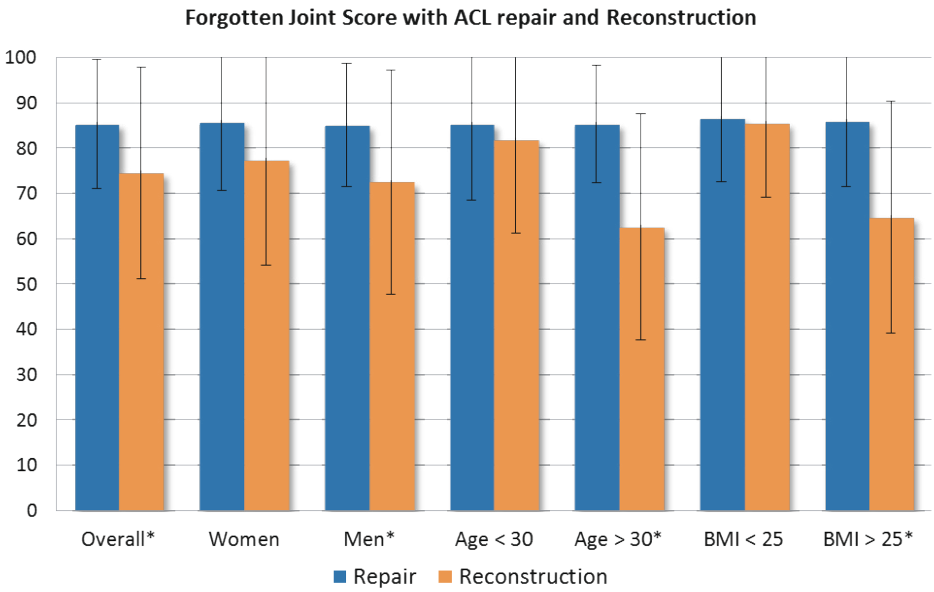
[a] Reported in median

[b] Reported in interquartile range

Joint awareness

Following arthroscopic primary ACL repair, patients had significantly improved joint awareness as compared to patients treated with ACL reconstruction (85.3 ± 14.2 vs. 74.5, ± 23.9, $P = 0.022$). In Figure 2, an overview regarding the FJS for different subgroups can be found. Following primary repair, significant improvement in joint awareness was noted in male patients (85.0 ± 13.6 vs. 72.5 ± 24.7, $P = 0.037$) as compared to reconstruction. Higher FJS scores were also noted following primary repair in female patients (85.7 ± 15.1 vs. 77.3 ± 23.1, $P = 0.188$) as compared to those undergoing ACL reconstruction, although this was not significant.

Figure 2.



Mean FJS in patients that underwent repair versus reconstruction between two- and five-years follow-up. The error bars represent standard deviation; *Asterix* indicates a statistically significant difference ($P < 0.05$) between both groups; BMI indicates Body Mass Index.

When comparing other subgroups, a significantly higher FJS scores were noted in patients older than 30 years (85.3 ± 12.9 vs. 62.6 ± 24.9, $P = 0.007$) and in patients with a BMI > 25 kg/m^2 (85.9 ± 14.5 vs. 64.7 ± 25.6, $P = 0.009$) treated with repair as compared to reconstruction. Post-hoc power analysis showed a power of 87.7% for different age groups and 87.8% for different BMI groups between repair vs. reconstruction at an α error probability = 0.05. There were no statistically significant differences noted between FJS scores in patients treated with primary repair or reconstruction surgery that were younger than 30 years old (85.3 ± 16.8 vs. 81.8 ± 20.6, $P = 0.571$) nor in patients with a BMI < 25 kg/m^2 (86.5 ± 14.0 vs. 85.5 ± 16.4, $P = 0.848$, respectively).

In all patients, 11 repair patients (22%) reported no awareness at all of their operated knees (FJS-12 = 100 points) in everyday life whereas only three reconstruction patients (9%) had no awareness at all but this was not statistically significant ($P = 0.094$).

Using multivariate regression analysis, while controlling for potential confounders age and follow-up length, the noted difference between FJS for repair patients as compared to reconstruction patients remained statistically different ($P = 0.045$; Table 2).

Table 2. Multivariate regression analyses for confounders on the FJS.

Variable	B	SE	Beta	P-value	95% CI (LB – UB)
Intercept	104.4	8.186		0.000	88.064 – 120.651
Age	- 0.194	0.191	- 0.110	0.312	- 0.547 – 0.185
FU	- 5.030	2.317	- 0.230	0.033	- 9.641 – - 0.419
Treatment	- 9.016	4.420	- 0.241	0.045	- 17.815 – - 0.218

B, unstandardized beta-coefficient; SE, standard error; Beta, standardized beta-coefficient; 95% CI LB – UB, 95%, confidence interval lower bound – upper bound; FU, follow-up; Treatment, primary ACL. repair vs. ACL reconstruction.

When comparing grafts, improved joint awareness was noted in patients treated with autograft tissue compared to allograft tissue; however, the difference did not reach significance due to the small number of patients (80.0 vs. 67.9, $P = 0.147$).

Discussion

The main finding of this study was that patients treated with primary ACL repair had less knee awareness - indicated by higher FJS scores - of their operated knees in everyday life compared to patients who were treated with ACL reconstruction at short-term (two to five years) follow-up. The FJS has recently been introduced as a tool to measure a patient's level of joint awareness.[17] A 'forgotten' joint excludes any subjective impairments such as instability, pain, or stiffness and integrates other variables including patient's expectation and psychological factors as well.[28] Furthermore, joint awareness, measured with the FJS-12, enables clinicians to assess both short-term outcomes regarding functional activity, while also allowing them to monitor changes over time, such as the development of osteoarthritis (OA).[17] Although the FJS is a relatively new, and not commonly used outcome measure in ACL surgery, this concept of 'joint awareness' can therefore be considered as an interesting tool to assess subjective patient-reported outcomes following surgery.

In the present study, patients following arthroscopic primary ACL repair had significantly less day-to-day knee joint awareness as compared to patients who underwent ACL reconstruction at short- to mid-term follow-up (85.3 vs. 74.5, respectively), which confirmed the hypothesis of this study. A possible explanation for this finding is that primary repair surgery is felt to be less invasive as opposed to reconstruction surgery, while also focusing on more tissue preservation. With reconstruction, on the other hand, the native ligament is removed, tunnels are drilled and graft site morbidity is present.[29] We speculate that it is these factors (preservation of the native ligament, avoidance of tunnel drilling and graft site morbidity) that contribute to decreased day-to-day knee joint awareness following primary repair as compared to ACL reconstruction.

When reviewing prior published studies, the literature concerning joint awareness after ACL surgery is scarce. Behrend et al. developed and validated the questionnaire in 2012 and initially designed the FJS-12 for arthroplasty surgery, but more recently they have also validated the questionnaire for ACL surgery.[22] In their study in 2017, significantly lower FJS were noted following reconstruction surgery compared to healthy controls during medium- (71.6 vs. 88.1) and long-term (70.1 vs. 90.0) follow-up.[23] Interestingly, in their study the authors found in their study that healthy controls were occasionally aware of their joints in daily life and did not score the maximum score of 100 (88.1 at short-term and 90.0 at 10-year follow-up). The FJS score in our primary repair group was 85.3 which is almost similar to healthy controls, wheares the reconstruction group did not approach this score of healthy controls (74.5). When comparing the findings of the FJS score in the reconstruction group in our study to the study of Berhrend et al., it was noted that the FJS score was quite similar to that found in their study (74.5 and 71.6, respectively), confirming the similarity found in the reconstruction group of both studies. Furthermore, these findings also suggests that the difference in FJS between repair and reconstruction are also clinically relevant when reviewing the literature (85.3 in our study as compared to 70.1 in the study of Berhrend et al.).

As previously mentioned, the FJS is, in comparison to other patient-reported outcomes, not limited by a ceiling effect,[22] and is therefore well suited to report on subjective patient-reported outcomes. The validated and context-specific minimal clinically important difference (MCID) has been determined between a value of 13-14 in patients with TKR.[30] It should be noted, that a validated MCID has not been developed for ACL surgery. A general method for defining the MCID is to use half of the standard deviation (SD) as an estimated MCID.[26] When reviewing the SD of the entire cohort, the noted difference in FJS scores of 10.8 was indeed more than half of the SD (9.7), and therefore our findings are considered clinically relevant differences for patients between primary repair and reconstruction. Nonetheless, it should be noted that studies determining the MCID for FJS in ACL surgery are needed.

Concerning age-specific outcomes, following primary repair compared to reconstruction, a significant difference of 22.7 points (85.3 vs. 62.6, $P = 0.007$) in FJS was noted in older patients (> 30 years old) in the present study. Clinical evidence relating age specific differences with regard to joint awareness following repair as compared to reconstruction are lacking. A possible explanation might be associated with the aforementioned development of posttraumatic OA in this older cohort. Several studies have shown that a high incidence of posttraumatic osteoarthritis occurs following ACL reconstruction.[31,32] It might be possible that with the preservation focus of primary repair surgery, there might be less development of OA as compared to ACL reconstruction surgery. In an experimental study, Murray et al. noted that following primary repair less cartilage damage was seen as compared to ACL reconstruction in porcine models.[33] Similarly, it might be possible that the older patients had more OA development following reconstruction when compared to primary repair, however future prospective studies will be necessary needed to further assess this.

Concerning gender-specific outcomes, a significantly higher FJS scores were noted in male patients following primary repair as compared to reconstruction (12.5-point difference), whereas the difference between repair and reconstruction was not statistically significant in female patients (8.4-point difference). This may be explained by the fact that this group was underpowered (24 patients in repair group and 14 patients in reconstruction group) according to our sample size calculation (21 in each group). Interestingly, joint awareness between female and male patients were equal following primary repair, whereas male patients had more joint awareness compared to females following ACL reconstruction. This is different from the literature as Ryan et al. noted similar patient-reported outcomes in their systematic review between male and female patients following ACL reconstruction.[34] It is not known why male patients had lower scores in our study, as none of the other factors were significantly different between both groups.

Finally, this study noted significantly less knee joint awareness in patients with a higher BMI following repair compared to reconstruction (85.9 vs. 64.7, $P = 0.009$). Higher BMI is generally associated with inferior outcomes following reconstruction surgery (e.g., less range of motion, more postoperative pain, lower IKDC scores and more likely to require additional surgery in the setting of ACL reconstruction).[35] A potential explanation for the larger difference in joint awareness between both procedures might be the higher weight-bearing pressure in their knees,[36] and that differences in joint awareness might be magnified in these patients by their body weight.

Limitations

Limitations certainly exist present in the present study. First, due to the retrospective design of the study, potential selection bias in the surgical treatment could have occurred. Secondly, age and follow-up time were not comparable between both groups, which could have influenced the outcomes in this study as a recent study found higher FJS with increasing age in the US general population, possibly due to a decrease in activity levels.[18] With regard to duration of follow-up, the potential development of OA may influence the joint awareness as lower FJS can be expected due to degenerative changes.[23] However, in our multivariate regression analysis, the difference in joint awareness remained statistically different between both cohorts. Although not statistically significant, there might be differences in other baseline characteristics between the groups, such as delay from injury to surgery or chondral or meniscus injuries that may have influenced outcomes in this study. Thirdly, the FJS-12 is only validated for ACL reconstruction and not specifically for ACL repair and future studies need to validate this. Nonetheless, we believe that the validation for ACL reconstruction enables us to perform this study since ACL reconstruction is the gold standard for surgical ACL treatment and primary repair was compared to this gold standard. Moreover, the FJS-12 was only completed after surgery; therefore, the pre-injury joint awareness was not taken into account. For this reason, no proportion of patients exceeding the MCID could be calculated. Finally, the different surgical techniques in the repair group (with or without additional suture augmentation) and in the reconstruction group (different grafts) could potentially have influenced our results although it was noted that the FJS scores in our reconstruction group were nearly identical to the FJS scores in the study by Behrend et al.[23]

Conclusion

Based on the data in this study, patients undergoing arthroscopic primary ACL repair can expect to have less daily awareness of their operated knee at short-to-mid-term follow-up compared to ACL reconstruction.

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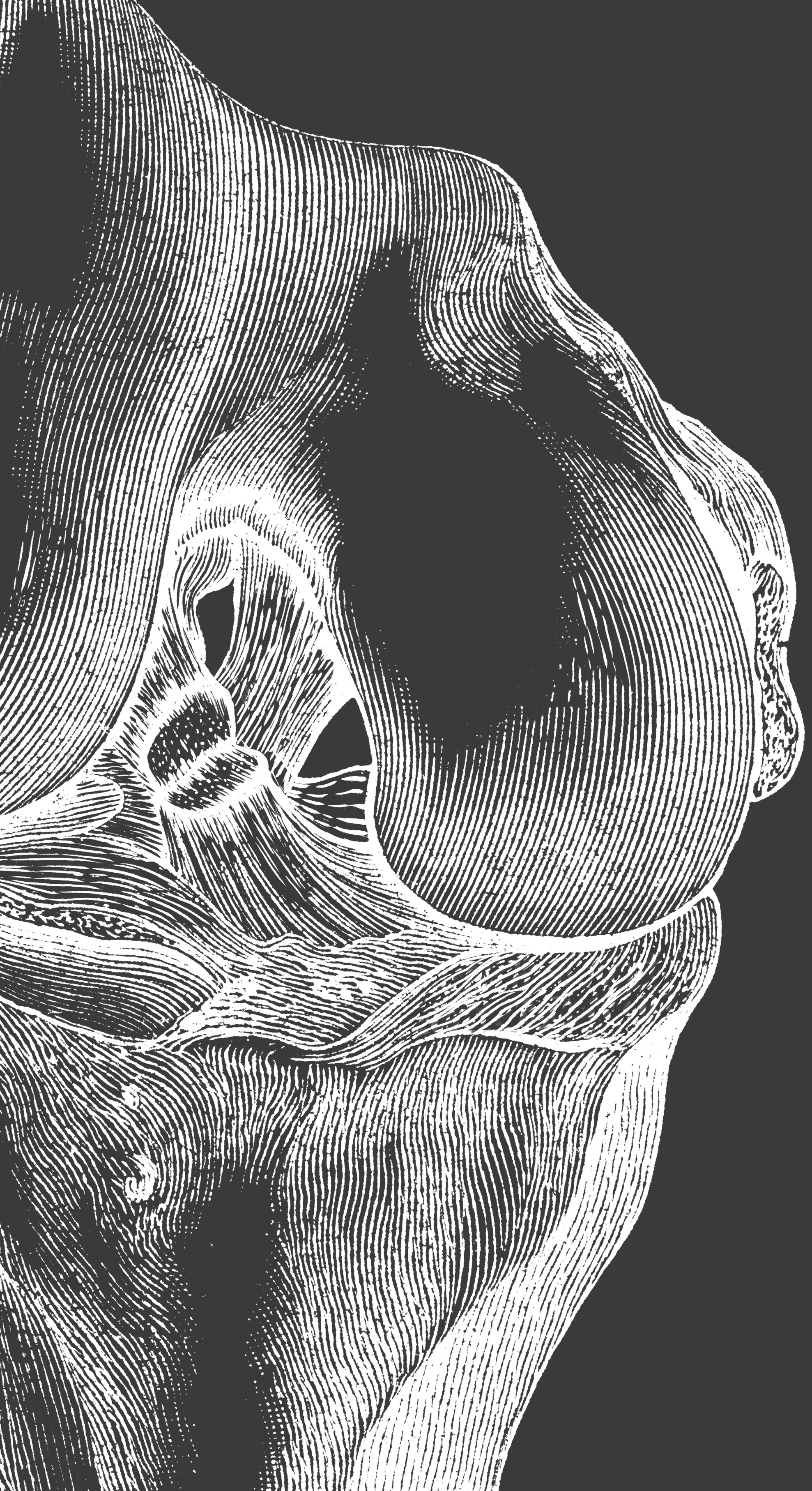

Chapter 11

A prospective comparison of postoperative pain and opioid consumption between primary repair and reconstruction of the anterior cruciate ligament

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Abstract

Background
Anterior cruciate ligament reconstruction (ACLR) is associated with postoperative pain and necessitates using perioperative nerve blocks and multimodal analgesic plans.

Purpose
To assess postoperative pain and daily opioid use between ACL repair and ACLR and also, to assess whether ACL repair could be performed successfully without using long-acting nerve blocks.

Study-design
Cohort study.

Methods
All eligible patients undergoing ACL surgery between 2019-2022 were prospectively enrolled. Patients were treated with primary repair if proximal tears with sufficient tissue quality were present, and otherwise undergoing single-bundle ACLR with either hamstring or quadriceps autografts. Patients were divided into three groups: ACLR with adductor canal nerve block (up to 20ml of 0.25% bupivacaine with 2mg dexamethasone), which is standard of care, and primary repair with and without nerve block. Pain scores on a visual analog scale and number of opioids used were recorded during the first 14 postoperative days (POD). Furthermore, patients completed the Quality of Recovery (QoR-15) survey and range of motion (ROM) was assessed. Group differences were compared using Mann-Whitney U tests and chi-square tests.

Results
Seventy-eight patients were included, of which 30 (39%) underwent ACLR, 19 (24%) ACL repair with nerve block, and 29 (37%) ACL repair without nerve block. Overall, repair patients used significantly fewer opioids than those treated with ACLR on POD 1 (1 vs. 3, $p=0.027$) and POD 2 (1 vs. 3, $p=0.014$), while also using less opioids in total (3 vs. 8, $p=0.038$). This difference was even more significant when only analyzing those patients who received postoperative nerve blocks (1 vs. 8, $p=0.029$). QoR-15 scores were significantly higher throughout the first postoperative week for repair patients, and they had more ROM (all $p<0.05$). Comparing repair patients with and without nerve block, there were no statistical differences in pain scores, opioid usage, nor QoR-15 scores (all $p>0.05$).

Conclusion
ACL repair patients experienced less postoperative pain during the first two weeks after surgery, while using significantly less opioids than those treated with ACLR. Furthermore, they had improved knee function and higher recovery quality than ACLR patients during the initial postoperative period. Finally, it seems that postoperative nerve blocks might not be necessary after ACL repair.

Introduction

Anterior cruciate ligament (ACL) tears are one of the most common surgically treated sports injuries, with over 200,000 procedures performed in the United States each year.[4] Currently, the surgical standard for patients with these injuries is ACL reconstruction.[13,32,34] Nevertheless, this procedure is associated with significant pain postoperatively, especially during the first days of surgery, necessitating the use of perioperative nerve blocks and multimodal analgesic plans.[3,8] Effective postoperative pain management, however, is essential for early mobilization, quick recovery, and patient satisfaction in patients treated for ACL injuries.[20]

In recent years, arthroscopic primary ACL repair has gained traction as an alternative to reconstruction for a select group of patients with proximal ACL tears.[11,29] By preserving native tissue and avoiding donor-site morbidity, this procedure is considered significantly less invasive than reconstructive surgery.[14,22] As a result, repair patients might experience less postoperative pain than those undergoing ACL reconstruction.[5] Given the potential risks of prolonged postoperative analgesic use and the current opioid epidemic in the United States,[21,25] it therefore seems intuitive to pursue less invasive surgical treatments, such as primary repair, that limit pain and avoid the need for excessive opioid use.

This study aimed to prospectively assess postoperative pain scores and daily opioid use between ACL repair and ACL reconstruction, and to further assess if ACL repair could be performed without using long-acting nerve blocks and thereby not increasing postoperative opioid usage. The hypothesis was that due to less postoperative pain, primary repair would reduce the need for opioid use as compared to ACL reconstruction, but that perioperative nerve blocks would still be needed for optimal postoperative pain management following this procedure.

Materials and methods

Patient selection

Following Institutional Review Board approval (IRB number: 2019-1403), a prospective cohort study was conducted between December 2019 and July 2022. All patients were treated using a previously described treatment algorithm in which patients with proximal ACL tears and sufficient tissue quality were primarily repaired, while a standard ACL reconstruction was performed otherwise.[16] Inclusion criteria were patients (i) aged between 18 to 55 years (ii) and treated with primary repair or ACL reconstruction (either with quadriceps (QT) or hamstring (HT) autograft). Exclusion criteria were patients with (i) a history of preoperative opioid use (defined as opioid use within three months of surgery), (ii) ACL revision surgery, (iii) multi-ligament knee injuries, (iv) bilateral knee injuries, (v) or insufficient follow-up.

During this period, 207 patients presented with isolated ACL injuries. Of these patients, 126 met the inclusion criteria and consented to participate in the study, of which follow-up could not be obtained for 45 patients. Ultimately, three patients were additionally excluded since they misinterpreted the prescribing regimen (as they took all prescribed narcotics rather than only using painkillers while experiencing significant pain), leaving 78 patients for final analysis.

At our institution, most patients treated with ACL reconstruction receive a peripheral adductor canal block (standard of care). For repair patients, however, this was based upon anesthesiologist preferences. To determine clinical outcomes, patients were therefore divided into three groups: ACL reconstruction with a nerve block (group A; n = 30), primary repair with a nerve block (group B; n =19), and primary repair without nerve block (group C; n = 29). For final analysis, patients treated with ACL reconstruction with a nerve block were first compared to patients treated with primary repair (with and without nerve block (group A vs. (B+C)). Then, only patients with a nerve block were included to compare outcomes between primary repair and ACL reconstruction (group A vs. B). Lastly, repair patients with and without nerve blocks were compared to assess if nerve blocks are actually needed following this procedure (group B vs. C).

Surgical techniques

All surgeries were performed by the senior author (GSD) either at the main hospital or ambulatory surgery center. Primary ACL repair using dual suture anchor fixation with suture augmentation was performed as previously described.[17] In brief, both bundles of the ACL were first identified, and then sutured separately from distal to proximal in an alternating and interlocking Bunnell-type pattern. Subsequently, two 4.5 mm x 20 mm holes were drilled or punched depending on the density of the bone, and then tapped. Then, the posterolateral (PL) suture anchor was deployed in the femoral cortex retensioning the PL bundle back to its origin. Next, the anteromedial (AM) suture anchor was pre-loaded with a suture augmentation and was subsequently used to refixate the AM bundle back to its origin. After the AM anchor was deployed, the suture augmentation was channeled through a small 2.5 mm tunnel, drilled from the AM cortex of the tibia to the central aspect of the anterior third of the tibial footprint. Finally, another suture anchor was then deployed for fixation of the suture augmentation into the anteromedial cortex of the tibia.

For non-repairable ACL tears (i.e., midsubstance tears or ligaments with poor tissue quality), a standard single bundle anatomic ACL reconstruction was performed using anteromedial drilling with either a QT or HT autograft [7,33]. Graft choice was based on the surgeon and patient preference, and it should be noted that a tourniquet was used during the graft harvesting.

Pain management protocol

As perioperative analgesia, all patients received spinal anesthesia (either 0.5% bupivacaine or 1.5% mepivacaine), intravenous (IV) Tylenol (up to 1mg), and IV Toradol (up to 30mg). Those patients receiving a postoperative nerve block received a peripheral adductor canal block that consisted of up to 20ml of 0.25% bupivacaine with 2mg dexamethasone. For local anesthetics injected at the portal and incision sites, reconstruction patients received up to 30ml of 0.25% bupivacaine, while those undergoing ACL repair received up to 10ml. Finally, all patients were prescribed 5mg Roxicodone (one or two tablets every four to six hours as needed), 7.5mg Meloxicam (one tablet per day up to 15 days) and 500mg Tylenol (one or two tables every six hours as needed) after surgery.

Postoperative management

All patients followed the same rehabilitation protocol. Patients were placed in a hinged brace in the operating room, which was locked in extension. The main focus during the first postoperative days was edema control and regaining early range of motion (ROM). Gentle ROM exercises were initiated immediately after surgery to avoid quadriceps atrophy, and weight bearing was allowed as tolerated, depending on concomitant meniscal treatment. Once quadriceps control was regained roughly four weeks after surgery, the brace was unlocked for ambulation. From that point, formal ACL rehabilitation using a mile-stone-based protocol was followed. When muscle strength (>90% isokinetic strength compared with contralateral leg) and full ROM were restored, gradual return to sports (RTS) was allowed, usually between six months to one year postoperatively [30].

Data collection

All patients were consented before participating. To compare outcomes, all patients were asked to complete six short surveys on postoperative days (POD) one, two, three, four, seven, and fourteen. First, patients were asked to complete their pain scores on a visual analog scale ranging from "no pain" to "unbearable pain" from 0 to 100.[10] Patients rated their pain both at rest, on average, and at its highest over the previous 24 hours. Secondly, patients recorded the number of analgesics used over the last 24 hours for POD one until four, while this was reported over the last three and seven days for POD seven and fourteen, respectively. This included the usage of 5mg Oxycodone, 7.5mg Meloxicam, 500mg Tylenol, and others. In addition, on POD one, four, seven, and fourteen, patients were asked to complete the Quality of Recovery (QoR-15). The QoR-15 is a validated 15-item patient-reported outcome survey that measures the quality of recovery after surgery and is scored between 0 and 100.[27] A higher score indicates a higher quality of recovery. All patient-reported data was collected using the mobile application MyCAP, which allows the patient to complete surveys associated with REDCap projects (Research Electronic Data Capture; Vanderbilt University, Nashville, TN).[24] Finally, charts were reviewed to assess patient demographics, including age, gender, side of injury, delay from injury to surgery, meniscal or chondral injuries, and ROM at the first postoperative visit (approximately one week after surgery and measured using a goniometer).

Statistical analysis

SPSS Version 25 (SPSS Inc., Armonk, NY) was used for all statistical analysis. Data was first tested for normal distribution using Shapiro-Wilk tests. As data was not normally distributed, descriptive analysis of continuous variables were presented as median with interquartile ranges (IQR), while discrete variables were presented as number (n) with percentage (%). Univariate analysis was conducted using Mann–Whitney U test for continuous variables, while Chi-square tests or Fisher exact tests (in case one of the numbers is < 5) were used to compare discrete variables. In case of multiple comparisons, an ANOVA test with Bonferroni correction was used. Considering an alpha error of 0.05 and power of study as 80%, 19 patients per group were needed to detect a 33% difference in the total number of opioid pills taken. Significance of statistical differences was attributed to p-value of < 0.05

Results

Patient demographics

A total of 78 patients were included, of which 30 (39%) underwent ACL reconstruction (group A), 19 (24%) underwent primary ACL repair with nerve blocks (group B), and 29 (37%) underwent primary ACL repair without nerve block (Group C). The overall median age at surgery was 32 years (IQR 23 – 43 years), 59% were male, median BMI was 25.1 (IQR 22.4 – 27.1), and median delay between injury surgery was 38 days (IQR 25 – 82 days). In patients treated with reconstruction, 13 (43%) underwent ACL reconstruction using HT autograft, while 17 (57%) received a QT autograft.

When comparing patients undergoing ACL reconstruction (group A) with ACL repair (group B + C), reconstruction patients were younger than those treated with ACL repair (22.3 vs. 39.6 years, p <0.001), but there were no significant differences in gender, side of injury, delay between injury to surgery, BMI and meniscal or chondral lesions between both groups (all p > 0.10; Table 1).

Table 1. Patient characteristics following primary ACL repair and ACL reconstruction

	Reconstruction (n = 30)		Primary repair (n = 48)		
	Median	IQR	Median	IQR	P-value
Age (years)	22.3	20.5 – 30.7	39.6	30.7 – 47.1	<0.001
Male gender; N (%)	19 (63%)		21 (44%)		0.536
Right side; N (%)	16 (53%)		25 (52%)		0.914
Delay (days injury-surgery)	45	25 – 88	35	25 – 72	0.444
BMI (kg/m^2)	24.7	22.5 – 26.5	25.2	22.3 – 28.2	0.307
FU (days)	14	14 - 14	14	14 - 14	0.519
Concomitant damage					
Meniscus injury; N (%)	25 (83%)		32 (67%)		0.106
Chondral injury; N (%)	5 (21%)		15 (31%)		0.276
Meniscal treatment					0.734
Partial meniscectomy; N (%)	8 (27%)		10 (21%)		
Repair; N (%)	13 (43%)		19 (40%)		
Both: N (%)	3 (10%)		2 (4%)		
Conservative: N (%)	1 (3%)		0 (0%)		

IQR indicates interquartile range; N, number of patients; BMI, body mass index; FU, follow-up

When comparing patients undergoing ACL reconstruction (group A) with ACL repair with nerve block (group B), reconstruction patients were younger than those treated with ACL repair (22.3 vs. (22.3 vs. 43.5 years, p <0.001). There were no differences in any of the other patient demographics (all p > 0.05).

When comparing repair patients with and without block (group B vs. C), there were no differences in age, gender, BMI, and chondral lesions (all $p > 0.05$). However, patients who did not receive a block had shorter delay between injury to surgery (29 vs. 61 days, $p = 0.011$) and less meniscal injuries than those who received a nerve block (55% vs. 86%, $p = 0.037$).

Part A: ACL reconstruction with block vs. ACL repair (with and without block)

Pain scores

When comparing preoperative VAS pain scores, no statistical differences were found in median pain scores between repair and reconstruction patients (8 vs. 10, $p = 0.399$). Postoperatively, patients treated with repair reported significantly lower average pain scores compared to those undergoing ACL reconstruction on POD 1 (median 22 vs. 53, $p = 0.004$), POD 2 (median 38 vs. 51, $p = 0.005$), POD 3 (median 25 vs. 32, $p = 0.040$), and POD 4 (median 20 vs. 29, $p = 0.015$). Although there was no statistical difference in pain scores on POD 7 (median 15 vs. 17, $p = 0.190$), repair patients did report lower average pain scores on POD 14 (median 8 vs. 10, $p = 0.032$; Table 2).

Table 2. Pain scores following ACL reconstruction and primary repair with and without nerve block

	(A) ACLR with block (n = 30)	(B) Repair with block (n = 19)	(C) Repair without block (n = 29)	ACLR vs. Repair	A vs. B	B vs. C
	Median (IQR)	Median (IQR)	Median (IQR)	P-value	P-value	P-value
Pre-op						
VAS Pain ave.	10 (4 – 19)	10 (0 – 20)	5 (0 – 13)	0.339	0.844	0.874
POD 1						
VAS Pain rest	40 (18 – 60)	20 (1 – 49)	20 (3 – 44)	**0.010**	**0.044**	0.728
VAS Pain ave.	53 (29 – 67)	22 (5 – 54)	21 (7 – 53)	**0.004**	**0.012**	0.404
VAS Pain max	71 (44 – 87)	45 (3 – 77)	53 (25 – 76)	**0.038**	0.056	0.591
QoR	68 (51 – 68)	75 (63 – 82)	69 (60 – 79)	**0.002**	**0.007**	0.276
POD 2						
VAS Pain rest	45 (31 – 62)	41 (15 – 57)	30 (13 – 50)	**0.025**	0.304	0.321
VAS Pain ave.	51 (40 – 65)	46 (20 – 55)	30 (18 – 50)	**0.005**	0.109	0.665
VAS Pain max	71 (60 – 82)	60 (30 – 80)	50 (36 – 78)	**0.010**	0.126	0.932
POD 3						
VAS Pain rest	30 (20 – 42)	19 (0 – 38)	10 (7 – 40)	**0.014**	0.084	0.816
VAS Pain ave.	32 (22 – 51)	25 (5 – 40)	24 (10 – 48)	**0.040**	0.134	0.665
VAS Pain max	50 (34 – 70)	45 (9 – 62)	41 (18 – 60)	0.060	0.139	0.717
POD 4						
VAS Pain rest	20 (14 – 43)	8 (0 - 39)	11 (1 – 33)	**0.024**	0.055	0.792
VAS Pain ave.	29 (20 – 50)	19 (5 – 42)	20 (7 – 33)	**0.015**	0.082	0.783
VAS Pain max	45 (30 – 65)	30 (10 – 53)	32 (10 – 40)	**0.027**	0.083	0.254
QoR	70 (64 – 79)	81 (79 – 88)	79 (66 – 87)	**0.005**	**0.002**	0.411

Table 2. Pain scores following ACL reconstruction and primary repair with and without nerve block *(Continued)*

	(A) ACLR with block (n = 30)	(B) Repair with block (n = 19)	(C) Repair without block (n = 29)	ACLR vs. Repair	A vs. B	B vs. C
	Median (IQR)	Median (IQR)	Median (IQR)	P-value	P-value	P-value
POD 7						
VAS Pain rest	15 (8 – 20)	6 (0 - 21)	10 (2 – 20)	0.093	0.085	0.904
VAS Pain ave.	17 (12 – 30)	15 (4 – 25)	12 (6 – 28)	0.190	0.397	0.759
VAS Pain max	30 (17 – 55)	30 (10 – 49)	30 (13 – 42)	0.423	0.676	0.321
QoR	75 (69 – 85)	82 (78 – 93)	82 (72 – 89)	**0.016**	**0.018**	0.321
POD 14						
VAS Pain rest	4 (3 – 10)	4 (0 – 10)	0 (0 – 10)	0.798	0.900	0.810
VAS Pain ave.	10 (5 – 18)	7 (0 – 11)	8 (1 – 15)	**0.032**	**0.043**	0.461
VAS Pain max	25 (10 – 33)	10 (2 – 40)	16 (5 – 32)	0.205	0.165	0.430
QoR	82 (72 – 87)	88 (81 – 97)	89 (80 – 95)	**0.008**	0.057	0.875

IQR indicates interquartile range; POD, postoperative day; VAS, visual analogue scale; ave, average; QoR, Quality of Recovery

Analgesic use

When reviewing analgesic use, it was noted that patients treated with primary repair used significantly fewer opioids than those treated with ACL reconstruction on POD 1 (median 1 vs. 3 pills, $p = 0.027$) and POD 2 (median 1 vs. 3 pills, $p = 0.014$). In addition, repair patients used significantly less opioids in total (median 3 vs. 8 pills, $p = 0.038$, respectively) and stopped taking opioids earlier after surgery than reconstruction patients (POD 1.5 vs. 3, $p = 0.015$; Table 3).

Quality of recovery

When reviewing QoR-15 scores, those undergoing primary repair reported significantly better quality of their postoperative recovery on POD 1 (71 vs. 68, $p = 0.002$), POD 4 (81 vs. 70, $p = 0.005$), POD 7 (82 vs. 75, $p = 0.016$), and POD 14 (88 vs. 82, $p = 0.008$; Table 2).

ROM

Patients who underwent primary repair had significantly more knee flexion when compared to patients who underwent reconstruction at one week after surgery (90° [IQR 73 – 90°] vs. 50° [IQR 44 – 81°], $p < 0.001$; Table 4).

Graft choice

There was no statistical difference in the total number of opioids used between patients treated with QT or HT autografts (6 vs. 11 pills, $p = 0.112$). Furthermore, no statistical differences were found in pain scores and QoR-15 scores during the first 14 days after surgery between both groups, while there was also no difference in ROM, respectively (all $p > 0.05$).

Part B: ACL reconstruction with block vs. ACL repair with block

Pain scores

No statistical differences were found in median preoperative pain scores between repair and reconstruction patients (10 vs. 10, $p = 0.884$). After surgery, patients treated with repair reported significantly lower average pain scores compared to those undergoing ACL reconstruction on POD 1 (median 22 vs. 53, $p = 0.012$). Throughout the first 14 postoperative days, repair patients reported lower median pain scores, although these did not reach statistical differences (all > 0.05) except on POD 14 (average pain 7 vs. 10, $p = 0.043$; Table 2).

Analgesic use

Regarding analgesic use, patients treated with primary repair used significantly fewer opioids than those treated with ACL reconstruction on POD 1 (median 0 vs. 3 pills, $p = 0.010$) and POD 2 (median 1 vs. 3 pills, $p = 0.043$). Overall, repair patients used significantly less opioids in total (median 1 vs. 8 pills, $p = 0.029$, respectively; Table 3).

Table 3. Number of opioids following ACL reconstruction and primary repair with and without nerve block

	(A) ACLR with block (n = 30)	(B) Repair with block (n = 19)	(C) Repair without block (n = 29)	ACLR vs. Repair	A vs. B	B vs. C
	Median (IQR)	Median (IQR)	Median (IQR)	P-value	P-value	P-value
POD 1	3.0 (1.0 – 5.3)	0.0 (0.0 – 2.0)	2.0 (0.0 – 4.5)	**0.027**	**0.010**	0.098
POD 2	3.0 (0.8 – 5.0)	1.0 (0.0 – 3.0)	1.0 (0.0 – 3.5)	**0.014**	**0.043**	0.973
POD 3	0.5 (0.0 – 2.3)	0.0 (0.0 – 1.0)	0.0 (0.0 – 1.5)	0.127	0.100	0.512
POD 4	0.0 (0.0 – 1.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.5)	0.389	0.195	0.388
POD 7a	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.764	0.592	0.692
POD 14[b]	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.260	0.094	0.077
Total# opioids	8.0 (2.8 – 13.3)	1.0 (0.0 – 10.0)	3.0 (0.5 – 10.5)	**0.038**	**0.029**	0.415
Last POD opioid use	3.0 (2.0 – 4.0)	1.0 (0.0 – 4.0)	2.0 (0.5 – 3.0)	**0.015**	0.082	0.771

IQR indicates interquartile range; POD, postoperative day; [a] Number of pills over the last three days; [b] Number of pills over the last seven days

Patients treated with primary repair had a significantly higher likelihood of using less than five narcotic pills in total as compared to those treated with ACL reconstruction (OR 3.3, p = 0.041), while they had a 6.5 higher likelihood of using opioids for less than two days after surgery, respectively (p = 0.009).

Quality of recovery

When reviewing QoR-15 scores, primary repair patients reported significantly better quality of their postoperative recovery on POD 1 (75 vs. 68, p = 0.007), POD 4 (81 vs. 70, p = 0.002), and POD 7 (82 vs. 75, p = 0.018), while the difference did not reach significance on POD 14 (88 vs. 82, p = 0.057; Table 2).

ROM

Those patients undergoing primary repair had significantly more knee flexion when compared to patients who underwent reconstruction at one week (90° [IQR 60 – 90°] vs. 50° [IQR 44 – 81°], p = 0.016; Table 4).

Part C: ACL repair with vs. without block

There were no statistical differences in pain scores, opioid use, and QoR-15 scores during the first 14 days after surgery between repair patients treated with and without nerve block (all p > 0.05; Table 1,2,3). However, patients without nerve blocks had significantly more knee flexion than patients with blocks at the first postoperative visit but this was not considered clinically relevant (90°; IQR 85 – 95° vs. 90°; IQR 60 – 90°, p = 0.017; Table 4).

Table 4. Range of motion after ACL reconstruction and primary repair with and without nerve block

	(A) ACLR with block (n = 30)	(B) Repair with block (n = 19)	(C) Repair without block (n = 29)	ACLR vs. Repair	A vs. B	B vs. C
	Median (IQR	Median (IQR	Median (IQR	P-value	P-value	P-value
Extension	0° (0 – 0°)	0° (0 – 0°)	0° (0 – 0°)	0.004	0.063	>0.999
Flexion	50° (44 – 81°)	90° (60 – 90°)	90° (85 – 95°)	<0.001	0.016	0.017

IQR indicates interquartile range

Discussion

The main finding of this study was that patients treated with primary repair had lower pain scores and used significantly fewer opioids than those treated with ACL reconstruction during the first two weeks after surgery. Furthermore, patients undergoing ACL repair experienced better quality of their recovery and had an earlier return of ROM when compared to patients who underwent reconstruction. Finally, it seemed that patients treated with primary repair did not experience enough pain to benefit from a postoperative nerve block.

An important factor influencing patient satisfaction following surgery is postoperative pain.[23] Although several improvements in surgical techniques and postoperative pain protocols have improved ACL reconstruction outcomes, patients often struggle with and complain of severe postoperative pain, leading to extensive postoperative analgesic use.[6,12] Nevertheless, since pain in the immediate postoperative period can be a significant restraint to starting an early rehabilitation program, adequate pain management enables immediate weight-bearing and ROM excises, lowering the risk of postoperative complications, including arthrofibrosis and quadriceps atrophy.[26,28] Therefore, it is important to assess surgical options that may reduce early postoperative pain, thereby improving patient outcomes and potentially leading to an earlier return to full activities.[30]

This prospective study noted that arthroscopic primary ACL repair patients experienced lower pain scores and used significantly fewer opioid pills than those treated with reconstructive surgery (median 3 vs. 8 pills). It should be noted that this difference was even more significant when only analyzing patients who received a postoperative nerve block (median 1 vs. 8 pills). Due to lower pain levels, this study also showed that primarily repairing a torn ACL leads to earlier return of ROM of the knee joint, confirming the results of a previous retrospective study assessing the same outcome.[18] As a result, patients treated with repair seem to have improved quality of recovery as compared to those treated with ACL reconstruction. The less invasive nature of ACL repair surgery likely plays an important role in these differences. With ACL repair, the native tissues of the ligament are preserved, only small tunnels are drilled (3.5mm vs. 7 to 11mm),[19] and there is no need for graft harvesting; thus, eliminating graft-site morbidity.[9,31]

When reviewing the literature, only two studies have assessed pain and postoperative opioid use following primary ACL repair. In 2021, Connelly et al. reported similar outcomes in a retrospective study in which ACL repair patients experienced less short-term postoperative pain and were prescribed fewer narcotics than those treated with ACL reconstruction.[5] Similar to the present study, patients treated with repair also underwent fixation using suture anchors. On the contrary, Barnett et al. did not find differences in pain scores and overall opioid intake between patients treated with repair as compared with ACL reconstruction.[1] When looking closely at their results, however, these patients underwent bridge-enhanced ACL repair (BEAR), performed via arthrotomy, that likely results in more pain than an arthroscopic ACL repair procedure. Therefore, it seems that based on the currently available evidence, repairing a torn ACL, rather than reconstructing it, leads to significantly lower pain scores, less overall opioid use, and improved physical comfort.

Interestingly, this study showed that patients treated with ACL reconstruction used 8 times more narcotics than those undergoing primary repairs with block and 2.5 times more than those without block. When reviewing those patients treated with repair, patients without long-acting nerve blocks had similar quality of recovery compared to those with a nerve block. However, it is important to note that patients with a block used less opioids than those who did not receive this block on POD 1 (0 vs. 2 pills) and in total (1 vs. 3 pills), but this was not significant. This can obviously be explained by the use of nerve blocks, which can reduce reported postoperative pain scores for up to 12 hours after surgery.[6] Furthermore, it should be noted that although there was a significant difference in knee flexion between both groups, this was not considered clinically relevant. Therefore, although the optimal pain management for patients undergoing ACL repair seems to include using long-acting nerve blocks, this procedure can be performed without while still effectively controlling postoperative pain due to the minimally invasive nature of surgery.

There are limitations to this study. First of all, although VAS scores have been proven reliable in assessing acute pain, determining pain perception remains relatively subjective and can be influenced by pain tolerance, anxiety, and psychological stress. Secondly, the nonrandomized nature of this prospective study could have induced potential selection bias, although the decision of receiving a nerve block was based on the preference of the anesthesiologist. Thirdly, it should be noted that repair patients were older than those undergoing reconstruction (39.6 vs. 22.3 years), which can be explained by the fact that proximal tears occur more often in older patients.[15] Nevertheless, this could have influenced the outcomes of this study due to the possible better pain tolerance in older patients. In addition, using a tourniquet during graft harvesting could have influenced the pain scores in this study, as this is associated with increased pain during the first 24 hours after surgery.[2] It should also be noted that the main goal of this study was to report the differences in pain and opioid use between repair and reconstruction patients rather than reporting the optimal pain management strategy and that 36% of patients were lost during follow-up. Finally, although subgroup analysis between both groups did not show any statistical differences, patients undergoing ACL reconstruction were treated with two types of soft tissue grafts (HT- and QT-autograft), which might have influenced the outcomes of this study.

Conclusion

ACL primary repair patients experienced less postoperative pain during the first two weeks after surgery even while using significantly less opioids than those treated with ACLR. Furthermore, they had improved knee function and higher recovery quality than ACLR patients during the initial postoperative period. Finally, it seems that postoperative nerve blocks might not be necessary after ACL repair.

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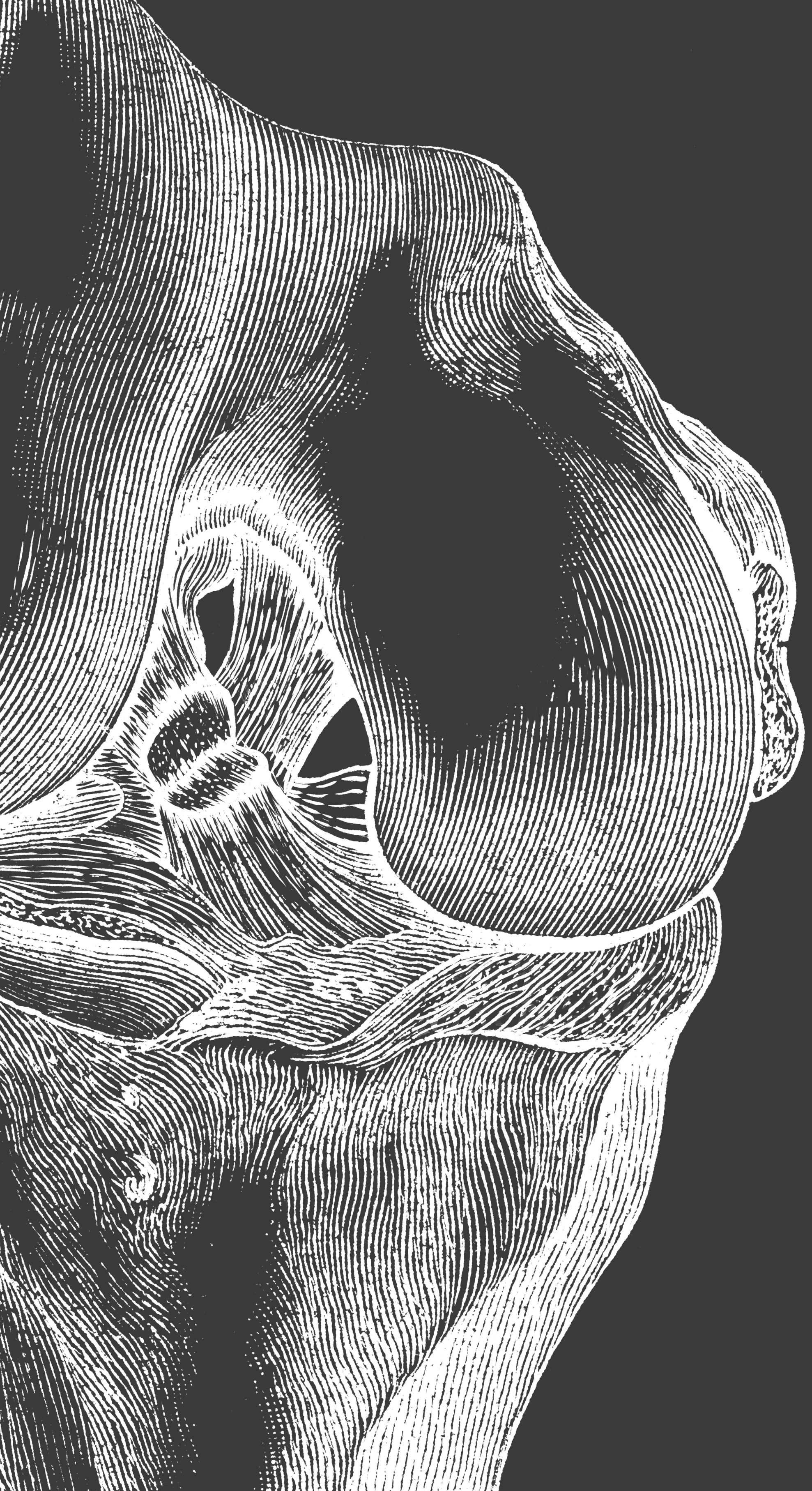

Chapter 12

Acute and delayed anterior cruciate ligament repair results in similar short to mid-term outcomes

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Abstract

Background

To assess whether primary repair of proximal ACL tears in the delayed setting leads to similar clinical and functional outcomes as compared to ACL repair in the acute setting.

Methods

All patients with proximal tears with good tissue quality treated in the acute (≤3 weeks post-injury) and delayed setting (>3 months post-injury) were retrospectively reviewed at minimum 2-year follow-up. Ipsilateral reinjury or reoperation and contralateral injury rates were recorded. Functional outcomes were evaluated using the Lysholm, modified Cincinnati, Single Assessment Numeric Evaluation, International Knee Documentation Committee subjective, Forgotten Joint Score-12, Anterior Cruciate Ligament–Return to Sport after Injury scale, and satisfaction scores. Finally, time to return to work, time to discontinue brace-usage, time to running, and time to return to sports were reviewed. Group differences were compared using chi-square tests and Mann-Whitney *U* tests.

Results

Sixty-nine patients were included, of which 34 (49%) were treated acutely and 35 (51%) in the delayed setting. Besides time from injury to surgery, patient demographics were similar between groups (all p>0.1). There were three reinjuries (9%) in the acute group and four in the delayed (11%; p>0.999). Reoperation, complication, and contralateral injury rates were similar between groups (all p>0.1), while functional outcomes were also comparable (all p>0.05).

Conclusion

This study found that acute and delayed primary ACL repair results in similar clinical and functional outcomes at short to mid-term follow-up. Therefore, the most important factors for repair surgery success seem to be tissue quality and tissue length, rather than acuity of the surgery.

Introduction

Anterior cruciate ligament (ACL) ruptures occur in over 200.000 patients in the United States each year and may lead to knee instability, functional impairments, and post-traumatic osteoarthritis (OA).[1,2] To restore knee stability in active patients, ACL reconstruction is often recommended over conservative treatment.[3] However, some disadvantages associated with this procedure persist, including loss of proprioceptive function, donor-site morbidity, and disappointing outcomes of revision surgery.[4–6] Therefore, arthroscopic primary ACL repair may represent a less morbid surgical option for patients with certain types of acute ACL injuries, although this treatment remains controversial.[7,8]

Several factors have been identified that contribute to the likelihood of successfully repairing a torn ACL, including surgical timing.[9] Although the ideal treatment window is debatable, several studies have advocated for early repair (within the first few weeks after injury) to optimize clinical outcomes.[7] A prolonged delay between injury and surgery can cause retraction and scarring of the ACL, which may lead to functional loss of healing potential.[10] Nevertheless, it has been suggested that some tears may even be repairable within the chronic phase[11], indicating that tissue length and quality may be more contributory to successful outcomes than acuity of the surgery. The current literature regarding primary repair in the delayed setting, however, remains limited.

The purpose of this study was to determine whether primary repair of proximal anterior cruciate ligament (ACL) tears in the delayed setting leads to the same outcomes as compared to ACL repair in the acute setting. The primary outcome of this study includes several patient-reported outcome measures (PROMs), and secondary outcomes include the failure and reoperation rates, and achievement of rehabilitation milestones. The hypothesis is that delayed repair will be inferior to acute repair in both PROMs and objective clinical assessments, while time to achieve rehabilitation milestones will be similar at short to medium-term follow-up.

Methods

Patient selection

This study was approved by our Institutional Review Board (IRB number: 2017-0404-CR3). A retrospective analysis of the prospectively collected data of the senior authors' database (GSD) was performed, in which all patients treated with arthroscopic primary repair for complete, isolated ACL tears between April 2008 and November 2018 were identified. All patients were treated according to the same surgical intra-operative treatment algorithm. With this treatment algorithm, primary ACL repair was performed in all patients presenting with proximal tears (i.e. when distal remnant length was sufficient to reattach the distal remnant back to the femoral insertion site) and with sufficient tissue quality to withstand suture passing (i.e. when the ligament can be tensioned without tearing the tissue). If the ligament was deemed non-repairable (i.e. midsubstance tear or insufficient tissue quality to withhold sutures), single-bundle ACL reconstruction was performed using various grafts. It is important to note that ACL repair was performed in all eligible patients, regardless of surgical delay.

During this time period, 189 patients underwent primary ACL repair. Patients were considered for inclusion if a minimum of two-year follow-up was available and if they were treated in the acute (within 3 weeks post-injury)[12], or in the delayed setting (after 3 months post-injury) due to late diagnosis, late referral, or other reasons[13]. Patients were excluded when treated in the subacute setting (n = 74), primary repair for distal ACL tears (n = 5), younger than 18 years of age (n = 29), or follow-up was insufficient (n = 12). Therefore, ultimately 69 patients treated with arthroscopic primary repair for proximal ACL tears were included in this study. Although this study demonstrates a unique analysis, it should be noted that some data has been reported on clinically in previous studies.[14–16]

Surgical technique

All surgeries were performed by the senior author (GSD). Primary ACL repair using dual suture anchor fixation was performed as previously described.[17] In brief, both ACL bundles were sutured individually from distal to proximal using in a Bunnell-type pattern using a Scorpion suture passer (Arthrex, Naples, FL). Each bundle was then reattached in anatomical fashion using a 4.75-mm BioComposite SwiveLock suture anchor (Arthrex). It is important to note that the availability of a new augmentation method (InternalBrace; Arthrex, Naples, FL) became clinically available in 2015 and then became standard of care in all patients. Following the same ligament suturing technique, the suture anchor of the anteromedial (AM) bundle is preloaded with an internal suture tape augmentation. After anchor deployment, the suture tape augmentation is channeled through a small 2.5 mm tibial tunnel. The suture augmentation is then tensioned in full extension and fixed to the anteromedial cortex of the tibia using single suture anchor fixation [18].

Post-operative management

All patients followed the same rehabilitation protocol in which early mobilization, passive range of motion (ROM) exercises, and swelling control were initiated within the first days following surgery. A knee-brace was worn in the first four weeks postoperatively with weight-bearing as tolerated. The brace was locked in extension until quadriceps muscle control was regained. After four weeks, formal physical therapy was continued as per guidance of their physical therapist. Sports activities were permitted at six to twelve months based upon sport-specific assessments.

Outcome measures

Patients were routinely evaluated at one week, one-, three-, and six months, and one-, two-, and five years. At each visit, patients underwent a standard clinical physical examination of the operated and contralateral knee performed by a member of the clinical team of the senior author (GSD), which included ROM, Lachman test, pivot shift test, and we recently started performing Rolimeter assessment (Aircast, Germany).

The primary outcome of this study includes several PROMs at a minimum of two years after surgery. Therefore, all patients, either seen in clinic or contacted for a telephone interview, were asked to complete a survey (in clinic or online) to evaluate functional outcomes after surgery. This survey included International Knee Documentation Committee (IKDC) Subjective form[19], the Lysholm Knee Score[20], modified Cincinnati Score[21], Single Assessment Numeric Evaluation (SANE)[22], Tegner activity scale[20], Forgotten-Joint-Score-12 (FJS-12)[23], Anterior Cruciate Ligament

Return to Sport After Injury (ACL-RSI) Scale (short-version)[24], and satisfaction scores, which was assessed on a Likert-scale (very satisfied – satisfied – neutral – unsatisfied – very unsatisfied).

The secondary outcomes of the present study were failure and reoperation rates. Clinical failure was defined as side-to-side difference >3 mm, grade ≥2 Lachman, and/or grade ≥2 pivot shift test, or a subjective feeling of instability. Furthermore, any occurrences of contralateral ACL tears, surgical interventions besides revision surgery, and complications other than failure or reoperations were recorded. If patients were unable to be seen in clinic due to COVID-19 or other reasons, their one-year physical examination was used for final analysis, and they were contacted for a telephone interview to assess if symptomatic instability, reinjury, revision surgery, or any other reoperation had occurred at a minimum of two years after surgery (Table 1).

Table 1. Clinical evaluation methods used for all patients*

	All included (n = 69)
In-person evaluation	56 (84%)
Online + telephone evaluation	5 (7%)
Telephone evaluation only	6 (9%)
Subjective outcomes	53 (77%)
Laxity assessment	13 (19%)

Asterisk indicated reported in number (%); PROMs, patient-reported outcome measurements

Finally, the time to return to work, time to discontinue brace usage, time to return to running, and time to return to sports (RTS) was reviewed. Therefore, all patients were asked to complete questions pertaining to the time from their surgery to these functional milestones at each of the visits.

Statistical analysis

SPSS Version 25 (SPSS Inc., Armonk, NY) was used for all statistical analysis. Data were first tested for normal distribution using Shapiro-Wilk tests. Due to non-normally distributed data, continuous variables were presented with median with their interquartile ranges (IQR), and nominal variables were presented with frequencies (%). Group comparisons were performed using Mann-Whitney *U* test for continuous variables and Chi-squared tests or Fisher exact tests (for samples with a value < 5 in the contingency table) for nominal data. A post-hoc sample size calculation was performed using the primary outcome variable IKDC subjective score. Using a standard deviation of 9 points, and a minimal clinically important difference (MCID) of 8.8 points, a total of 16 patients in each study group were needed to achieve a power of 80%.[25–27] The sample sizes of 34 and 35 in the acute and delayed groups, respectively, show that there is sufficient power to detect differences in the IKDC. Furthermore, these group sizes are sufficient to detect MCID between the groups in Lysholm knee score, Tegner activity levels, and FJS-12.[15,20,28,29] However, this study was underpowered for failure analysis, as sample size calculation showed that 203 patients in each group were needed to assess a 5% difference in failure rate between both groups. Significance of statistical differences was attributed to p-value of < 0.05.

Results

Patient demographics

Sixty-nine patients were included in this study, of which 34 (49%) were treated acutely and 35 (51%) in the delayed setting. Overall follow-up was 86%, including 79% in the acute group and 89% in the delayed group. The median age at surgery was 37 years (IQR 29 – 45 years), 67% were males, median BMI was 25.1 kg/m^2 (IQR 23.4 – 27.0 kg/m^2), and 59% of patients underwent right-sided knee surgery. The median follow-up time was 2.2 years (range 2.0 – 10.9 years). Most common injury mechanism was skiing (28%), followed by soccer (15%) and basketball (15%; Table 2). Additional suture augmentation was added in 49% of all patients. Besides time from injury to surgery (15 days, IQR 11 – 19 days vs. 149 days, IQR 106 – 285 days, $p < 0.001$), there was no statistical difference between groups for demographics, concomitant injuries, and sports participation (all $p > 0.2$; Table 2). In the delayed group, 63% of patients underwent conservative treatment first, while the reason for delayed surgery was unknown or due to other causes in the remaining 37%. In the delayed group, some form of reattachment of the ACL to the PCL was seen in 37% of patients and to the femoral notch in 30%.

Table 2. Patient demographics of patients treated with primary ACL repair

	All included (n = 69)	Acute (n = 34)	Delayed (n = 35)	P-value
Age (years); median (IQR)	37 (29 – 45)	39 (32 – 47)	36 (26 – 42)	0.171
Male gender; freq. (%)	46 (67%)	22 (65%)	24 (69%)	0.733
Right side; freq. (%)	41 (59%)	20 (59%)	21 (60%)	0.921
Delay (days injury-surgery); median (IQR)	91 (15 – 152)	15 (11 – 19)	149 (106 – 285)	<0.001
BMI (kg/m^2); median (IQR)	25.1 (23.4 – 27.0)	25.1 (23.6 – 26.8)	25.5 (23.2 – 27.3)	0.838
Meniscal injury; freq. (%)	38 (55%)	16 (47%)	22 (63%)	0.187
Medial meniscus	18 (26%)	7 (21%)	11 (31%)	0.305
Lateral meniscus	27 (39%)	11 (32%)	16 (46%)	0.256
Meniscus treatment; freq. (%)				
Repair	9 (13%)	4 (12%)	5 (14%)	0.743
Meniscectomy	23 (33%)	10 (29%)	13 (37%)	
Repair + Meniscectomy	3 (4%)	1 (3%)	2 (6%)	
Conservative	3 (4%)	1 (3%)	2 (6%)	
Chondral injury; freq. (%)	19 (28%)	11 (32%)	8 (23%)	0.377
Suture augmentation; freq. (%)	34 (49%)	18 (53%)	16 (46%)	0.548
Preinjury Tegner; median (IQR)	6 (5 – 7)	6 (5 – 7)	6 (5 – 7)	0.531
Tear location; median (IQR)[a]	78% (74% – 83%)[b]	78% (74% – 83%)[c]	79% (73% – 83%)[d]	0.900
Follow-up (years); median (IQR)	2.2 (2.1 – 2.9)	2.3 (2.1 – 2.9)	2.2 (2.0– 2.9)	0.239

[a] indicates that ACL tear location is calculated as distal remnant divided by total remnant length on preoperative MRI [42]; [b], Preoperative MRI was available in 53 patients; [c], Preoperative MRI was available in 29 patients; [d], Preoperative MRI was available in 23 patients N, number of patients; BMI, body mass index; Freq., frequencies; SD, standard deviation.

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Primary outcomes

For subjective analysis, only patients with intact repaired ACLs and who completed outcome surveys were included (n = 53). No statistically significant differences in subjective IKDC scores were found between the acute and chronic group (93, IQR 87 – 96 vs. 99, IQR 83 – 95, p = 0.190). Based on the Tegner scale, 70% in both groups had returned to their preinjury level of sports participation (p >0.999). Finally, no significant differences were found in all other subjective outcomes and functional milestones between both groups (all p > 0.05; Tables 3 and 4).

Table 3. Patient-reported outcomes of those treated with acute (<3 weeks) versus delayed (>3 months) repair*

	Acute (n = 28)	Delayed (n = 25)	P-value
Subjective IKDC; median (IQR)	93 (87 – 96)	88 (83 – 95)	0.190
Lysholm; median (IQR)	95 (87 – 100)	93 (83 – 100)	0.352
Modified Cincinnati; median (IQR)	97 (88 – 100)	92 (87 – 100)	0.262
SANE; median (IQR)	90 (85 – 100)	90 (80 – 95)	0.423
Satisfied; n (%)	21 (88%)[a]	22 (96%)[b]	0.667
FJS-12; median (IQR)	83 (73 – 96)[c]	88 (74 – 95)[d]	0.940
ACL-RSI; median (IQR)	81 (73 – 96)[e]	78 (55 – 86)[f]	0.226
Postoperative Tegner; median (IQR)	6 (5 – 6)	6 (5 – 7)	0.548

* PROMs of those patients without failure of treatment or completed surgical evaluation before re-injury; SANE, Single Assessment Numeric Evaluation; IKDC, International Knee Documentation Committee; FJS-12, Forgotten Joint Score-12; ACL-RSI, Anterior Cruciate Ligament Return to Sport After Injury; [a]Reported in 24 patients; [b]Reported in 23 patients; [c]Reported in 26 patients; [d]Reported in 25 patients; [e]Reported in 24 patients; [f]Reported in 22 patients.

Table 4. Patient-reported milestones of those treated with acute (<3 weeks) versus delayed (>3 months) repair*

	Acute (n = 25)	Delayed (n = 22)	P-value
Time to return to work; days	7 (3 – 14)	9 (7 – 19)	0.066
Time to discontinue brace; days	30 (23 – 42)	28 (21 – 32)	0.482
Time to return to running; months	2.0 (1.4 – 4.2)	2.4 (1.4 – 3.3)	0.854
Time to return to sports; months	6.0 (3.7 – 8.9)	6.0 (4.3 – 7.9)	0.869

Asterisk indicates reported in median with IQR

Secondary outcomes

At latest follow-up, 59 patients (90%) underwent successful ACL repair, while seven (10%) sustained a reinjury at a median follow-up of 1.1 years (IQR 0.7 – 2.0 years). There were three reinjuries (9%) in the acute group and four in the delayed group (11%), which was not statistically significant (p > 0.999). Of all patients with reinjuries, five were converted to ACL reconstruction without further complications, two were treated conservatively. Furthermore, no statistical differences were found in reoperations (12% vs. 3%, p = 0.154), nor in complications (0% vs. 3%, p > 0.999), or contralateral failures (3% vs. 0%, p = 0.493) between the acute vs. delayed group.

Reoperations observed in the acute group included three patients with additional meniscus lesions that required a partial meniscectomy and one with cartilaginous injury that underwent chondroplasty. In the delayed group, there was one patient who required a partial meniscectomy. Complications observed in the acute group included one patient in which the tip of the self-retrieving suture passer broke off intraoperatively and was lost in the ACL fibers. No specific complications occurred in the delayed group. Finally, one patient in the acute group sustained a contralateral failure at 10.4 years after the initial surgery, while no contralateral failures were observed in the delayed group.

Thirty-two of 34 (94%) patients in the acute group and 26 of 35 (74%) patients in the delayed group returned for clinical evaluation at a median follow-up of 2.3 years (IQR 2.1 – 2.9 years). For those patients without failure, 86% of the both the acute and chronic group had a negative Lachman, while 14% in both groups had a grade one with firm endpoint. Additionally, 93% of the acutely treated patients and 86% of the delayed treated patients had a negative pivot examination, whereas 7% and 14% had a grade one finding. Furthermore, all patients achieved full ROM. Rolimeter measurements showed a median manual side-to-side difference of 1.2 mm (range 0.7 – 2.0 mm) in eight acutely repaired patients, and 2.0 mm (range 0.6 – 3.2 mm) in five delayed repaired patients, but these groups were too small for further analysis.

Discussion

The most important finding of this study was that acute and delayed primary repair of the ACL resulted in similar clinical outcomes at short to mid-term follow-up. Furthermore, this study found that similar subjective outcomes and functional milestones could be achieved in both groups. Given these findings, the most important factors for success of repair surgery seem to be tissue quality and length of the tissue rather than acuity of the surgery.

Over the last decade, primary ACL repair has seen renewed interest in the orthopaedic literature.[8,30] In both historical and more recent studies, several surgeons utilizing repair techniques have advocated for performing surgery in the acute or subacute phase because it is thought that early repair gives improved outcomes over late repair.[31,32] Even though primary ACL repair within two to three weeks after injury may optimize surgical outcomes, there remains, however, debate regarding the optimal timing of surgery. A recent case-control study, for example, reported that patients have an increased likelihood of undergoing primary ACL repair if surgery was performed within four weeks after injury (OR 3.3, $p < 0.001$) rather than after four weeks.[33] Several studies have found that a longer delay between injury and repair surgery may cause retraction and resorption of the torn ACL, leading to suboptimal tissue quality and insufficient tissue length for reattachment to the femoral wall.[34] Therefore, primary ACL repair is less likely to be performed in the chronic setting as compared to the acute setting.

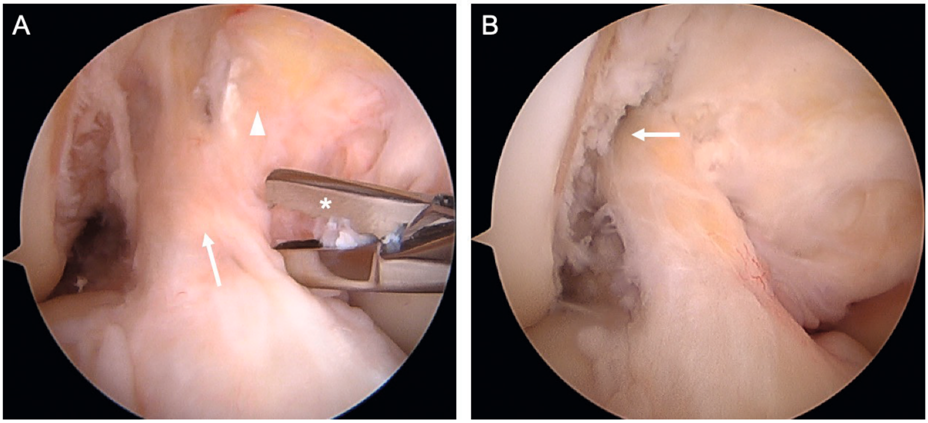
In this study, similar outcomes were found between patients treated in the acute and delayed settings. In all cases, optimal conditions required for successful repairing a torn ACL were present (Figure 1). First of all, all patients presented with a proximal tear with sufficient tissue length to reattach the ligament to its anatomical insertion site. Secondly, good to excellent tissue quality that could withstand intrasubstance suturing and tensioning of the remnant towards the anatomical attachment site was also observed during arthroscopy. Although these conditions are typically observed in the acute setting, this study seems to provide evidence suggestive that a chronically torn ACL, in some cases, still has potential to heal when tissue length and quality of tissue are sufficient.

Figure 1.

Preoperative sagittal MRI image reveals a proximal ACL tear. The ACL is attached to the PCL (arrow).

Nevertheless, the hypothesis that chronic ACL tears still have some healing potential contradicts the historical thought that the ACL cannot be reliably repaired in the delayed setting since the ligament remnant can potentially retract and resorb after several weeks.[35] One of the explanations for these optimal circumstances for primary ACL repair might be that the ACL could scar onto the posterior cruciate ligament (PCL) or to the roof of the femoral notch, after which the quality and length of the tissue may be maintained (Figure 2).[36] Specifically, Lo et al. showed that in roughly 66% of patients with chronic ACL injuries, reattachment of the ACL to the PCL was observed during ACL reconstruction surgery.[36] Given these findings, tear type and tissue quality, rather than acuity of surgery, seem to be the most important determining factors as to whether a torn ACL can be successfully repaired.

Figure 2.



(A) The ACL *(asterisk)* is noted to be scarred to the PCL *(triangle)*. Using an arthroscopic scissors *(arrow)*, the ligament is freed up and mobilized. (B) Primary ACL repair using dual anchor fixation is finished. As seen, the ligament has good tissue quality and sufficient tissue length to be reattached to the femoral wall *(asterisk)*.

When reviewing clinical outcomes of primary ACL repair of larger case-series and cohort studies, only studies that performed primary repair in the acute setting could be identified in the literature.[30] A recent meta-analysis reported an 11% failure rate, 9% reoperation rate, and all subjective outcomes good to excellent at mean time from injury to surgery of 14 days (range 0 – 547 days).[7] More importantly, this meta-analysis also reported that the current evidence level is still low and that as of yet there are few longer-term outcome studies for this procedure. It is clear that future studies are needed to evaluate both the short and long-term clinical outcomes of selective arthroscopic primary ACL repair more extensively.

In this study, acute ACL repair did not result in arthrofibrosis or postoperative stiffness. Various historical studies have suggested avoiding ACL reconstruction in the early phase after injury to avoid these risks.[37] Recent studies with modern-day arthroscopic techniques and rehabilitation protocols, however, have shown that acute ACL surgery is not associated with an increased risk of postoperative stiffness.[12] Furthermore, it has been shown that patients undergoing acute ACL reconstruction (within 8 days post-injury) have significantly less quadriceps muscle atrophy and improved one-leg hop test at the 6-month follow-up time point as compared to those treated after 6 to 10 weeks post-injury.[38] On the contrary, a subset of patients treated acutely might undergo unnecessary surgery as they might achieve successful coping with their ACL deficiency following non-operative treatment. However, a longer delay between injury to surgery may increase the risk for meniscal and cartilage lesions[39], potentially leading to subsequent premature degenerative joint changes[40], while also increasing the indirect costs by requiring longer sick leave time. Given the multifactorial nature of this decision, all patients should be carefully counseled about the risks and benefits of undergoing ACL surgery in the acute or delayed setting. Nevertheless, if patients first undergo conservative treatment before proceeding with ACL surgery, this study shows that ACL repair with good outcomes can still be achieved when tear type and tissue quality are both sufficient.

There are limitations to this study. First, given the study's retrospective design, there could have been a potential selection bias. Secondly, it is important to note that this study was underpowered for the secondary outcome treatment failure. In addition, the lost to follow-up rate in the acute group was higher than in the chronic group (21% vs. 11%), which could have influenced the present study results. Finally, the median follow-up period was relatively short (median 2.2 years, range 2.0 – 10.9 years), and most patients should be followed-up at least until the mid-term interval to confirm that there are no differences in clinical outcomes between both groups.

Conclusion

This study showed that acute and delayed primary ACL repair resulted in similar clinical and functional outcomes at short to mid-term follow-up. Therefore, the most important factors for success of repair surgery seem to be tissue quality and length of the tissue, rather than acuity of the surgery.

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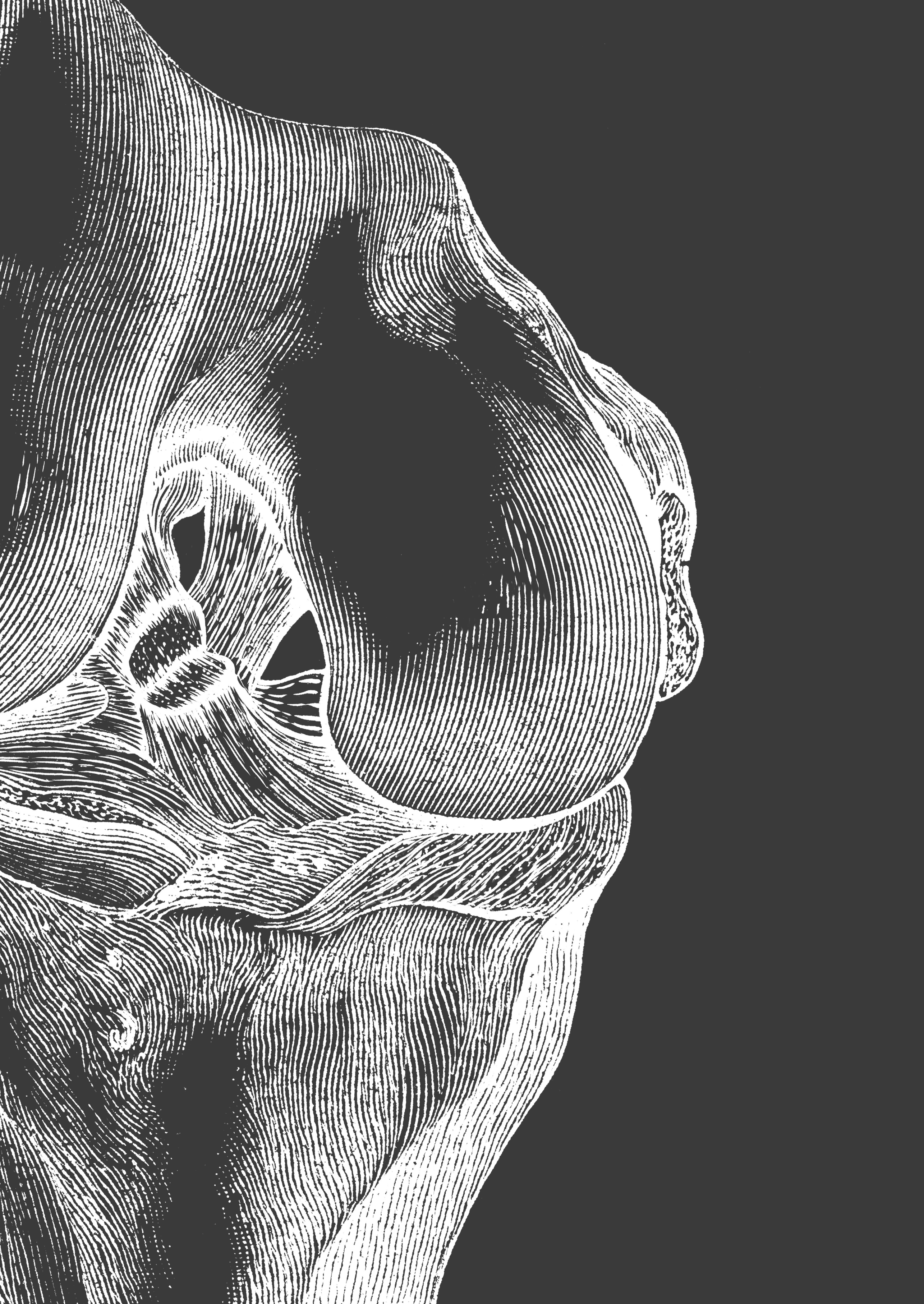
Part 5

General discussion, future perspectives and conclusions



Chapter 13

General discussion and future perspectives

This thesis assessed whether patients with acute ACL injuries should be treated early and evaluated if there is a role for primary repair in the treatment algorithm for (some of) these patients. Therefore, it was first investigated if it is advantageous to treat acute ACL injuries early, and the rationale and different repair procedures were then assessed. The following section assessed the patient selection for primary repair to understand which patients could be treated with the primary repair procedure. Lastly, this thesis evaluated the latest outcomes of primary repair to understand if it is safe to repair a torn ligament and assessed if primary repair has advantages compared to reconstructive surgery. In this general discussion, the main findings of the thesis will be discussed, as well as the implications for daily practice, and directions for further research.

Acute treatment of ACL injuries

In this thesis, the current treatment algorithm for acute ACL injuries (**chapter 3**) and the potential for ACL repair were reviewed first (**chapter 2**). This thesis showed several advantages of treating patients early after acute ACL injuries, including the possibility of performing ACL repair.

Currently, the most optimal treatment strategy for patients with ACL injuries still needs to be determined[1,2], and opinions and guidelines vary significantly among surgeons and centers around the globe. Patients with ACL injuries can be treated conservatively or surgically, depending on several patient factors.[3,4] In the Netherlands, the guideline recommends a structured, supervised rehabilitation program followed by optional ACL reconstruction in case of persistent knee instability.[5] With this treatment algorithm, patients can become copers, which has the advantage of not performing surgery on all patients, reducing the risk of surgical complications, and preventing overtreatment. However, there are also several disadvantages, as a significant number of patients (between 40% to 90% depending on age and activity level) ultimately require ACL surgery.[6] As patients must undergo two rehabilitation periods, before (3 to 6 months) and after surgery (9 to 12 months), this increases the time from injury to full recovery in those attempting to return to sports activities fully. Therefore, it is important to carefully review the advantages and disadvantages of the timing of surgery.

This thesis showed a high level of evidence that patients can undergo isolated ACL reconstruction early without increased risk of postoperative stiffness (**chapter 3**). This is important as it was historically reported that patients treated acutely had a significantly higher risk of developing arthrofibrosis.[7] Several modern advancements, such as the introduction of minimally invasive arthroscopic techniques, more anatomical ACL reconstruction and the adoption of early motion protocols, have likely played a critical role in avoiding postoperative stiffness.[8] Furthermore, no clinical and functional differences in outcomes were noted between patients treated early and in the delayed setting after ACL injury. Although the outcomes of **chapter 3** did not show lower incidence of meniscal and chondral lesions in patients treated early, other studies have shown that the ACL-deficient knee is more at risk of developing secondary injuries due to future episodes of instability.[9,10] It can be debated that the follow-up in our study was insufficient to show a significant difference between both groups. Finally, another advantage of early surgical treatment includes avoiding potential quadriceps atrophy, as patients must restore quadriceps strength two times in case of delayed ACL reconstruction.[11]

As it seems safe to undergo ACL surgery in the acute setting, it is important to assess which patients are potential copers and thus can be treated with conservative treatment and identify potential non-copers who might benefit from early ACL surgery. In the literature, age and activity levels have been identified as the strongest predictors of coping with ACL deficiency.[12] This is not surprising, as it is generally stated that younger patients participating in higher demanding sports have an increased risk for ACL injuries and tend to have a higher chance of failing conservative treatment.[6] Older patients, on the contrary, can be initially treated conservatively by adjusting their activity levels, thereby preventing surgery.[1,2,6] Therefore, early ACL surgery should be considered in younger patients and those with high activity levels. As shown in **chapter 3,** early surgery may also lead to shorter sick leave for these patients, potentially resulting in a lower economic burden.

By treating acute ligament knee injuries early, some patients might benefit from primary repair as a treatment option.[13–16] In recent years, several different repair techniques have been proposed. Including primary ACL repair with static augmentation, repair with dynamic augmentation (dynamic intraligamentary stabilization; DIS), and bridge-enhanced ACL restoration (BEAR). Although the goal of all these procedures remains ligament preservation by repairing the torn ligament ends, significant differences between these tear locations depending on ACL repair techniques exist, as shown in **chapter 2.** The differences in healing capacity between tear locations can explain the rationale behind the different techniques.[17–19] This will be further outlined in the following discussion section. It should also be noted that the term "ACL repair" includes a wide range of surgical techniques and that this thesis (mainly) focuses on direct suture repair with static augmentation. Besides tear location, it is also important to note that tissue quality is crucial in achieving good clinical outcomes (**chapter 2**). Although this is most commonly seen in the acute setting, some patients, however, can still benefit from the advantages of primary repair when treated in the delayed setting (**chapter 12**).

Given the recent resurgence of interest in preservation techniques, it is therefore not only important to identify patients who would benefit from early ACL surgery in general but also to assess the clinial and functional outcomes between acute ACL repair and conservative treatment. Only with this knowledge the orthopaedic community can determine the optimal treatment strategy for patients with acute ACL tears, and future studies are obviously needed.

Patient selection for ACL repair

Previous studies have shown that patient selection is key for successful outcomes following primary ACL repair as proximal ACL tears perform better in repair surgery.[20] This part of the thesis aimed to assess and further understand which patients present with proximal ACL tears and how to identify them. These findings can help orthopaedic surgeons evaluate which patients are eligible for primary ACL repair preoperatively.

As mentioned, the role of tear location and tissue quality has recently been identified in the literature for optimal outcomes after primary repair.[13] Our study on the arterial anatomy of the ACL (**chapter 4**) found that in situ adult ACLs demonstrated the most significant relative perfusion within the proximal third of the ligament (nearly two times greater than the middle third and three times greater than the distal third). Learning from this quantitative MRI study, the higher concentration of vessels and increased relative blood flow to the third proximal ACL may indicate that this region may have greater healing potential than midsubstance tears and, thus, can be repaired directly. The outcomes of historical studies focusing on tear location of the ACL indeed showed better outcomes after primary repair of proximal tears as compared to those torn at the midsubstance[13], and more recent studies have shown promising clinical results after direct suture repair of proximal tears.[21–23] It should be noted, however, that it remains unclear if vascularity is actually re-established after ACL repair, and future histological and clinical studies are needed in this area. On the contrary, one could also argue that proximal tear types can be treated non-operatively, as a recent study reported spontaneous healing of the ACL without surgical intervention in a small subset of patients.[24] Interestingly, all patients in this group had a proximal ACL tear and showed a healed and continuous ACL with homogenous signals at the final MRI follow-up while being clinically stable during physical examination. However, no predictive role between tear location and coping after ACL injury has been found in the literature.[12]

Given these recent developments in tear-location depending ACL repair techniques, it might be possible that in the future, patients with acute proximal tears indicated for surgery may undergo direct suture repair (either with static or dynamic augmentation), while those with midsubstance tears will be treated with primary repair with some form of biological augmentation. ACL reconstruction, on the other hand, can then be used for patients presenting with chronic tears or those with poor tissue quality. This treatment algorithm will make treating patients with ACL injuries more personalized than the current 'one size fits all' approach.

In order to determine which patient is eligible for what specific ACL procedure, precise measurement of tear location is required. Over the last decade, the quality of MRI in evaluating ACL injuries has significantly increased, especially with high-resolution scanners, and can now be used to distinguish between tear locations rather than only assessing if the ligament is torn.[25] Previously, some studies have suggested using the modified Sherman classification (type I: >90% distal remnant length, type II: 75–90%, or type III: 25–75%) to correlate different tear locations with several ligament preservation techniques.[26,27] However, it remains difficult to differentiate, and thus indicate for repair surgery, between different types with this classification system since clear definitions are lacking. Due to this limitation, a new and straightforward measurement protocol was designed to more accurately predict the eligibility for primary repair compared to the tear type classification (**chapter 5**). This protocol showed excellent inter- and intraobserver reliability between an experienced musculoskeletal magnetic resonance radiologist, a musculoskeletal radiologist fellow, and an orthopedic research fellow. Although this study did not correlate these findings to arthroscopy, this study showed that only 24% of all ACL tears occur in the proximal quarter of the ligament, which is lower than previously reported studies.[28,29] Nevertheless, one out of four patients presenting with acute ACL injuries could benefit from the advantages of repairing a torn ACL.

With this MRI measurement protocol, it was then assessed which patient and radiological factors are associated with a more proximal tear location (**chapter 6**). This is an important study as it provides more insight into patient characteristics associated with eligibility for primary repair. In this study, it was noted that older age was correlated with a higher likelihood of proximal tear location. This is in line with previous studies that showed a higher incidence of proximal

ACL tears in older patients and might be explained by some form of mucoid degeneration due to the decreasing blood supply that comes with aging.[12,15] However, it could also be argued that older patients have lower energy knee injuries and fewer injuries of other knee structures than younger patients, as multivariate regression analyses showed that bone bruises in both compartments and posterolateral corner injury decreased the likelihood of a proximal tear. Therefore, less overall knee damage may result in a more proximal tear location, which is generally more often seen in older patients and those with lower activity levels. Nevertheless, the exact reason still needs to be determined and is most likely multifactorial. No other patient or anatomical risk factors were identified that influenced the tear location of the ACL.

Outcomes of ACL repair

After promising early results of developers and early adopters, more studies have recently been published on modern-day ACL repair.[15,20,30,31] In the last part of this thesis, the clinical outcomes of this procedure and factors associated with improved outcomes were assessed.

Based on a recent systematic review with meta-analysis[20], **chapter 7** describes a systematic review with a meta-analysis assessing the outcomes of primary repair with static augmentation in the literature. The overall failure rate in 414 patients treated with primary repair was 8%, while reoperation and complication rates were low at mean follow-up of 2.0 years (range 0.4–4.5 years). Over the last few years, more than 15 systematic reviews have been published on this topic, and most have shown similar promising findings. However, it is important to note that all reviews also identified low quality and low overall level of evidence in the current literature on ACL repair. Thus, the body of high-quality studies is limited, and the quest to determine the exact role of primary repair in the treatment algorithm of proximal ACL injuries is still ongoing. Currently, we are including patients in the REPAIR trial (**appendix**), a randomized controlled trial designed to assess if primary repair is at least equivalent to the current surgical standard of ACL reconstruction in both subjective and objective outcomes.[32]

In order to improve the predictability of outcomes of ACL repair techniques, risk factors for re-injury should be identified. It is well known from the ACL reconstruction literature that failure rates are higher in younger and more active patients[33–36], but there is much controversy regarding ACL repair in this patient group.[37] The current literature shows limited evidence regarding the effectiveness of this procedure in younger patients, with widely varied failure rates in the scarce literature (0 to 41%). In our cohort, we also showed high failure rates in younger patients (21 years and younger; **chapter 8**). This could have been influenced by the high rate of female patients in this patient group (70.1%), as previous studies have demonstrated that young female athletes are more prone to graft failure than their male peers.[38] Although there are certainly several theoretical advantages of primary repair in young patients (growth deficits can be avoided while potentially reducing the risk of osteoarthritis), caution must be exercised when considering this treatment in young patients.

Recently, some studies have suggested that anterolateral ligament injuries are present in almost 90% of patients.[39] This is one of the most important risk factors for grade three pivot shift in patients with acute ACL injuries and is more often seen in young patients. Some surgeons have therefore suggested treating anterolateral structures in high-risk patients (i.e. young patients and those with highly demanding knee sports) to improve clinical outcomes.[40–42] Recent comparative studies have shown that concomitant anterolateral ligament or lateral extra-articular procedures are associated with significantly lower failure rates after ACL reconstruction.[43] Given these findings, improved outcomes with may be expected in young patients who are more at risk of failure after primary ACL repair since these procedures can protect the repaired ligament, thereby preventing subsequent injury. Future studies, however, are needed to confirm this hypothesis.

Irrespective of age, there are, however, several (theoretical) advantages of repairing a torn ACL rather than reconstructing it due to fundamental differences in surgical morbidity between both procedures. As mentioned in the introduction, primary repair surgery is a relatively quick procedure in which the native ligament can be preserved, thereby preserving the blood supply and nerve fibers and potentially preserving proprioception.[44–46] In addition, there is no need for graft harvest, which prevents donor-site morbidity.[47–49] Besides these potential benefits, this thesis showed additional benefits of repairing a torn ACL over ACL reconstruction, which will be discussed in more detail in the next sections. Nevertheless, for all patients, the advantages of primary repair should be critically weighted over the risks and uncertainties of this new procedure. This includes, as mentioned earlier, that ACL repair is most commonly performed in the acute setting and that a subset of patients will therefore be surgically overtreated, the higher reported failure rates in younger patients, and the lack of high-quality and long-term evidence supporting primary ACL repair.

Earlier research has shown that repair patients regained their ROM in a shorter time frame than those undergoing ACL reconstruction.[47] At the start of this thesis, it was unclear if this indeed facilitates an easier recovery as milestones are potentially reached earlier. Therefore, a clinical evaluation of return to sports rates and an assessment of the timeline of rehabilitation milestones was performed (**chapter 9**). Notably, 70% of adult patients returned to knee-strenuous sports and 60% to their pre-injury level, and similar numbers have been reported in non-elite athletes treated with ACL reconstruction.[50] For elite athletes, however, return to sport rates could be lower in those treated with primary repair than those treated with reconstructive surgery. The average time to return to work was seven days, the time to return to running was 90, and the time to fully return to play was 180 days following ACL repair. Compared to outcomes of the gold standard of ACL reconstruction in the literature, these milestones seem to be reached earlier after ACL repair.[51,52] From a cost-effectiveness perspective, this could also result in a substantial economic advantage of primary repair over ACL reconstruction, as patients can return earlier to work or sports activities. Nevertheless, it should be noted that rehabilitation and return-to-play protocols for repair still need to be established, and earlier return to sports may lead to higher failure rates, especially in the young patient population.

In addition, this thesis showed that patients who underwent primary repair had less everyday knee awareness (i.e. more often a forgotten knee joint) of their operated knees than those treated with reconstruction (**chapter 10**). Over the last decades, outcomes of ACL surgery have improved, and patient expectations have increased. Nevertheless, several studies have not found any significant differences between new surgical techniques with better biomechanical properties. The currently established outcomes assessment tools seem to lose their discriminatory abilities, while this is essential to compare clinical outcomes between surgical procedures over time.[53,54] Therefore, the FJS-12 score was used to evaluate everyday joint awareness and we believe that this validated outcome metric should be used more often to evaluate outcomes of ACL surgery.[55] This is because a "forgotten" joint excludes any subjective impairments such as instability, pain, or stiffness and can therefore even discriminate between minor differences not detected with the traditional PROMs.[56] Primary repair may, therefore, potentially lead to closer restoration of native knee function than ACL reconstruction, but randomized studies are warranted to assess this further.

Finally, due to the lower surgical morbidity, it was previously suggested that patients treated with repair might experience less postoperative pain than those treated with reconstruction. This is relevant given the potential risks of prolonged postoperative analgesic use and the current opioid epidemic, especially in the United States.[57,58] This thesis indeed showed in a prospective study that patients undergoing ACL repair experienced significantly less postoperative pain and used fewer opioids than those treated with ACL reconstruction (**chapter 11**), confirming a recent retrospective study assessing the same outcomes.[59] Given these findings, repair patients seem to have less postoperative pain, earlier return of range of motion, and subsequent easier recovery than those treated with ACL reconstruction, which is an important finding of this thesis.

Although this thesis showed promising outcomes following ACL repair, it is important to note that the mean age was relatively high in most of these studies. In general, it is felt that this procedure is most commonly advocated in the slightly older patient population, which makes it is difficult to directly compare these outcomes with those found in the ACL reconstruction literature. It should also be noted that early surgical treatment remains controversial in older patients as subset of patients can be treated conservatively and do not need surgery.[1,2,6] Nevertheless, a progressively increasing group of slightly older recreational athletes desire to maintain their active lifestyles, and a recent study showed that the success of conservative treatment is low in this patient group (aged 25 to 40 years with high Tegner scores).[6] As a result, patients may need to modify their lifestyle and change sports, as nonoperative treatment may lead to residual instability.[60] Given the minimally invasive nature of the surgery with less postoperative pain, the low reported failure rates, quick return to work and sports activities, and less joint awareness, this procedure seems to be an excellent treatment in this growing patient group. However, future studies must further assess which patient should benefit from early surgery, especially in the older patient population.

Conclusion

This thesis shows that treating patients early after ACL injury is safe without increasing the risk of complications. Furthermore, primary repair seems a viable treatment option for selected patients, as a growing body of evidence supports primary repair in patients with proximal ACL tears. The work in this thesis, but certainly also by others, emphasizes that although the ACL can heal by means of primary repair, patient selection is critical for successful outcomes. The ideal candidate for primary repair seems to be recreational athletes older than 22 years of age with a proximal ACL tear of good to excellent tissue quality. To predict which patients are eligible for ACL repair, MRI scans can adequately help orthopedic surgeons to make a preoperative assessment. Nevertheless, to establish the definitive role of primary repair in the treatment algorithm of ACL injuries, high-quality comparative studies are needed to compare ACL repair with reconstruction and conservative treatment.

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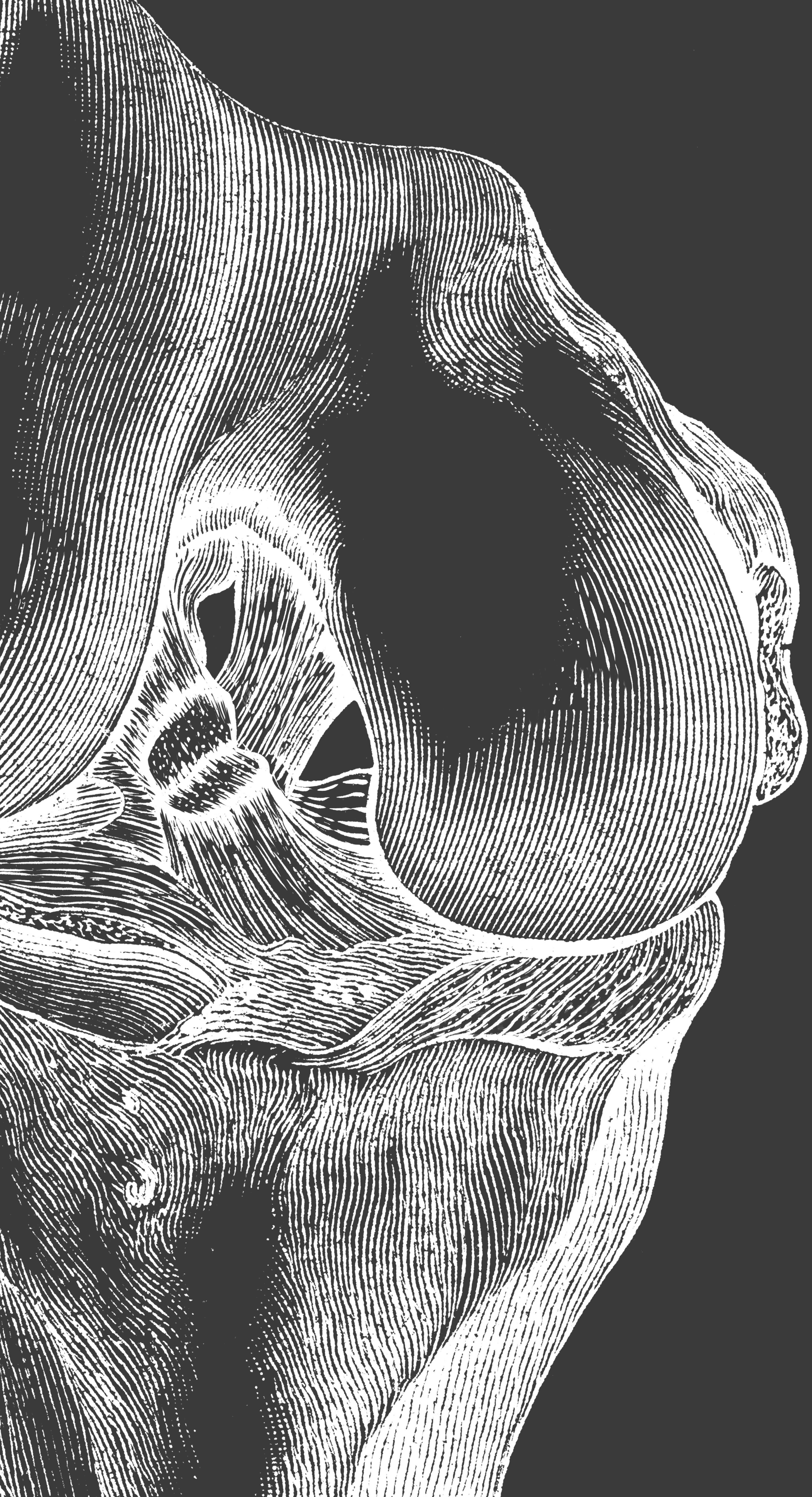


Chapter 14

Summary (in English and Dutch)

Summary in english

The main objective of this thesis was to investigate the optimal treatment of acute anterior cruciate ligament (ACL) injuries and the role of primary repair as a treatment option for these type of injuries. **Chapter 1** provides an overview of this thesis, in which the potential benefits of early treatment for ACL injuries, various available repair procedures, patient selection for primary repair, and the comparative outcomes of primary repair versus reconstructive surger are introduced.

In **chapter 2**, a comprehensive review of the rationale and treatment principles behind modern ACL repair is presented. The chapter focuses on the different repair procedures and their evidence-based overview, including direct suture repair with or without augmentation for proximal tears and primary repair with biological augmentation for midsubstance tears. The differences in healing capacity between tear locations explain the rationale behind these techniques. Furthermore, it was found that older age, early surgery after injury, and lower activity levels were associated with better treatment outcomes.

Historical studies have indicated that performing ACL surgery in the acute phase can increase the risk of complications, such as stiffness and arthrofibrosis. To address this, **chapter 3** investigated the safety of early ACL surgery using modern arthroscopic surgery and rehabilitation protocols and did not find significant differences in clinical and functional outcomes between patients treated early or with delayed reconstruction after ACL injury. It was also noted that early ACL surgery may be cost-effective and does not increase the risk of postoperative stiffness. Although the appropriate candidates for early surgical treatment remains unclear, younger patients and those with high activity levels seem to be the best candidates, and identifying them early can be advantageous.

In **chapter 4**, our study on the arterial anatomy of the ACL reveals that the proximal third of the ligament demonstrates the highest relative perfusion, indicating greater healing potential compared to midsubstance tears. This suggests that direct repair has a higher likelihood for success in patients with proximal tears, while midsubstance tears require biological augmentation, such as using a collagen-based scaffold called bridge-enhanced ACL repair (BEAR). However, it is still uncertain whether vascularity is fully restored after ACL repair, and further histological and clinical investigations are needed in this field.

In **chapter 5**, a new MRI measurement protocol was introduced to determine the tear location of the ACL accurately. The study found that assessing the distal and proximal remnant lengths on preoperative MRIs could reliably quantify the tear location. Furthermore, it was shown that 24% of all ACL tears occur in the proximal quarter of the ligament, and these patients might be eligible for primary repair. This highlights the importance of identifying the specific tear location rather than simply confirming the presence of an ACL tear.

In **chapter 6**, it was shown that older age was linked to a higher probability of proximal tear location in the ACL, while no specific anatomical risk factors were found to influence tear location measured on preoperative MRIs. This is important as this might help the surgeon in assessing the preoperative likelihood for successful repair. The higher incidence of proximal

tears in older patients is unknown but may be due to mucoid degeneration or variations in injury mechanisms.

Chapter 7 of the thesis presented a systematic review with meta-analysis of the outcomes of primary repair with static augmentation for proximal ACL tears. The review indicated that this procedure could be a viable treatment option in the short term, with a low failure rate (8%) and low reoperation and complication rates observed in 414 patients. Furthemore, it was noted that patients with younger age had a higher likelehood of treatment failure as compared to older patients. Nevertheless, more comparative studies with larger patient groups are needed to better understand its outcomes compared to ACL reconstruction, the current standard approach.

In **chapter 8**, it was found that ACL repair had higher failure rates in patients aged 21 years and younger compared to older patients in the short term (37% vs 3.5%). While primary repair has theoretical advantages for young patients, such as avoiding growth deficits and potentially reducing the risk of osteoarthritis, their higher demands on the repaired ACL might compromise its strength. It is crucial to provide younger patients with comprehensive information regarding the risks and benefits of this procedure, as isolated primary ACL repair might not be strong enough. Older patients, however, can benefit from isolated primary repair with low failure rates and good functional outcomes.

In **chapter 9**, the time of patients returning to their pre-injury sports level after primary ACL repair was investigated. This retrospective study demonstrated that the average time to return to work after surgery was seven days, resuming running took 90 days, and complete return to sports activities required 180 days. These milestones seem to be achieved earlier with primary repair compared to results described in the ACL reconstruction literature. However, it is important to note that further research is needed to establish standardized rehabilitation protocols and conduct comparative studies with ACL reconstruction.

In **chapter 10**, it was observed that patients who underwent primary ACL repair had lower knee awareness in their everyday lives compared to those who underwent ACL reconstruction, as indicated by lower Forgotten Joint Scores (FJS). This finding is important because it suggests that primary repair may result in a closer restoration of native knee function, with fewer subjective impairments such as instability, pain, or knee stiffness. The FJS-12 questionnaire is valuable for assessing various aspects of ACL surgery, including the risk of posttraumatic osteoarthritis. We recommend utilizing this outcome measure more frequently to assess and compare the outcomes of ACL surgery.

In **chapter 11**, it was shown that patients who undergo repair experience less postoperative pain, resulting in decreased opioid usage and a more favorable recovery quality. Considering the risks associated with prolonged postoperative analgesic use and the ongoing global opioid epidemic, this is an important finding of this thesis. These findings, coupled with the earlier restoration of range of motion and reduced joint awareness, highlight the advantages of primary ACL repair.

In **chapter 12** of this thesis, the question of whether ACL ruptures can only be repaired in the acute setting was investigated. For this study, patients who underwent repair within three weeks or after three months were included to determine whether both acute and delayed ACL repair yield similar clinical outcomes and functional milestones. Tissue quality and length, rather than timing, are therefore the key factors for a successful outcome in primary ACL repair. Therefore, we recommend orthopedic surgeons to assess the tissue during knee joint inspection before deciding on ACL repair or reconstruction, regardless of the timing of the surgery.

Finally, **chapter 13** presents a comprehensive analysis of the conducted studies, examining the feasibility of early surgical intervention for acute ACL ruptures and investigating the current and future role of primary ACL repair in the treatment algorithm of acute ACL tears. Additionally, it provides insights into future directions for further research on arthroscopic primary ACL repair.

Samenvatting in het nederlands

Het primaire doel van dit proefschrift was om de behandeling van acute voorste-kruisband (VKB) letsels en de rol van primair hechten binnen het huidige behandelingsalgoritme te onderzoeken. In **hoofdstuk 1** werd een algemene inleiding van dit proefschrift gepresenteerd, waarin de voordelen en nadelen van vroege behandeling van acute VKB letsels, verschillende VKB hechtprocedures, patiëntselectie voor deze hechtingsprocedures, en de resultaten van primair hechten in vergelijking met VKB reconstructie werden geintroduceerd.

Hoofdstuk 2 biedt een uitgebreid overzicht van de behandelingsprincipes achter modern VKB hechten. Dit hoofdstuk identificeerde verschillende locatieafhankelijke hecht technieken, waaronder direct hechten van de VKB met of zonder augmentatie (intern verstevigen met sterke hechtdraad) voor proximale scheuren en primair hechten met biologische augmentatie voor scheuren in het midden van het ligament. De verschillen in genezingscapaciteit tussen scheurlocaties verklaren de rationele achter deze technieken. Deze studie liet verder zien dat oudere leeftijd, vroege behandeling nadat de blessure is opgelopen en lagere activiteitsniveaus geassocieerd zijn met betere behandelingsresultaten.

Historische studies hebben aangetoond dat het uitvoeren van VKB chirurgie in de acute fase het risico op complicaties, zoals stijfheid en arthrofibrose, kan vergroten. In **hoofdstuk 3** werd onderzocht of met hedendaagse arthroscopische chirurgie en moderne revalidatie protocollen er toch voordelen zijn aan het vroegtijdig behandelen van patienten met VKB rupturen. De bevindingen van deze studie waren dat er geen significante verschillen in klinische en functionele resultaten zijn tussen patiënten die vroeg werden behandeld of met vertraagde reconstructie na een acute VKB ruptuur. Tevens bleek het acuut opereren van VKB rupturen het risico op postoperatieve stijfheid niet te verhogen en zelfs mogelijk kosteneffectief te zijn. Desondanks blijft het identificeren van geschikte kandidaten voor vroegtijdige chirurgische behandeling onduidelijk. Over het algemeen worden jonge patiënten en die met hoge activiteitsniveaus beschouwd als geschikte kandidaten voor vroege operatie, en het vroegtijdig identificeren van deze patiëntengroep lijkt volgens onze studie gunstig.

In **hoofdstuk 4** werd onderzoek gedaan naar de arteriële bloedvoorziening van de VKB. Hieruit bleek dat het proximale derde deel van het ligament de hoogste relatieve doorbloeding vertoonde, wat wijst op een groter potentieel voor genezing in vergelijking met scheuren in het midden van het ligament. Dit suggereert dat proximale scheuren direct kunnen worden gehecht, terwijl middelste scheuren biologische augmentatie vereisen, zoals het gebruik van een op collageen gebaseerd scaffold genaamd Bridge-Enhanced ACL Repair (BEAR). Het is echter nog onduidelijk of de bloedtoevoer volledig herstelt na primair hechten en verder onderzoek op dit gebied is noodzakelijk.

In **hoofdstuk 5** van dit proefschrift werd een nieuw MRI-meetprotocol geïntroduceerd om de locatie van VKB-scheuren nauwkeurig te kunnen bepalen. Uit dit onderzoek bleek dat het beoordelen van de lengte van de distale en proximale restanten op preoperatieve MRI's betrouwbaar de locatie van de scheur kon kwantificeren. Bovendien werd aangetoond dat 24% van alle VKB-scheuren zich in het proximale kwart van het ligament bevindt, wat kan betekenen dat deze patiënten mogelijk in aanmerking komen voor primair hechten. Dit benadrukt het belang van het identificeren van de specifieke scheurlocatie in plaats van alleen het bevestigen van de aanwezigheid van een VKB-scheur op de MRI.

In **hoofdstuk 6** werd onderzocht welke kenmerken van patiënten of blessurekarakteristieken van invloed zijn op de locatie van de VKB-scheur. Uit deze studie bleek dat een hogere leeftijd geassocieerd was met een grotere kans op een proximale scheurlocatie, terwijl er geen specifieke anatomische risicofactoren werden gevonden die de locatie van de scheur beïnvloeden. De hogere incidentie van proximale scheuren bij oudere patiënten kan mogelijk worden toegeschreven aan mucoid degeneratie of variaties in blessuremechanismen.

Hoofdstuk 7 presenteerde een systematische review met meta-analyse waarin de recentste resultaten van primair VKB-hechten met statische augmentatie werden onderzocht. Deze studie toonde aan dat primair hechten goede resultaten laat zien op korte-termijn, met een laag falingspercentage (8%) en lage heroperatie- en complicatiepercentages. Er is echter meer onderzoek nodig met grotere patiëntengroepen en vergelijkende studies om een beter begrip te krijgen van de resultaten in vergelijking met VKB-reconstructie, de huidige standaardbenadering.

In **hoofdstuk 8** werd geconstateerd dat VKB-hechten hogere falingpercentages had bij patiënten van 21 jaar en jonger in vergelijking met oudere patiënten op korte termijn (37.0% vs 3.5%). Hoewel primair hechten theoretische voordelen heeft voor jonge patiënten, zoals het vermijden van groeideformaties en mogelijk het verminderen van het risico op osteoartritis, kunnen hun hogere eisen aan de gehechte VKB de sterkte ervan compromitteren. Het is van cruciaal belang om jongere patiënten uitgebreide informatie te verstrekken over de risico's en voordelen van deze procedure, aangezien geïsoleerd VKB hechten waarschijnlijk niet sterk genoeg is. Oudere patiënten daarentegen kunnen profiteren van geïsoleerd primair hechten met lage falingpercentages en goede functionele resultaten.

In **hoofdstuk 9** is onderzocht hoe snel patiënten na primair hechten van de VKB terugkeerden naar hun oorspronkelijke sportniveau. Deze retrospectieve studie toonde aan dat de gemiddelde tijd om weer aan het werk te gaan na operatie zeven dagen was, het hervatten van hardlopen 90 dagen duurde en de volledige terugkeer naar sportactiviteiten 180 dagen vergde. Deze mijlpalen werden eerder bereikt na een primair hechting in vergelijking met resultaten beschreven in de VKB-reconstructie literatuur. Het is echter belangrijk op te merken dat er meer onderzoek nodig is om gestandaardiseerde revalidatieprotocollen vast te stellen en vergelijkende studies uit te voeren met VKB-reconstructie.

In **hoofdstuk 10** is geconstateerd dat patiënten na primair VKB hechten, minder bewust zijn van hun geopereerde knie in het dagelijks leven in vergelijking met patiënten die een VKB-reconstructie hebben ondergaan, zoals blijkt uit lagere Forgotten Joinst Scores (FJS). Deze bevinding is van belang omdat het suggereert dat primair hechten kan leiden tot een nauwere herstel van de oorspronkelijke kniefunctie, met minder subjectieve beperkingen zoals instabiliteit, pijn of stijfheid van de knie. De FJS-12-vragenlijst is een waardevol instrument om verschillende aspecten van VKB-chirurgie te beoordelen, waaronder het risico op posttraumatische osteoartritis. We raden aan om deze uitkomstmaat vaker te gebruiken om de resultaten van VKB-chirurgie te beoordelen en te vergelijken.

In **hoofdstuk 11** werd aangetoond dat patiënten die primair hechten ondergaan, minder postoperatieve pijn ervaren, wat resulteert in verminderd gebruik van opioïden en een betere kwaliteit van revalidatie gedurende de eerste twee weken na de operatie in vergelijking met patiënten die een VKB-reconstructie ondergaan. Gezien de risico's die gepaard gaan met langdurig postoperatief gebruik van pijnstillers en de voortdurende wereldwijde opioïde epidemie, is dit een belangrijke bevinding van dit proefschrift.

In **hoofdstuk 12** van dit proefschrift werd onderzocht of VKB-rupturen uitsluitend in de acute fase gehecht kunnen worden. In deze studie weren patiënten geincludeerd die binnen drie weken of na drie maanden werden geopereerd en toonde aan of dat zowel acute als uitgestelde VKB-hechten vergelijkbare klinische resultaten en functionele mijlpalen opleveren. Weefselkwaliteit en lengte, in plaats van timing, zijn daarom de belangrijkste factoren voor een succesvolle uitkomst bij primair VKB-hechten. Daarom raden wij orthopedisch chirurgen aan om, ongeacht het tijdstip van de operatie, eerst het weefsel te beoordelen tijdens de inspectie van het kniegewricht voordat zij beslissen over het hechten of reconstrueren van de VKB.

In **hoofdstuk 13** wordt teruggeblikt op de uitgevoerde studies, waarbij wordt besproken of acute VKB-rupturen daadwerkelijk vroeg kunnen worden geopereerd en wat de huidige en toekomstige rol is van primair VKB-hechten binnen het behandelspectrum voor acute VKB rupturen. Ten slotte worden er inzichten gegeven in de toekomstige richtingen voor verder onderzoek naar arthroscopisch primair VKB-hechten.

Part 6

Appendices

A

Appendices - A

Repair versus reconstruction for proximal anterior cruciate ligament tears: a study protocol for a prospective multicenter randomized controlled trial

Abstract

Background

For active patients with a tear of the anterior cruciate ligament (ACL) who would like to return to active level of sports, the current surgical gold standard is reconstruction of the ACL. Recently, there has been renewed interest in repairing the ACL in selected patients with a proximally torn ligament. Repair of the ligament has (potential) advantages over reconstruction of the ligament such as decreased surgical morbidity, faster return of range of motion, and potentially decreased awareness of the knee. Studies comparing both treatments in a prospective randomized method are currently lacking.

Methods

This study is a multicenter prospective block randomized controlled trial. A total of 74 patients with acute proximal isolated ACL tears will be assigned in a 1:1 allocation ratio to either (I) ACL repair using cortical button fixation and additional suture augmentation or (II) ACL reconstruction using an all-inside autologous hamstring graft technique. The primary objective is to assess if ACL repair is non-inferior to ACL reconstruction regarding the subjective International Knee Documentation Committee (IKDC) score at two-years postoperatively. The secondary objectives are to assess if ACL repair is non-inferior with regards to (I) other patient-reported outcomes measures (i.e. Knee Injury and Osteoarthritis Outcome Score, Lysholm score, Forgotten Joint Score, patient satisfaction and pain), (II) objective outcome measures (i.e. failure of repair or graft defined as rerupture or symptomatic instability, reoperation, contralateral injury, and stability using the objective IKDC score and Rollimeter/KT-2000), (III) return to sports assessed by Tegner activity score and the ACL-Return to Sports Index at two-year follow-up, and (IV) long-term osteoarthritis at 10-year follow-up.

Discussion

Over the last decade there has been a resurgence of interest in repair of proximally torn ACLs. Several cohort studies have shown encouraging short-term and mid-term results using these techniques, but prospective randomized studies are lacking. Therefore, this randomized controlled trial has been designed to assess whether ACL repair is at least equivalent to the current gold standard of ACL reconstruction in both subjective and objective outcome scores.

Background

Historical overview of ACL repair

The first documented surgical treatment of an anterior cruciate ligament (ACL) injury consisted of open repair in 1895 when Mayo Robson repaired a proximally avulsed ACL and posterior cruciate ligament back to the femur in a 41-year old male with good outcomes at six-year follow-up.[1] In the twentieth century, Ivar Palmar[2,3] and Don O'Donoghue[4,5] reported on open primary repair as a treatment of ACL injuries, and in the early 1970s open primary repair became a popular treatment for ACL injuries.[6-9]

Feagin and Curl were the first to present the outcomes of open repair in 1972 and noted good outcomes at short-term follow-up.[8] A few years later in 1976, however, they noted a deterioration of outcomes at mid-term follow-up in their cohort.[10] Similarly, several other surgeons and researchers noted good short-term[11-16] but disappointing mid-term outcomes[17-21]. With these disappointing results and the promising outcomes of ACL reconstruction, several (randomized) prospective studies were started in the 1980s comparing open ACL repair with open ACL reconstruction.[19,22-24] These prospective studies noted more reliable outcomes with ACL reconstruction when compared to ACL repair, which ultimately led to an abandonment of open ACL repair and to the current gold standard of ACL reconstruction for all patients.[9]

In 1991, Sherman et al. were the first analyzing the disappointing mid-term outcomes of open ACL repair by performing an extensive subgroup analysis.[21] The authors found that a trend towards better outcomes in patients with proximal avulsion type tears and good tissue quality when compared to patients with midsubstance tears and/or tears with poor tissue quality. Unfortunately, the inclusion of the aforementioned prospective trials was already completed before the study by Sherman et al. was published, and thus the prospective trials contained all tear types including patients that might not have been ideal candidates for ACL repair (i.e., those with midsubstance tears or tears with poor tissue quality).

When critically reviewing the historical literature, and bearing in mind these findings by Sherman et al., it can be noted that the results of open repair of proximal ACL tears were indeed better. A recent systematic review of all historical studies on open repair noted that outcomes of open repair of proximal ACL tears showed 83 to 90% clinical stability, 80% return to sports, 79% good to excellent Lysholm score and 86% satisfaction in 539 patients in 11 studies.[25] These findings indicate that ACL repair may have been prematurely abandoned for all tear types and perhaps may be a good treatment option for patients with proximal tears. Furthermore, outcomes of ACL repair can be expected to improve when benefiting from modern development, such as arthroscopy (instead of open repair) and modern rehabilitation (instead of casting and immobilization).

Rationale for ACL repair

The rationale behind better outcomes of ACL repair of proximal tears compared to midsubstance tears is that better vascularity is present at the proximal end of the ligament[26] and, as a result, proximal tears have healing potential for reattachment that is similar to medial collateral ligament (MCL) tears.[27] The reason for the continued pursuit of repair as a treatment of ACL injuries can also be explained by the potential advantages of repair over reconstruction. With ACL repair, the native tissue can be preserved along with proprioception which may provide patients with a more normal feeling of the knee compared to ACL reconstruction.[28,29] Also, ACL repair is a less invasive surgery when compared to ACL reconstruction as no or only small tunnels need to be drilled and no graft tissues need to be harvested, leading to lower surgical morbidity,[30-33] faster return of range of motion and fewer complications[34]. Furthermore, in case of failure of both treatments, revision surgery following primary repair is expected to be similar to primary reconstruction (no or only small tunnels have been drilled or grafts harvested), whereas revision of reconstruction surgery can be complicated by tunnel malpositioning or widening and pre-existing hardware and is associated with inferior outcomes compared to primary ACL reconstruction.[35-37]

Recent literature on ACL repair

With the recognized relevance of tear location in ACL repair and the potential advantages of this treatment, several surgeons and researchers have pursued the concept of ACL repair of proximal tears.[38-47] Most of these studies were retrospective small case series reporting good short-term outcomes with an overall reported failure rates of 6 to 9%, reoperation rates of 0 to 4% and patient-reported outcome measures (PROMs) >85% of the maximum score.[48] Three studies have also shown that the good outcomes are maintained at mid-term follow-up.[44,45,49] One prospective study has compared the outcomes of repair (n = 20) versus reconstruction (n = 20) in patients with proximal tears and reported similar outcomes regarding functional outcomes, failure rates and laxity examination.[46] However, no randomized studies or studies with sufficient number of patients to assess differences between the treatments have been performed, and a recent systematic review also concluded higher-level evidence studies for ACL repair are currently lacking.[48] Recent studies have also suggested that primary repair with suture augmentation results in lower failure rates when compared to primary repair without suture augmentation.[42,48]

The current surgical gold standard of treating ACL injuries is ACL reconstruction using autograft tissue of either hamstring tendons, patellar tendon or quadriceps tendon. As for all new surgical techniques, the outcomes of arthroscopic ACL repair need to be compared to the current gold standard in order to assess whether this treatment can be used for standard patient care. Therefore, a randomized controlled trial (RCT) comparing ACL repair with ACL reconstruction is needed. The ACL study group of the Dutch Arthroscopy Association also recently declared that "*the application of ACL repair could be considered in a medial ethical committee-approved study until there is high-grade and long-term evidence regarding the efficacy of modern-day ACL repair.*"

Goal and hypotheses

The goal of this multicenter non-inferior prospective randomized controlled trial is therefore to compare the outcomes of arthroscopic ACL repair with suture augmentation to ACL reconstruction for patients with proximal tears in a 1:1 allocation ratio. The primary outcome is the subjective International Knee Documentation Committee (IKDC) score and the secondary outcomes are other patient-reported outcomes, objective outcomes and return to sports. It is hypothesized that patients following ACL repair with suture augmentation have non-inferior primary and secondary outcomes when compared to ACL reconstruction due to the less invasive surgery.

Methods

This study and manuscript have been designed in accordance to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines.

Study design

This study is a multicenter prospective RCT with randomization into two treatment arms: (I) arthroscopic ACL repair with suture augmentation and (II) arthroscopic ACL reconstruction surgery. This study is a non-inferiority study with the hypothesis that arthroscopic ACL repair is non-inferior to (equivalent or better than) arthroscopic ACL reconstruction. All patients with proximal tears will be randomized during the operation into one of these treatment arms and will be followed up to ten-years postoperatively.

Study sample

Potential candidates will be selected from five participating orthopaedic surgery departments, of which one is an academic hospital, three are teaching hospitals and one is a private hospital. Inclusion and exclusion criteria for participation in the study are displayed in Table 1. In general, potential inclusion involves all patients with acute, isolated, complete, proximal ACL tears that have a desire to return to pre-injury activities and exclusion involves all concomitant ligamentous and osteoarthritic injuries and skeletally immature patients. A flowchart of the study is shown in Figure 1. Patients can withdraw their participation in this study at any time point, at which their data will be deleted.

Table 1. Inclusion and exclusion criteria for participating in this trial

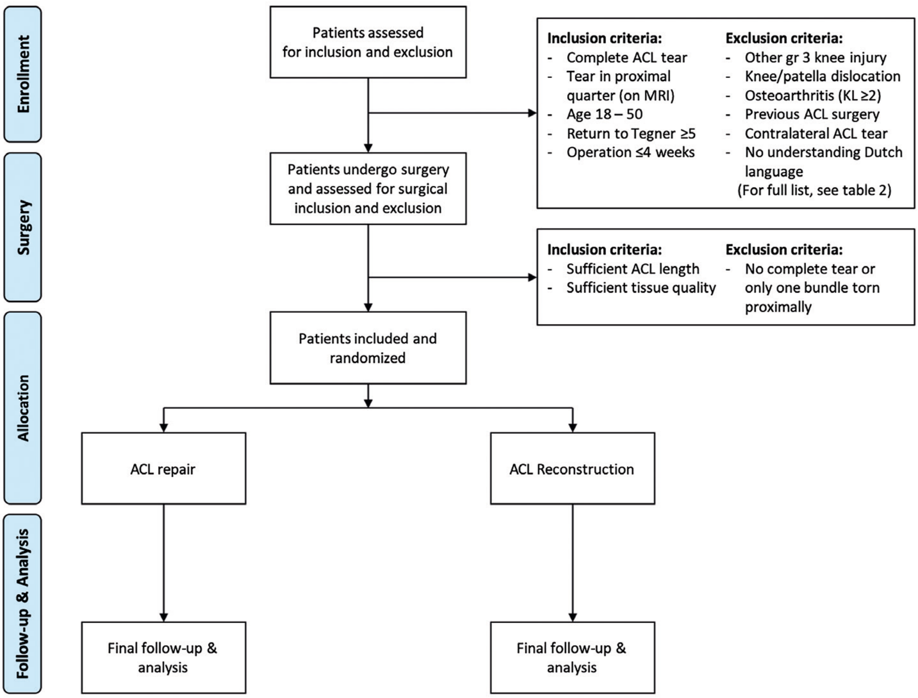
Inclusion criteria	Exclusion criteria
Pre-operative	
Complete primary ACL tear on physical examination and MRI	Complete ipsilateral concomitant knee ligament injury requiring surgery
Tear in proximal quarter on MRI[50,51]	Concomitant ipsilateral knee dislocation or patellar dislocation
Age 18 – 50 years[22,52]	Osteoarthritis KL grade ≥2
Preinjury Tegner level ≥5 & desired Tegner level ≥5[53]	Previous ipsilateral ACL reconstruction/repair
Operation within 4 weeks of injury[54]	Intra-articular corticosteroids 6 months prior
	No understanding of Dutch language or not capable of understanding the study and participation
	No preoperative flexion of 90 degrees
	Grade 3 pivot shift indicating gross ligament instability that requires additional procedures
	Gross lower leg malalignment requiring bony osteotomies
	Muscular, neurological or vascular diseases that influence rehabilitation or surgery
	Prolonged use medication use of prednison or cytostatics

Table 1. Inclusion and exclusion criteria for participating in this trial *(Continued)*

Inclusion criteria	Exclusion criteria
	Pregnancy during injury or surgery
	Osteoporosis that influence rehabilitation or surgery
Intra-operative	
Sufficient tissue length for retensioning to femoral insertion	No complete tear at arthroscopy or only one bundle (AM or PL) with proximal tear
Sufficient tissue quality to withhold sutures	Grade 3 or grade 4 cartilage lesions

ACL indicates anterior cruciate ligament; MCL, medial collateral ligament; LCL, lateral collateral ligament; PCL, posterior cruciate ligament; PLC, posterolateral corner.

Figure 1.



Flowchart of the REPAIR-trial

Randomization

All patients will be consented preoperatively for the study. Patients are taken into the operating room, general or epidural anesthesia is induced, and the leg is prepped and draped for standard arthroscopic knee surgery with a tourniquet high at the upper thigh. Then standard anteromedial and anterolateral portals are created, and the knee is assessed for cartilage, meniscus and ligamentous injuries. After cartilage and meniscus injuries are addressed, the tear type of the ACL and eligibility for this study is assessed. First, it should be confirmed whether a proximal tear is present (i.e., whether the distal remnant of the ACL is of sufficient length to be reattached to the anatomical femoral footprint of the ACL) and whether sufficient tissue quality is present (i.e., whether the ligament remnant is of sufficient quality to withhold suture passage and can be tensioned towards the femur).

If these conditions are present, patients are randomized between both treatment arms, and if these conditions are not present, the patient is excluded, and standard ACL reconstruction will be performed. A computer block randomization of 10 patients per block will be done digitally prior to the study, and the allocation concealment is performed by sequentially numbered, opaque, sealed envelopes containing the name of the procedure in a randomized order. The envelopes are placed in the operating room and opened when the surgeon deems the ACL tear eligible for the study. A participant timeline is shown in Figure 2.

Surgical techniques

Prior to the start of the trial, a cadaver session will be held in order to standardize the technique of ACL repair and ACL reconstruction for all surgeons and to minimize the learning curve. All surgeons have extensive experience with ACL reconstruction and three out of six participating centers have experience with ACL repair.

The surgical technique of arthroscopic ACL repair has been more extensively described in the literature.[39,43,55] In brief, first the native torn ACL will be sutured with a loop using FiberWire sutures and advanced with one to two passes, so that the sutures exit the avulsed ligament towards the femur. Then, a small tunnel will be drilled from the native femoral insertion towards the lateral epicondyle using an ACL drill guide. The sutures will be passed through a TightRope button along with an additional FiberTape. The sutures and TightRope will be passed through the femoral tunnel and the button will be flipped. Then, a small tunnel will be drilled through the tibia from the anteromedial cortex towards the anterior part of the tibial footprint, and the FiberTape will be channeled through the tibial tunnel and, after cycling the knee, the FiberTape is fixed into the anteromedial cortex using a suture anchor at full extension. Finally, the repair sutures will be tensioned and tied in order to reapproximate the ACL towards the femoral footprint at 90° flexion.

For ACL reconstruction, a standard all-inside autograft hamstring tendon anatomic reconstruction technique is used.[56,57] First, autologous hamstrings (semitendinosus and gracilis tendon) are harvested to the preference of the surgeon and will be prepared for graft usage with a minimum graft diameter of 8 mm.[58,59] Then, femoral and tibial sockets are independently drilled in retrograde fashion using a FlipCutter drill. The graft is placed into the sockets, the knee is cycled in order to achieve optimal tension of the graft, and the graft is then fixed at the femoral and tibial side using a cortical button.

Rehabilitation

Both treatment arms undergo the same rehabilitation program and consists of a milestone-based program according to the Dutch national guidelines for rehabilitation following ACL reconstruction and consists of three phases.[60-62] The first phase focuses on controlling swelling, restoration of range of motion and return of quadriceps muscle control, and generally takes 4 to 8 weeks. The second phase focuses on resuming light sporting activities and work without symptoms, and phase three focuses on full return to sports activities and heavy work. In case of meniscus repair, the first 6 weeks patients are partial weight bearing, range of motion is restricted to 0-90° and patients are not allowed deep bending or squatting for 4 months. Although the rehabilitation is milestone based and no strict time goals can be set, generally cycling on a stationary bike is allowed at 4-6 weeks, running at 10-12 weeks and return to sports and pivoting activities at a minimum of 9 months postoperatively.

Blinding

Blinding for patients is not possible due to different scars, different postoperative radiographs and practical reasons. However, the data analysis will be performed in blinded fashion.

Primary outcomes/endpoint (Table 2)

The primary outcome of this non-inferiority RCT is the subjective patient reported outcome (PROM) at two-year follow-up consisting of the subjective IKDC score[63] (Dutch validation[64]), as to a recent RCT on a similar topic.[65,66] The primary endpoint is the subjective IKDC at two-years postoperatively. Patients will ultimately be followed for 10 years.

Table 2. This chart provides an overview of which outcomes are collected at the different follow-up visits

	Pre	3 mns	6 mns	9 mns	1 yr	2 yrs	5 yrs	10 yrs
Primary outcomes								
IKDC subjective	X	X	X	X	X	X	X	X
Secondary outcomes								
KOOS	X	X	X	X	X	X	X	X
Lysholm	X	X	X	X	X	X	X	X
Forgotten Joint Score	X	X	X	X	X	X	X	X
Satisfaction & pain	X	X	X	X	X	X	X	X
Failure		X	X	X	X	X	X	X
Reoperation		X	X	X	X	X	X	X
Contralateral injury	X	X	X	X	X	X	X	X
IKDC objective	X	X	X	X	X	X	X	X
KT-1000	X	X	X	X	X	X	X	X
Return to sports		X	X	X	X	X	X	X
Tegner score	X	X	X	X	X	X	X	X
ACL-RSI		X	X	X	X	X	X	X
Osteoarthritis (X-ray)	X							X
AE, SAE, SUSAR	X	X	X	X	X	X	X	X

IKDC indicates International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; AE, adverse events; SAE, serious adverse event; SUSAR, Suspected Unexpected Serious Adverse Reaction; Pre, preoperatively; mns, months; yr(s), year(s).

Secondary outcomes (Table 2)

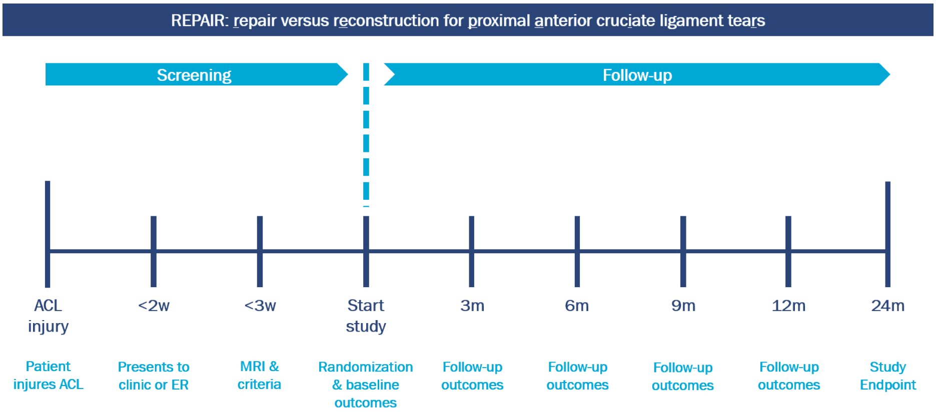
The secondary outcomes of this RCT are fourfold and consist of (I) other subjective outcomes, (II) objective outcomes, (III) return to sports, and (IV) long-term osteoarthritis.

Other collected PROMs for this study are the Knee Injury and Osteoarthritis Outcome Score (KOOS)[67] (Dutch validation[68]), Lysholm score[69] (Dutch validation[70]), and Forgotten Joint Score (FJS)[28] (Dutch validation[71]). Furthermore, patient satisfaction and pain scores are collected using a numeric rating scale (range 0 – 10).

The objective outcomes consist of failure of ACL repair/graft, reoperation, contralateral injury, and laxity. Failure is defined as a (traumatic) rerupture or symptomatic instability with activities. Reoperation is defined as any new operation on the same knee for any other reason than revision (e.g., symptomatic meniscus tear, hardware irritation, infection or stiffness/arthrofibrosis). Contralateral injury was defined as a complete ACL rupture of the contralateral ACL. Stability is defined as the laxity found with physical examination using the IKDC objective score form,[72] which includes the Lachman, anterior drawer and pivot shift test, and side-to-side differences is assessed using KT-2000 or Rollimeter.

Return to sports is defined as (I) returning to sports, (II) returning to the same sport, and (III) returning to the preinjury level of sport. The preinjury and postoperative Tegner activity scale are also collected, which enables comparison with other studies[73] (Dutch validation[70]). Finally, confidence of return to sports and fear of reinjury are assessed using the ACL-Return to Sports Index (ACL-RSI) score[74] (Dutch validation[75]).
Osteoarthritis will be reviewed at ten-year follow-up. Radiographs of both knees will be performed, and the operated knee will be compared to (I) the contralateral knee if no operation occurred in that knee, and (II) the ipsilateral knee radiograph preoperatively. The Kellgren-Lawrence (KL) grade will be used to assess the incidence and grades of osteoarthritis.

Figure 2.



Timeline for patients in the REPAIR-trial

Sample size

The sample size calculation was based on the primary outcome of this study (subjective IKDC score), similar to another RCT design on this topic.[65] It has been shown that a difference of 8.8 points in the subjective IKDC score is the minimal clinically important difference (MCID).[76] Using this non-inferiority limit of 8.8 points, and a standard deviation of 11 points[42,65,77] along with a two-sided alpha of 0.05, a power of 90%, and a lost-to-follow-up rate of 10%, a total of 37 patients in each group (74 patients in total) are needed to assess the primary outcome of this non-inferiority RCT. This sample size is also sufficient for the MCID of KOOS[78] and Lysholm score.[79] Given the recent studies that showed that 30-40% of the acute tears will have repairable proximal ACL tears,[50,80] we estimate that approximately 200 patients will be needed to be screened preoperatively to achieve the sample size of 74 patients.[81]

Statistical analysis

Both an intention to treat analysis and per protocol analysis will be performed for this non-inferiority study. Comparison of nominal variables between ACL repair and ACL reconstruction will be performed using two-by-two tables with Pearson's Chi-square test or Fisher's exact test (in case one of the cells is <5). For comparison of continuous variables, first tests for normal distribution of values are performed and independent t-tests are used of normal distributed values and non-parametric t-tests are used for not-normally distributed values.

A mixed model analysis for repeated measures will be performed to assess differences between both groups. Furthermore, a multivariate regression analysis will be performed for the primary endpoint of IKDC at two-years follow-up in order to correct for potential confounders. Statistical analysis will be performed using SPSS version 25.0 (IBM Software, Armonk, NY, USA). All tests are two-sided and a p-value of <0.05 is considered statistically significant.

Discussion

This study reports on the study design of the REPAIR-trial (**R**epair versus r**E**construction for **P**roximal **A**nterior cruciate l**I**gament tea**R**s). Few studies have examined the outcomes of repair versus reconstruction with favorable outcomes for ACL reconstruction [22-24]. However, these studies were performed over 30 years ago and are limited by the fact that all tear types were repaired rather than only proximal tears and that repair was performed using an arthrotomy.[9,25,82] Recently, four RCT studies have been designed to assess the outcomes of ACL repair[65,83-85] but these are either performed in midsubstance tears,[65,83] assess the outcomes of dynamic intraligamentary stabilization (DIS) versus ACL reconstruction,[65,83] repair versus DIS[84] or Bridge-Enhanced ACL Repair (BEAR) with reconstruction[85]. Our current RCT differs from these studies as only proximal tears will be treated rather than all tear types and as the ligament will be reattached to the femoral footprint in a minimally invasive way.

The renewed interest of repair of proximal tears can be explained by improved understanding of patient selection. Research has shown that proximal tears have a better vascularity compared to midsubstance tears[26] and therefore have excellent healing capacity by reattachment to the femoral wall which is similar to the healing capacity of MCL tears.[27] Both historical studies on open ACL repair,[9,25,82] and more recent studies on repair with DIS (also known as Ligamys) have shown that the clinical outcomes are indeed better when repairing proximal tears. Two studies have shown failure rates of repair with DIS in midsubstance tears of 24% in all patients and 36% in competitive athletes with midsubstance tears.[86,87] Our current study applies strict patient selection criteria of proximal tears and good tissue quality. As the length of distal remnant and possibility of repair can only be assessed intraoperatively, randomization in this study should perform during surgery after the surgeon has confirmed the possibility of repair. Consequently, patients will be consented that they might be excluded during surgery if a non-repairable tear is present, and these patients will undergo standard ACL reconstruction.

It should be noted that there is also a potential disadvantage of ACL repair. By performing ACL surgery in the early phase (since early surgery prevents ligament retraction and preserves tissue quality that is both needed for repair[4,5,88]), it is likely that too many ACL surgeries will be performed. Current day standards recommend that patients following ACL injury will be treated conservatively first as approximately half of the patient may be copers and do not need surgical intervention.[53,60,89] By performing surgery on all ACL injured patients, patients will undergo surgery while they might be copers and do not need surgery. This risk is minimized in this study by only including patients aged 18 – 50 and only patients that desire to return to sports. It would be best if it is known preoperatively which patients will not do well with conservative treatment and ultimately require ACL surgery, as this both increases the chance of performing ACL repair and as early reconstruction outcomes decreases the risk for meniscal and chondral damage[60] at longer follow-up when compared to delayed reconstruction.

Several studies have recently reported good short-term outcomes of arthroscopic ACL repair using different techniques: in some studies femoral fixation consisted of using two suture anchors,[42,44] one suture anchor (for both bundles)[40,45,46] or transosseous tunnels with or without cortical button fixation[39,41,43,55,90], and some studies used ACL repair without[40,41,45,46] or with[39,43,55,90] additional suture augmentation. For this study, femoral fixation will consist of cortical button fixation with additional suture augmentation (FiberTape) in order to protect the repair in the early phases of rehabilitation, because it has been suggested that additional suture augmentation leads to lower rerupture rates.[42,48]

This study has been designed to assess the outcomes following repair and reconstruction of proximal ACL tears. We hypothesize that the repair treatment is a good treatment for proximal tears as it has potential advantages over ACL reconstruction: the surgery is short and minimally invasive, it has a low complication rate, rehabilitation is easier, and in case ACL repair fails then primary reconstruction surgery can be performed. Non-inferiority of arthroscopic ACL repair compared to arthroscopic ACL reconstruction may lead to a treatment algorithm in which patients with proximal avulsion tears can be repaired in the acute setting whereas patients with midsubstance tears will undergo ACL reconstruction in either the acute or delayed setting.[91,92]

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B

Appendices - B

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Appendices - C

C

Phd portfolio

Name PhD student:	Daan Vermeijden
PhD period:	2019 - 2024
Promotor:	Prof. dr. G.M.M.J. Kerkhoffs
Copromotors:	dr. M.V. Rademakers and dr. J.P. van der List

PhD training

General courses	**Year**	**Workload (ECTS)**
BROK ('Basiscursus Regelgeving Klinisch Onderzoek')	2021	1.0
Specific courses		
AO Trauma Course: Basic Principles of Fracture Management	2023	1.0
Advanced Trauma Life Support	2021	1.0

Oral presentations and podium presentations	**Year**	**Workload (ECTS)**
Vermeijden HD, Rilk S, Huluba K, Yang XA, Van der List JP, DiFelice GS. *A Prospective Comparison of Postoperative Pain and Opioid Consumption between Primary Repair and Reconstruction of the Anterior Cruciate Ligament.* E-poster presentation at 12th Biennial Congress of the European Federation of National Associations of Orthopaedics and Traumatology (EFORT), Boston, USA *Presented by S. Rilk*	2023	0.25
Vermeijden HD, Rilk S, Huluba K, Yang XA, Van der List JP, DiFelice GS. *A Prospective Comparison of Postoperative Pain and Opioid Consumption between Primary Repair and Reconstruction of the Anterior Cruciate Ligament.* E-poster presentation at 14th Biennial Congress of the International Society of Arthroscopy,Knee Surgery, and Orthopaedic Sports Medicine *Presented by S. Rilk*	2023	0.25

Vermeijden HD, Van der List JP, Benner JL, Rademakers, MV, Kerkhoffs GMMJ, DiFelice GS. *ACL Primary Repair with Suture Augmentation: systematic review with meta-analysis.* Podium presentation at the 53th Biennial Congress of the Eastern Orthopedic Association. Atlantic City, USA *Presented by S. Rilk*	2022	0.25
Vermeijden HD, Rilk S, Huluba K, Yang XA, Van der List JP, DiFelice GS. *A Prospective Comparison of Postoperative Pain and Opioid Consumption between Primary Repair and Reconstruction of the Anterior Cruciate Ligament.* Podium presentation at the 53th Biennial Congress of the Eastern Orthopedic Association. Atlantic City, USA *Presented by S. Rilk*	2022	0.25
Vermeijden HD, Van der List JP, DiFelice GS. *The role of age on failure rates and outcomes following arthroscopic primary repair of proximal anterior cruciate ligament tears.* Podium presentation at the 50th of The American Orthopaedic Society for Sports Medicine (AOSSM) and the Arthroscopy Association of North America (AANA) Combined Annual Meeting. Nashville, USA *Presented by G.S. DiFelice*	2021	0.25
Vermeijden HD, Van der List JP, DiFelice GS. *The Multiple Ligament Injured Knee: When is Primary Repair an Option?* Podium presentation at the 51th Biennial Congress of the Eastern Orthopedic Association *Presented by G.S. DiFelice*	2020	0.25
Vermeijden HD, Van der List JP, DiFelice GS. *The role of age on failure rates and outcomes following arthroscopic primary repair of proximal anterior cruciate ligament tears.* Podium presentation at the 12th of the International Society of Arthroscopy, Knee Surgery, and Orthopaedic Sports Medicine. Cancun, Mexico	2019	0.5
Vermeijden HD, Van der List JP, Jonkergouw A, DiFelice GS. *Less awareness of the knee following arthroscopic primary repair versus reconstruction of the anterior cruciate ligament.* E-poster presentation at 12th Biennial Congress of the International Society of Arthroscopy, Knee Surgery, and Orthopaedic Sports Medicine. Cancun, Mexico	2019	0.5

(Inter)national conferences	Year	Workload (ECTS)
Combined 61st NOF Congress and NOV congress, Rotterdam, The Netherlands	2024	1.0
24th Anniversary NVA Congress, Amsterdam, The Netherlands	2024	0.5
12th Biennial Congress of the International Society of Arthroscopy, Knee Surgery, and Orthopaedic Sports Medicine, Cancun, Mexico	2019	1.0
86th Annual Meeting of American Academy of Orthopaedic Surgeons, Las Vegas, NV, USA.	2019	1.0
VOCA Congress, Amsterdam, Netherlands.	2018	0.5

Other	Year	Workload (ECTS)
Invited peer-reviewed for: Journal of ISAKOS	2021	0.25

Teaching	Year	Workload (ECTS)
Supervising		
Alex Yang, Primary ACL repair, Orthopaedic Surgery, HSS	2019	1.0
Kurt Huluba, Primary ACL repair, Orthopaedic Surgery, HSS	2021	1.0
Ashwin Joeloemsingh, Primary ACL repair, AUMC	2023	1.0

Parameters of Esteem	Year
Grants	
Anna Fonds research grand	2022
Anna Fonds travel grand	2019
A.S.C. Academy travel grand	2019
Stichting Fundatie van Vrijwouwe van Renswoude travel grand	2019
Scholten-Cordes Fonds travel grand	2019

Appendices - D

List of publications

Peer reviewed articles

Published/accepted

D

1. Rilk S, Goodhart GC, O'Brien R, von Rehlingen-Prinz F, **Vermeijden HD**, Van der List JP, DiFelice GS. Revision Rates After Anterior Cruciate Ligament Primary Repair Compared To Reconstruction Are Increased in Young Patients But Comparable in Adults: A Systematic Review and Meta-Analysis. *Knee Surgery, Sports Traumatology, Arthroscopy. 2024. doi: 10.1002/ksa.12239.*
2. Holuba K, Rilk S, **Vermeijden HD**, O'Brien R, van der List JP, DiFelice GS. Acute Percutaneous Repair of Medial Collateral Ligament With Suture Augmentation in the Multiligamentous Injured Knee Results in Good Stability and Low Rates of Postoperative Stiffness. *Arthroscopy, Sports Medicine, and Rehabilitation. 2023;5(6).*
3. **Vermeijden HD**, Huluba K, Yang XA, O'Brien R, Van der List JP, DiFelice GS. A prospective comparison of postoperative pain and opioid consumption between primary repair and reconstruction of the anterior cruciate ligament. *Orthopaedic Journal of Sports Medicine. 2023;11(9):23259671231187442.*
4. Rilk S, Goodhart GC, O'Brien R, **Vermeijden HD**, Van der List JP, DiFelice GS. Anatomic Arthroscopic Primary Repair of Proximal Anterior Cruciate Ligament Tears. *Arthroscopy Techniques. 2023;15;12(6):e879-e888.*
5. **Vermeijden HD**, Yang XA, Dougles DN, Rademakers MV, Kerkhoffs GMMJ, Van der List JP, DiFelice GS. Age and Bone Bruise Patterns Predict Tear Location in the Anterior Cruciate Ligament. *Arthroscopy, Sports Medicine, and Rehabilitation. 2023;5(1):41-50.*
6. Xiuyi YA, **Vermeijden HD**, Holuba K, Obrien B, DiFelice GS. Bilateral simultaneous anterior cruciate ligament tears treated with single staged simultaneous primary repair: A case report. *International Journal of Surgery Case Reports. 2022;99:107670.*
7. **Vermeijden HD**, Edoardo M, Marzilli F, Yang XA, Van der List JP, Ferreti A, DiFelice GS. Primary Repair versus Reconstruction in Patients with Bilateral Anterior Cruciate Ligament Injuries: What do Patients Prefer? *Advances in Orthopedics. 2022;13;2022:3558311.*
8. **Vermeijden HD**, Yang XA, van der List JP, Rademakers MV, Kerkhoffs GMMJ, DiFelice GS. Primary repair with suture augmentation for proximal anterior cruciate ligament tears: a systematic review with meta-analyses. *Knee. 2022 Jul 38:19-29.*
9. Holuba K, **Vermeijden HD**, Xiuyi YA, Obrien B, van der List JP, DiFelice GS. Treating Combined Anterior Cruciate Ligament and Medial Collateral Ligament Injuries Operatively in the Acute Setting Is Potentially Advantageous. *Arthroscopy. 2022;8;S0749-8063(22)00398-X.*
10. Lin KM, **Vermeijden HD**, Klinger CE, Dyke JP, Rodeo SA, DiFelice GS. Differential regional perfusion of the human anterior cruciate ligament: a quantitative MRI assessment. *Journal of Experimental Orthopaedics. 2022 May 30;9(1):50.*

11. Xiuyi YA, **Vermeijden HD**, Holuba K, Obrien B, DiFelice GS. Primary Repair of Medial Collateral Ligament Tears with Suture Augmentation. *Video Journal of Sports. Medicine. 2022;2(5).*

12. Yang XA, **Vermeijden HD**, Obrien B, van der List JP DiFelice GS. Percutaneous Coracoclavicular Tightrope Reduction of a Displaced Distal Clavicular Fracture: A Case Report. *Journal of Orthopaedic Experience & Innovation. 2021;2(2).*

13. **Vermeijden HD**, Yang XA, van der List JP, Rademakers MV, Kerkhoffs GMMJ, DiFelice GS. Early and Delayed Surgery for Isolated ACL and Multiligamentous Knee Injuries Have Equivalent Results: A Systematic Review and Meta-analysis. *American Journal of Sports Medicine. 2022;51(4):1106-1116.*

14. van der List JP, **Vermeijden HD**, Sierevelt IN, et al. Repair versus reconstruction for proximal anterior cruciate ligament tears: a study protocol for a prospective multicenter randomized controlled trial. *BMC Musculoskelet Disorders. 2021;30;22(1):399.*

15. **Vermeijden HD**, Van der List JP, O'Brien RJ, DiFelice GS. Primary repair of anterior cruciate ligament injuries: current level of evidence of available techniques. *The Journal of Bone & Joint Surgery Reviews. 2021;6;9(5).*

16. **Vermeijden HD**, Van der List JP, Chen,YT, DiFelice GS. Black Bone Disease with Synovial Pigmentation Observed During Anterior Cruciate Ligament Surgery: a Case Report. *International Journal of Surgery Case Reports. 2021;81:105819.*

17. **Vermeijden HD**, Yang XA, Van der List JP, DiFelice GS. Validating the Forgotten Joint Score-12 after Primary Anterior Cruciate Ligament Repair. *Arthroscopy, Sports Medicine, and Rehabilitation. 2021;5;3(3):e893-e900.*

18. **Vermeijden HD**, Yang XA, Van der List JP, DiFelice GS. Acute and Delayed Anterior Cruciate Ligament Repair Results in Similar Short to Mid-term Outcomes. *Knee. 2021;29:142-149.*

19. **Vermeijden HD**, Van der List JP, DiFelice GS. Arthroscopic Primary Repair of the Posterior Cruciate Ligament. *Journal of Knee Surgery. 2020;28(1):23-29.*

20. **Vermeijden HD**, Van der List JP, DiFelice GS. Arthroscopic Primary Repair of Proximal Anterior Cruciate Ligament Tears with Suture Augmentation. *Video Journal of Sports. Medicine. 2021;1(3).*

21. **Vermeijden HD**, Van der List JP, DiFelice GS. The role of age on the failure rates and patient-reported outcomes following arthroscopic primary repair of proximal anterior cruciate ligament tears. *Arthroscopy. 2021;37(4):1194-1201.*

22. **Vermeijden HD**, Cerniglia B, Dougles DN, Rademakers MV, Kerkhoffs GMMJ, Van der List JP, DiFelice GS. Distal remnant length can be measured reliably and predicts primary repair of proximal anterior cruciate ligament tears. *Knee Surgery, Sports Traumatology, Arthroscopy. 2021;29(9):2967-2975.*

23. **Vermeijden HD**, Van der List JP, DiFelice GS. Primary repair of the lateral collateral ligament using additional suture augmentation. *Arthroscopy Techniques, 2020;9(8):e1073-1077.*

24. **Vermeijden HD**, Yang XA, van der List JP, DiFelice GS, Rademakers M V., Kerkhoffs GMMJ. Trauma and femoral tunnel position are the most common failure modes of anterior cruciate ligament reconstruction: a systematic review. *Knee Surgery, Sports Traumatology, Arthroscopy. 2020;28(11):3666-3675.*

25. **Vermeijden HD**, van der List JP, O'Brien R, DiFelice GS. Return to sports following arthroscopic primary repair of the anterior cruciate ligament in the adult population. *Knee. 2020;27(3):906-914.*
26. Van der List JP, **Vermeijden HD**, Sierevelt IN, DiFelice GS, van Noort A, Kerkhoffs GMMJ. Arthroscopic primary repair of proximal anterior cruciate ligament tears seems safe but higher level of evidence is needed: a systematic review and meta-analysis of recent literature. *Knee Surgery, Sports Traumatology, Arthroscopy. 2020;28(6);1946-1957.*
27. **Vermeijden HD**, Yang XA, van der List JP, DiFelice GS. Large variation in indications, preferred surgical technique and rehabilitation protocol for primary anterior cruciate ligament repair: a survey among ESSKA members. *Knee Surgery, Sports Traumatology, Arthroscopy. 2020;28(11):3613-3621.*
28. **Vermeijden HD**, Van der List JP, DiFelice GS. Arthroscopic primary repair of the anterior cruciate ligament with single-bundle graft augmentation. *Arthroscopy Techniques. 2020;19;9(3):e367-373.*
29. **Vermeijden HD**, O'Brien R, Van der List JP, DiFelice GS. Patients forget about their operated knee more following arthroscopic primary repair of the anterior cruciate ligament than following reconstruction. *Arthroscopy. 2020;36(3);797-804.*
30. **Vermeijden HD**, Van der List JP, DiFelice GS. Arthroscopic posterior cruciate ligament primary repair. *Sports Medicine and Arthroscopy Review. 2020;28(1)23-29.*
31. **Vermeijden HD**, Jonkergouw A, Van der List JP, DiFelice GS. The multiple ligament injured knee: when is primary repair an option? *Knee, 2019;27(1):173-182.*
32. Van der List JP, **Vermeijden HD**, DiFelice GS. Anterior cruciate ligament reconstruction following failed primary repair: surgical technique and a report of three cases. *Minerva Ortopedica e Traumatologica. 2019;70(2):70-77.*
33. **Vermeijden HD**, Leenen LPH, van Polen M, Dijkgraaf MGW, Hietbrink F. Analysis of two treatment modalities for the prevention of vomiting after trauma: orogastric tube or anti-emetics. *Injury. 2017;48(10):2106-2111.*

Editorials and letters

1. Rilk S, Gabriel GS, **Vermeijden HD**, van der List JP, DiFelice GS. Anterior cruciate ligament primary repair is a valid treatment option for proximal tears with good to excellent tissue quality in the acute, sub-acute and delayed setting – A letter to the editor. *Journal of ISAKOS, 2024;9(4):740-741.*
2. Rilk S, Saithna A, Ferreti A, et al. The modern-day ACL surgeon's armamentarium should include multiple surgical approaches including primary repair, augmentation, and reconstruction: A letter to the Editor. *Journal of ISAKOS. 2023;5;S2059-7754(23)00465-0.*

Bookchapters

1. **Vermeijden HD,** Van der List JP, DiFelice GS. Arthroscopic Primary Repair of the Cruciate Ligaments. Evidence-Based Management of Complex Knee Injuries: Restoring the Anatomy to Achieve Best Outcomes. *2020, pp 144-156.*

Appendices - E

Acknowledgments

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Appendices - F

About the author

Harmen Daniel (Daan) Vermeijden (born March 11, 1993, in Amsterdam) grew up in Amersfoort, where he completed his pre-university education at Het Nieuwe Eemland. He then pursued his medical studies at the Vrije Universiteit (VU) Amsterdam. During his training, he developed a keen interest in orthopaedic and trauma surgery, gaining valuable early experience at Bergman Clinics in Naarden, an orthopaedic surgery center.

In 2019, Daan moved to New York to work as a research fellow at the Hospital for Special Surgery, where he collaborated with Dr. DiFelice on research focused on arthroscopic primary repair of the anterior cruciate ligament. This research became the foundation for his thesis at Amsterdam University Medical Centers under supervision of prof. Gino Kerkhoffs. To date, his research has resulted in more than 30 publications and several presentations on international meetings on the topic of primary ACL repair.

In 2021, he returned to the Netherlands and began working as a non-training orthopaedic surgery resident, first in Alkmaar under the supervision of Dr. Lucien Keijser, and later at TergooiMC's orthopaedic department under Dr. Ton Vervest. During this time, he balanced his clinical responsibilities with ongoing research. The following year, he commenced his residency in orthopaedic surgery at Amsterdam University Medical Centers under the supervision of Dr. Matthias Schafroth. He completed his general surgery training at Onze Lieve Vrouwe Gasthuis under Prof. Carel Goslings and is currently working once again at the orthopaedic department in Alkmaar. Daan is currently living in Amsterdam and aims to complete his orthopaedic residency training in 2028.