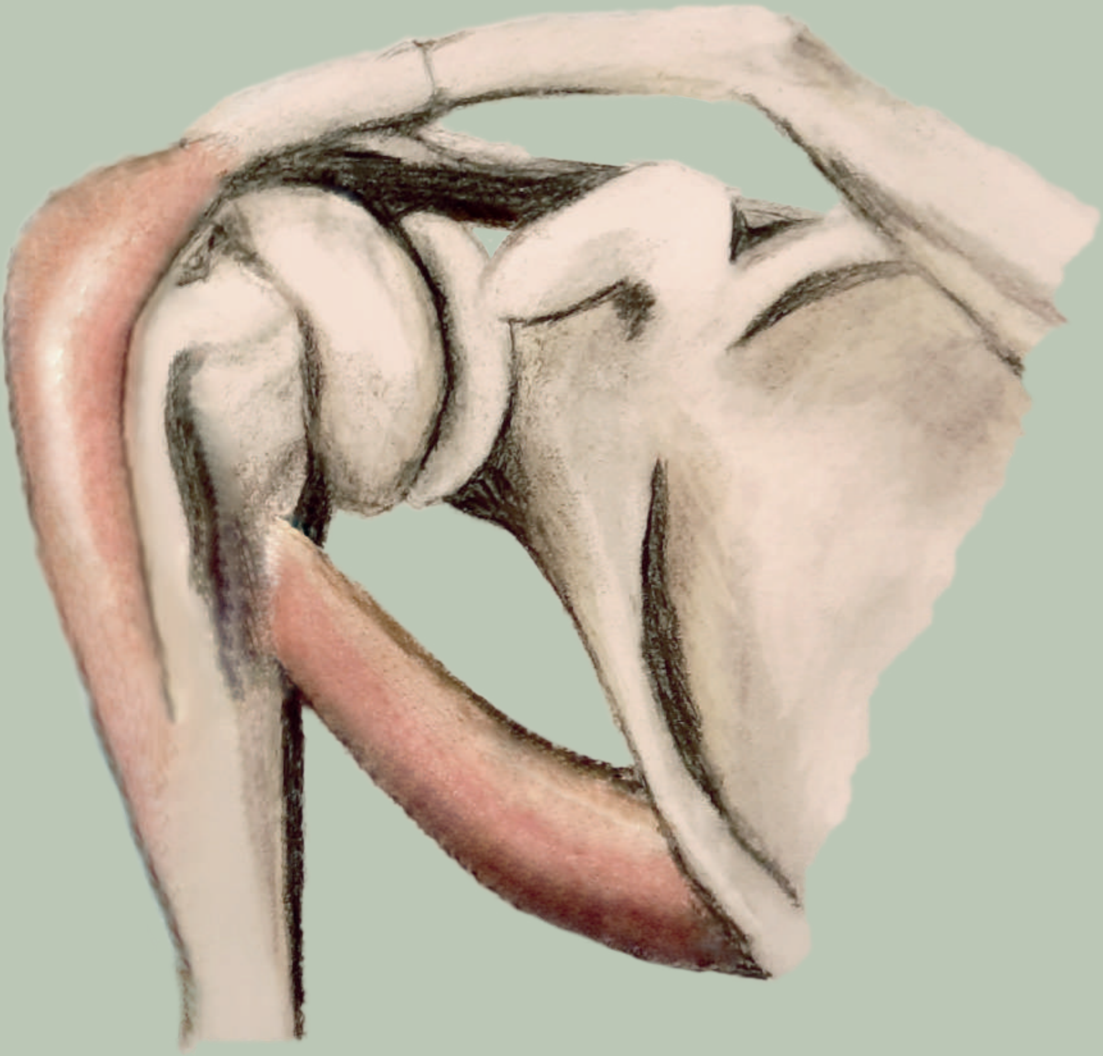
Adductor co-contraction during abduction: A Friend or Foe

An electromyography assessment and analysis of factors that may determine adaptation in asymptomatic individuals and patients with Subacromial Pain Syndrome.



Celeste Laurena Overbeek

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Celeste Laurena Overbeek

Colophon

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GENERAL INTRODUCTION

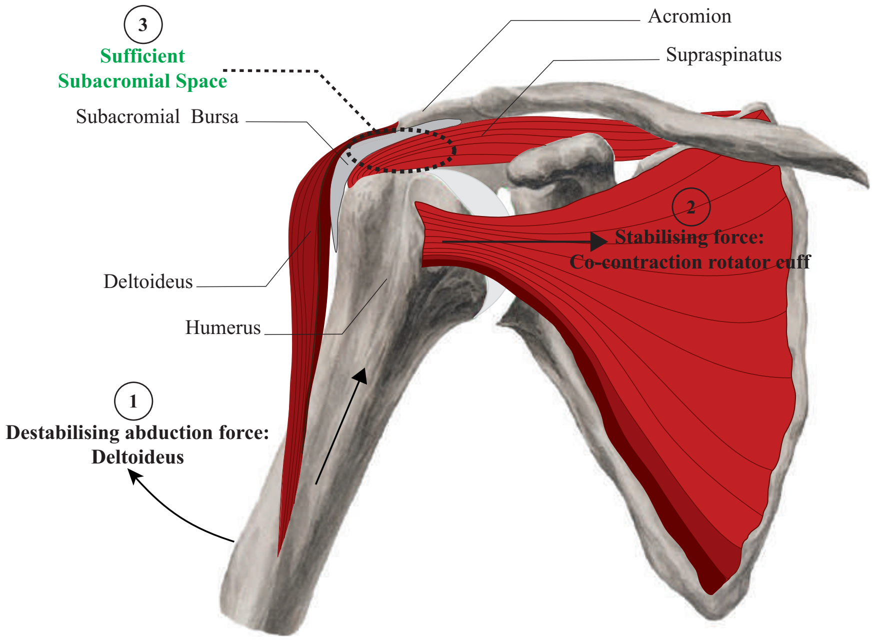
The first publication on subacromial pain dates from 1934[1]. In an ongoing search on the aetiology of this common pain disorder, more than four thousand articles have been published. From the 1970's until 2010 the condition was viewed as a consequence of "impingement" of the rotator cuff tendons and other subacromial tissues by the coracoacromial arch[1]. This turned out to be an overly simplistic representation of the problem, resulting in high recurrence rates after subacromial decompression procedures[2]. Subsequently, the condition has been described by a myriad of names to point at different proposed causes, until in 2014 clinicians concluded that given the lack of knowledge on the aetiology, calling it a pain syndrome is more appropriate[3]. Since then, the term "Subacromial Pain Syndrome (SAPS)" has increasingly been adopted to describe this clinical entity[3].

SAPS is characterised by pain in the subacromial region, that worsens during or subsequent to abduction of the arm[4,5]. Patients may experience (antalgic) loss of arm function and trouble sleeping[4,5]. With prevalence rates ranging between 15% and 22%, SAPS has far-reaching consequences for an individual's ability to perform daily activities, quality of life and health-care consumption[6]. Multiple treatment approaches are available, however up to 40% of patients report persisting complaints after treatment and the clinical course is disappointing in terms of resuming daily activities[7-10]. Hence, here is a need for improvement of therapeutic strategies in SAPS, and to achieve this, a more evidence-based hypothesis on the cause of pain and discriminating factors has to be constructed. In the maze of potential causes for subacromial pain proposed in literature so far, a few things seem to be certain, and have formed the base for this thesis:

1. **There is a relative discrepancy between the volume of subacromial tissues and the volume of the subacromial space.** In patients with SAPS, the subacromial tissues are inflamed with consequent swelling, but there is only limited space for expansion[4,11]. Furthermore, dynamic narrowing of the subacromial space during motion occurs, further narrowing the space[12,13].
2. **In the aetiology of SAPS, factors associated with ageing play a role.** The incidence of SAPS follows a specific age pattern; it develops from midlife onwards showing that age-related factors play a role in the pathogenesis[14-18].
3. **Coping and adaptation determine whether patients develop symptoms or not.** Starting between the age of 30 and 40, asymptomatic degenerative changes in the shoulder become common[14,19]. Most of the individuals remain asymptomatic while a minority develops SAPS, suggesting that coping and adaptation are of vital importance[4,19].

This thesis

A characteristic finding in patients with SAPS is exacerbation of pain during active abduction[4,5]. Open MRI and roentgenographic studies have shown that this may be the result of insufficient humeral head depression during abduction, with cranialisation of the humerus towards the acromion[4,5,12,13]. We theorise that patients with SAPS could benefit from mechanical unloading of subacromial tissues by active contribution of humeral head depressors. In both research and clinical practice, there has been a focus on the rotator cuff, while the arm adductors, specifically the teres major, may contribute strongly to depression of the humerus during abduction as well[20-24]. Since adductor co-contraction has so far predominantly been interpreted as a finding specific for shoulder injury, we have put one question central in this thesis, to evoke a shift in thinking[25]:



Young healthy shoulder

Adequate humeral depression during abduction by rotator cuff co-contraction

Figure 1 | Simplified representation of selected glenohumeral forces. *Destabilising cranial force generated by deltoideus during abduction, counteracted by medial directed force of rotator cuff.*

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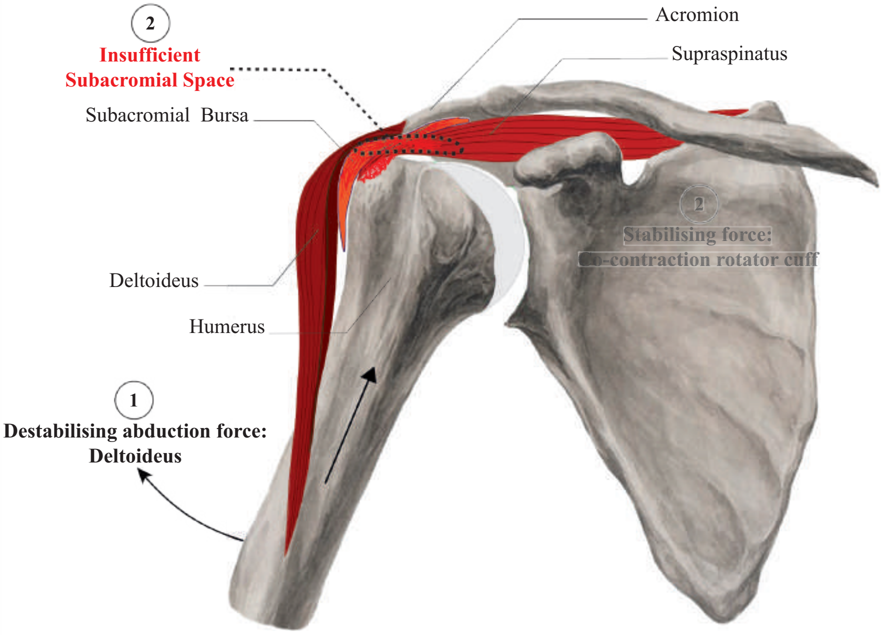
Background

In the young and healthy shoulder, cranially directed forces during abduction are counteracted by co-contraction of the rotator cuff muscles, predominantly the subscapularis and infraspinatus[21,22]. In this way, it is prevented that the humerus moves cranially towards the acromion, thus entrapping subacromial tissues (**Figure 1**). During ageing however, shoulder tissues are subject to marked degeneration, which particularly concerns the rotator cuff muscles[14,16,26-31]. This may have two consequences. First, due to reduced contribution of the upper parts of the rotator cuff to the abduction movement, the deltoid has to compensate, which results in a more cranially, instead of mediocranially directed force. Second, reduced stabilising force by the rotator cuff may jeopardise counteraction of cranial deltoid forces. These changes both could lead to cranialisation of the humerus and painful compression of subacromial tissues, which is depicted in **Figure 2**.



Painful irritation of subacromial tissues during abduction
Insufficient humeral depression, e.g. due to rotator cuff degeneration

Figure 2 | Simplified representation of selected glenohumeral forces. *Destabilising cranial force generated by deltoideus during abduction, not sufficiently counteracted by rotator cuff, leading to painful irritation of subacromial tissues.*

The arm adductors, as mentioned earlier, exert a medio-caudally directed force on the humerus and are capable of counteracting cranial deltoid forces during abduction[21,22]. Previous studies have shown that arm adductors, specifically the latissimus dorsi, teres major, and, to a lesser extent, the pectoralis major, may significantly contribute to humeral head depression during abduction[21,22]. We theorised that in the ageing shoulder, due to rotator cuff degeneration, increasing co-contraction of the arm adductors may be necessary for mechanical unloading of subacromial tissues during abduction (**Figure 3**)[14,16,27-31].

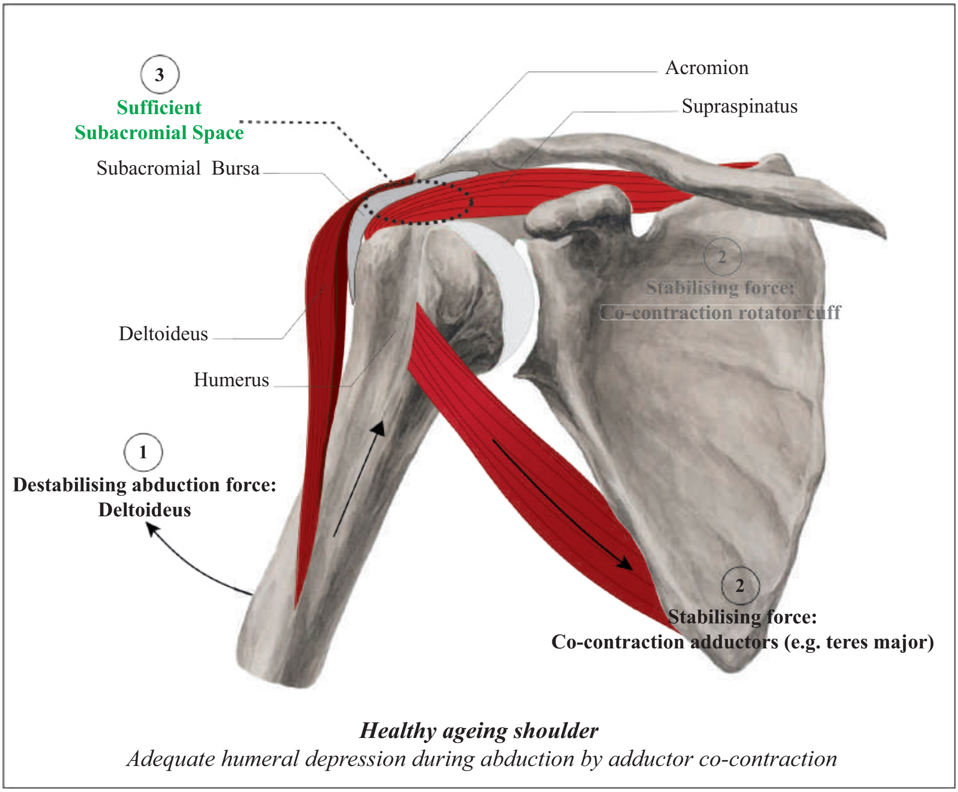


Figure 3 | Simplified representation of selected glenohumeral forces. *Destabilising cranial force generated by deltoideus during abduction, not sufficiently counteracted by rotator cuff, instead counteracted by co-contraction of adductors (e.g., teres major, latissimus dorsi).*

Following this line of reasoning, we explored the role of adductor co-contraction in individuals without shoulder complaints and in patients with SAPS in PART 1 of this thesis. In PART 2, factors that may determine adaptation of adductor activation patterns and perception of pain in SAPS are discussed.

PART I - The role of adductor co-contraction in the asymptomatic and symptomatic ageing shoulder (chapters 1-4).

- Chapter 1. To assess possible changes in adductor co-contraction during ageing, a cross-sectional analysis with electromyography (EMG) on co-contraction of the latissimus dorsi, teres major and pectoralis major was assessed in a wide age range of individuals without shoulder complaints[32].
- Chapter 2. Co-contraction of the latissimus dorsi, teres major and pectoralis major was compared between patients with SAPS and age-matched asymptomatic controls[33].
- Chapter 3. A prospective longitudinal cohort study comparing patients with SAPS at baseline and at 4 years of follow-up, to assess whether an increase of adductor co-contraction is associated with a favourable course of SAPS[23].
- Chapter 4. The effect of subacromial lidocaine infiltration on adductor co-contraction patterns was assessed in patients with SAPS, to evaluate potential causal relationships[34].

PART II - Factors that may determine adaptation of adductor activation patterns and perception of pain in SAPS (chapter 5-8).

The ability to adapt adductor activation patterns may depend on various psychosocial and biomechanical factors, among which is motor complexity[35,36]. This factor is rather new in the field of orthopaedic research and not fully validated yet, but may provide important insight[37-40]. It is proposed to describe the available spectrum of motor solutions for a given task, which should allow for learning through exploration and uniform load distribution across muscles[37-40].

- Chapter 5. Motor complexity of arm elevation trajectories was assessed in 120 asymptomatic shoulder controls between 18 to 70 years[35].
- Chapter 6. Force complexity was compared between 40 patients with SAPS and 30 matched asymptomatic controls[36].
- Chapter 7. A narrative review summarising the evidence of loss of proprioception in SAPS was performed, as proprioception is vital to counteract upward migration of the humerus during abduction and thus may play a role in SAPS[41-45].
- Chapter 8. The association between psychosocial functioning and persistence of complaints 4 years after routine care in patients with SAPS was evaluated[46].

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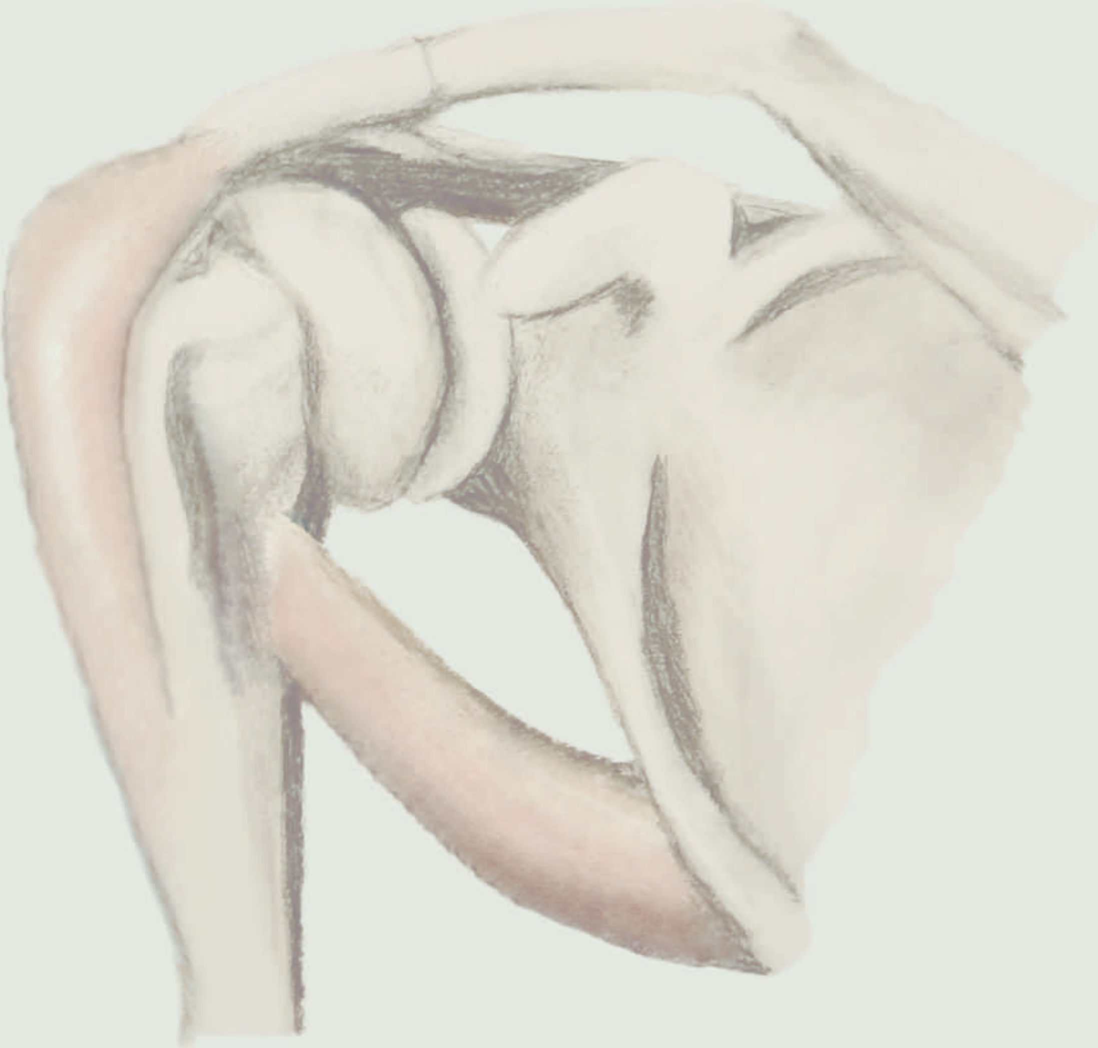
PART I |

The role of adductor co-contraction in the asymptomatic and symptomatic ageing shoulder



1

Middle-aged adults co-contract with arm Adductors during arm Abduction, while young adults do not. Adaptations to preserve pain-free function?

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ABSTRACT

Middle-aged individuals co-contract with adductor muscles during abduction. This may be crucial for counteracting deltoid forces, depressing the humerus and ensuring free passage of subacromial tissues underneath the acromion during abduction. We questioned whether adductor co-contraction is always present, or develops during ageing, in which case it may explain the age-related character of common shoulder conditions such as Subacromial Pain Syndrome. In a cross-sectional analysis with electromyography (EMG), activation patterns of the latissimus dorsi, teres major, pectoralis major and deltoid muscle were assessed during isometric force tasks in 60 asymptomatic individuals between 21 and 60 years old. Co-contraction was expressed as the degree of antagonistic activation relative to the same muscle's degree of agonistic activation, resulting in an activation ratio between -1 and 1, where lower values indicate more co-contraction. Using linear regression analyses, we found age-related decreases in the activation ratio of the latissimus dorsi (regression estimate: -0.004, 95% CI: -0.007 – 0.0, p-value: 0.042) and teres major (regression estimate: -0.013, 95% CI: -0.019 – -0.008, p-value: <0.001). In contrast to young individuals, middle-aged individuals showed a high degree of adductor co-contraction during abduction. This may indicate that during ageing, alterations in activation patterns are required for preserving pain-free shoulder function.

INTRODUCTION

Shoulder pain is the second most common musculoskeletal disorder in the general population, with prevalence rates ranging between 15% and 22%[1-3]. The incidence of shoulder pain increases with ageing, suggesting that age-related factors play a role in the pathogenesis[4-8]. Numerous studies have investigated the effect of ageing on the shoulder complex (e.g., rotator cuff degeneration), however factors that may directly relate to the onset and/or perpetuation of shoulder pain are yet unidentified[4].

In the most common age-related shoulder condition, the Subacromial Pain Syndrome (SAPS), repetitive overloading of subacromial tissues during abduction may be the key factor leading to complaints[9-11]. A recent study showed that during abduction, patients with SAPS have significantly less activation of two potent humeral depressors, the latissimus dorsi and teres major, than asymptomatic controls[12]. This finding explains overloading of subacromial tissues in SAPS, but also supports a stabilising function of the latissimus dorsi and teres major in asymptomatic adults that was only recently suggested[13].

Based on the results of this study, we questioned whether adductor co-contraction is always present, or develops during ageing, in which case it may explain the age-related character of age-related shoulder conditions such as SAPS. In this cross-sectional analysis we assessed the effect of age on the degree of latissimus dorsi, teres major and pectoralis major co-contraction in asymptomatic individuals.

PATIENTS AND METHODS

Data of three individual cohorts were combined, resulting in a study population of 60 participants, between 21 and 60 years old, with no current or past shoulder complaints. This age range covers the age at which common non-osteoarthritic shoulder complaints, such as SAPS, generally develop[14]. The first group of twenty participants aged 19 to 50 years was recruited between February 2010 through October 2010[15]. Second, ten asymptomatic participants aged between 35 and 60 years were recruited in September 2012[16]. The third group, comprising thirty asymptomatic participants was evaluated between January 2016 and November 2016. Exclusion criteria were: less than 18 years old, limited range of motion during physical examination, malignancy, neurologic/muscle disease, symptomatic osteoarthritis, rheumatoid arthritis, adhesive capsulitis, diabetes mellitus, previous injury/ fracture or infection of the shoulder, a pacemaker in situ, or insufficient Dutch language skills. Asymptomatic shoulder pathology was not ruled out. All participants were analysed at the laboratory of Kinematics and Neuromechanics (Leiden University medical Centre, Leiden, the Netherlands). The review board of the institutional medical ethical committee approved this study (P09.243, P11.002 and P15.046) and all participants gave written informed consent.

Assessment of muscle activation patterns

We were interested in evaluating the activation patterns of muscles that may translate the humerus cranially (towards the acromion) or caudally (away from the acromion) during abduction. In biomechanical evaluations and a recent systematic review on the topic, it has been shown that the deltoid muscle (DM) is the most potent cranial translator of the humerus during abduction[13,17]. The arm adductors, specifically the latissimus dorsi (LD), teres major (TM), and, to a lesser extent, the pectoralis major (PM), are the strongest caudal translators (humeral depressors) during abduction[13,17]. Of these muscles, the activity during an isometric abduction and adduction task was determined, in order to obtain a standardised degree of task-specific activation. Participants were measured while standing and facing a computer monitor which gave force feedback information. The target arm was in external rotation at the side touching a 1-dimensional force transducer at the wrist. This set-up was previously described in detail[15]. During a resting task and isometric ab- and adduction tasks, electromyography (EMG) of three muscles involved in humeral depression during abduction, i.e., the LD, TM and PM, and the main humeral elevator, i.e., the medial part of the DM was recorded with surface EMG-electrodes (DelSys system Bagnoli-16, Boston, MA, USA, two parallel 10 mm silver bar electrodes, inter-electrode distance 10 mm, bandwidth 20–450 Hz, gain adjusted to 1000)[15]. Electrodes were placed at the middle of the muscle bellies, with the silver bar contacts perpendicular to the muscle fibres. The electrode for the LD was placed 6 cm below the angulus inferior scapulae; for the TM 4 cm cranial and 2 cm lateral to angulus inferior scapulae; for the PM 1 cm below the clavicle and for the DM 2-4 cm below the acromion, laterally. For conductivity, the skin was abraded with scrubbing cream, cleaned with alcohol and conductive cream was applied to the electrode contact bars prior to adherence to the skin. The EMG and force signals were analogue-digital (AD) converted and simultaneously recorded at a sample rate of 2500 Hz with 16-bit resolution. Post-processing of the EMG consisted of offset removal (1Hz recursive low-pass Butterworth filter), rectification and enveloping using the moving average over intervals of 0.1 seconds and averaging to a single value per task ($\mathrm{mEMG}^{IP/OP}$) through custom made software in Matlab (MathWorks inc., version R2016a, Natick, USA).

For the assessment of muscle activation, participants first performed a maximal abduction and maximal adduction task. The lowest value of either of these maximums was set as the maximum voluntary force (MVF). Subsequently, a target force of 60%

with a tolerance of ± 3.75% of the MVF was presented to the participants on a computer screen[15]. Finally, participants performed a 15-second isometric force task in abduction and adduction where they attempted to exert a force level within the target force tolerances (60% MVF ± 3.75%). The target force level was equal during the abduction and adduction task for the purpose of computing a standardised measure of the degree of antagonistic versus agonistic activation. The mean of the post-processed EMG-data of when the exerted force lied within the target force tolerances ($mEMG^{IP/OP}$) was used for the analyses.

Outcome measure

For this study, we were interested in the degree of adductor activation during abduction, i.e., adductor co-contraction. Analysing the plain EMG-amplitude, hampers comparability between participants and studies and therefore it is preferable to normalise EMG-output. This can be done using the maximum voluntary contraction, however this method may be limited in symptomatic participants due to the unpredictability when pain is present[18]. The EMG-assessment used in the current study has and will be applied in patients with pain, and therefore EMG was standardised using the Activation Ratio (AR) for generalisability (Eq.1)[15].

$$AR_{muscle} = \frac{mEMG^{IP} - mEMG^{OP}}{mEMG^{IP} + mEMG^{OP}} \qquad \textbf{Eq.1}$$

where muscle represents the LD, TM, PM or DM and the superscripts IP and OP indicate ‘in phase’ agonist activation and ‘out of phase’ antagonist muscle activation respectively, in relation to the force task in abduction or adduction.

The AR indicates the task related degree of antagonist activation relative to the same muscle’s degree of agonist activation, and has been proved reliable[15]. The AR ranges between -1 and 1 and equals 1 in case of sole agonist muscle activation and decreases with antagonist muscle activation, i.e., co-contraction, up to -1 with the muscle being solely active as antagonist. An AR = 0 indicates equal activity during the agonist and antagonist task.

In order to prevent overestimation of the degree of co-contraction as assessed with the AR, the post-processed mean EMG-amplitude during the agonistic task ($mEMG^{IP}$, i.e., the activity of the deltoid muscle during abduction and the activity of adductors during adduction) was verified to be twice the mean EMG-amplitude of the 10% lowest EMG-signals during the relative rest, abduction or adduction task (a signal-to-noise ratio of $SNR \geq 2.0$). In case this condition was not met or in case EMG-data was corrupt (e.g., loose electrode), the ARs were excluded.

Statistical analysis

Descriptive statistics

Categorical data are described with numbers and percentages; continuous parameters with means, standard deviation (SD) and 95% confidence intervals (95% CI) or with medians and percentiles depending on the distribution of data. The Statistical Package of Social Sciences (SPSS®) version 23 (IBM® Corp, Armonk, NY, USA) was used for statistical analysis.

The activation ratio, force task and age, were verified to have normal distributions by visual interpretation of histograms. Missing values in activation ratios were verified to be missing completely at random (e.g., loose electrode) or at random (e.g., not meeting the SNR) and imputed with multiple imputation based on the study group, sex, arm dominance, assessment of dominant arm, force task and AR, using 50 iterations, to avoid possible bias, use all available data and increase power[19]. For statistical analyses, we used the pooled results automatically generated by SPSS® in multiple imputed datasets. The analyses were additionally performed on the original database for verification of the results using multiple imputation. Results are presented as intercepts with unstandardised regression estimates and corresponding 95% CI intervals and p-values. A two-sided p-value of 0.05 or less was considered statistically significant.

Association between age and activation ratios

For the primary study question, the association between the independent variable age and dependent variable AR was assessed using linear regression analysis, with controlling for the magnitude of force task, sex and the assessment of the dominant arm (or non-dominant arm).

Mediation analysis

To rule out that a possible association between age and AR was explained by differences in the torque level at which participants performed the measurements, a mediation analysis was performed. This was done using the product-method, where four associations were tested: 1) age and AR, 2) age and force task, 3) force task and AR and 4) age and AR, corrected for force task[20]. If either of the associations assessed in step 1-3 is non-significant, it is unlikely that force task is a mediator[20]. As verification, we assessed whether the unstandardised beta describing the association between age and AR (step 1) changed significantly when controlling for force task (step 4). For this, we calculated the standardised z-score from Eq. 2 and determined the corresponding p-value with standard statistical tables.

$$z = \frac{B1 - B2}{\sqrt{SE_{B1}^{2} + SE_{B2}^{2}}} \qquad \textbf{Eq.2}$$

Where B1 represents the unstandardised beta from step 1 and B2 the unstandardised beta from step 4. The SE describes the standard errors associated with B1 and B2 respectively.

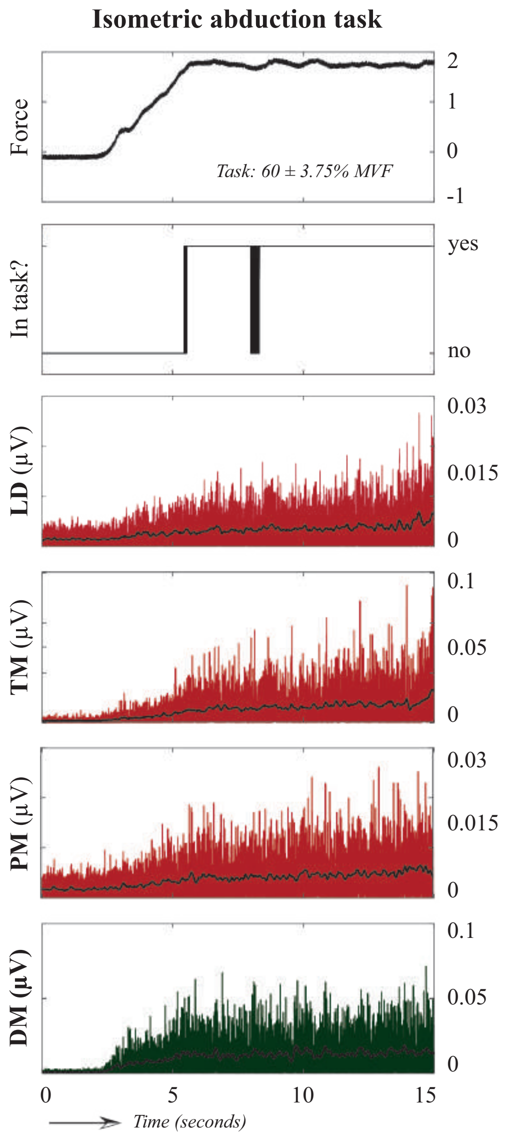

Figure 1 | Rectified and offset-subtracted electromyography during a 15 second isometric abduction force task at 60 ± 3.75% of the Maximal Voluntary Force (*MVF*). The line curve represents the processed signal with which the *activation ratio* is determined. In the latter panel, it is indicated whether patients were in or out of the force task; in-task EMG data was used for the assessment of co-contraction. It shows that with abduction, mainly achieved with deltoid muscle (DM) activation, there is concomitant increased activation of the pectoralis major (PM), latissimus dorsi (LD) and teres major (TM) activation (i.e., co-contraction).

RESULTS

Baseline characteristics of the study group are presented in **Table 1**. Multiple imputation was performed for nine missing values in the activation ratio of the LD (4 due to a technical problem with the amplifier, 4 due to not reaching the SNR and 1 because of a loose electrode); six missing values in the AR of the TM (3 due to a technical problem with the amplifier, 2 due to not reaching the SNR and 1 because of a loose electrode); six missing values in the AR of the PM (4 due to a technical problem with the amplifier, 1 due to not reaching the SNR and 1 because of a loose electrode) and lastly three missing values in the AR of the DM, all due to a technical problem with the amplifier.

Table 1 | Demographics of asymptomatic participants

Demographics	**Asymptomatic participants**	
Total group (n=60)		
Age, yrs (mean, SD)	42 (13)	Range 21 – 60
Female (n, %)	27	45
Right side dominance (n, %)	50	83
Dominant side assessed (n, %)	45	75
Per group		
Cohort 2010 (n=20)		
Age, yrs (mean, SD)	25 (2.5)	Range 21 – 29
Female (n, %)	5	25
Right side dominance (n, %)	16	80
Dominant side assessed (n, %)	19	95
Cohort 2012 (n=10)		
Age, yrs (mean, SD)	50 (6.6)	Range 39 – 59
Female (n, %)	5	50
Right side dominance (n, %)	10	100
Dominant side assessed (n, %)	10	100
Cohort 2016 (n=30)		
Age, yrs (mean, SD)	51 (5.7)	Range 39 – 60
Female (n, %)	17	57
Right side dominance (n, %)	24	80
Dominant side assessed (n, %)	16	53

SD, standard deviation; n, number; yrs., years; NA, not applicable.

Association between age and activation ratios

A typical example of the raw antagonistic (EMG^{OP}) signals of the LD, TM and PM and raw agonistic (EMG^{IP}) signal of the DM with simultaneously exerted force is presented in **Figure 1**. The associations between age and activation ratio of the LD, TM, PM and DM are illustrated in **Figure 2** and described by the regression models in **Table**

2. For the LD, higher age was associated with lower ARs (-0.004, 95% CI: [-0.007, 0.0], p=0.042). The AR of the TM also decreased with increasing age (-0.013, 95% CI: [-0.019, -0.008], p<0.001). There was no significant association between age and the AR of the PM. Lastly, the AR of the assessed abductor, the DM, decreased with increasing age (-0.003, 95% CI: [-0.005, 0.0], p=0.046), although the regression model did not explain much variance in the AR of the DM (adjusted R^2 of 0.024). Except for an association between male sex and a higher AR of the TM (0.17, 95% CI: [0.015, 0.32], p=0.031), sex the assessment of the dominant arm or the magnitude of force task were not related with the ARs (**Table 2**).

The analyses were performed on the original dataset with missing values and on the imputed dataset and outcomes obtained from the original dataset (**Appendix 1**).

Table 2 | Association between age and activation ratios in asymptomatic participants

	Activation Ratio			
Independent variables	*Estimate*	*95% CI*	*p-value*	*Adjusted R^2*
LD				
Intercept	0.96	(0.77 – 1.2)	–	0.17
Age (years)	-0.004	(-0.007 – 0.00)	**0.042**	
Force task (N)	-0.073	(-0.23 – 0.086)	0.367	
Sex (female is ref.)	0.095	(-0.007 – 0.20)	0.068	
Assessment of dominant arm (yes is ref.)	-0.038	(-0.15 – 0.069)	0.484	
TM				
Intercept	1.2	(0.88 – 1.4)	–	0.42
Age (years)	-0.013	(-0.019 – -0.008)	**<0.001**	
Force task (N)	-0.20	(-0.43 – 0.025)	0.082	
Sex (female is ref.)	0.17	(0.015 – 0.32)	**0.031**	
Assessment of dominant arm (yes is ref.)	0.11	(-0.044 – 0.27)	0.160	
PM				
Intercept	0.75	(0.59 – 0.90)	–	-0.011
Age (years)	-0.001	(-0.004 – 0.002)	0.543	
Force task (N)	0.090	(-0.038 – 0.22)	0.169	
Sex (female is ref.)	-0.002	(-0.087 – 0.084)	0.967	
Assessment of dominant arm (yes is ref.)	0.023	(-0.063 – 0.11)	0.605	
DM				
Intercept	0.98	(0.84 – 1.1)	–	0.024
Age (years)	-0.003	(-0.005 – 0.00)	**0.046**	
Force task (N)	-0.028	(-0.14 – 0.087)	0.635	
Sex (female is ref.)	0.002	(-0.075 – 0.079)	0.965	
Assessment of dominant arm (yes is ref.)	0.034	(-0.042 – 0.11)	0.383	

Multivariable regression analysis with dependent variable *activation ratio* and independent variables *age, force task, sex* and *assessment of the dominant arm*. LD, latissimus dorsi; TM, teres major; PM, pectoralis major; DM, deltoid muscle. Adjusted R^2 represents the mean adjusted R^2 from multivariable regression analyses with 20 iterations. Significant values at the level of alpha=0.05 are in bold.

Mediation analysis

We did not perform a mediation analysis for the PM since there was no significant relation between the AR of the PM and age (step 1 of mediation analysis). Simple regression analyses between age and force task (0.002, 95% CI: [-0.005, 0.008], p=0.596) and between force task and ARs of the LD (-0.007, 95% CI: [-0.16, 0.14], p=0.928), TM (-0.11, 95% CI: [-0.36, 0.14], p=0.375) and DM (-0.036, 95% CI: [-0.13, 0.062], p=0.476) revealed no significant associations. Furthermore, the changes in non-standardised beta describing the relation between age and AR of the LD, TM or DM after controlling for force task, were negligible (at maximum 1%, all p>0.99). Thus, force task was not a mediator in the association between ARs and age.

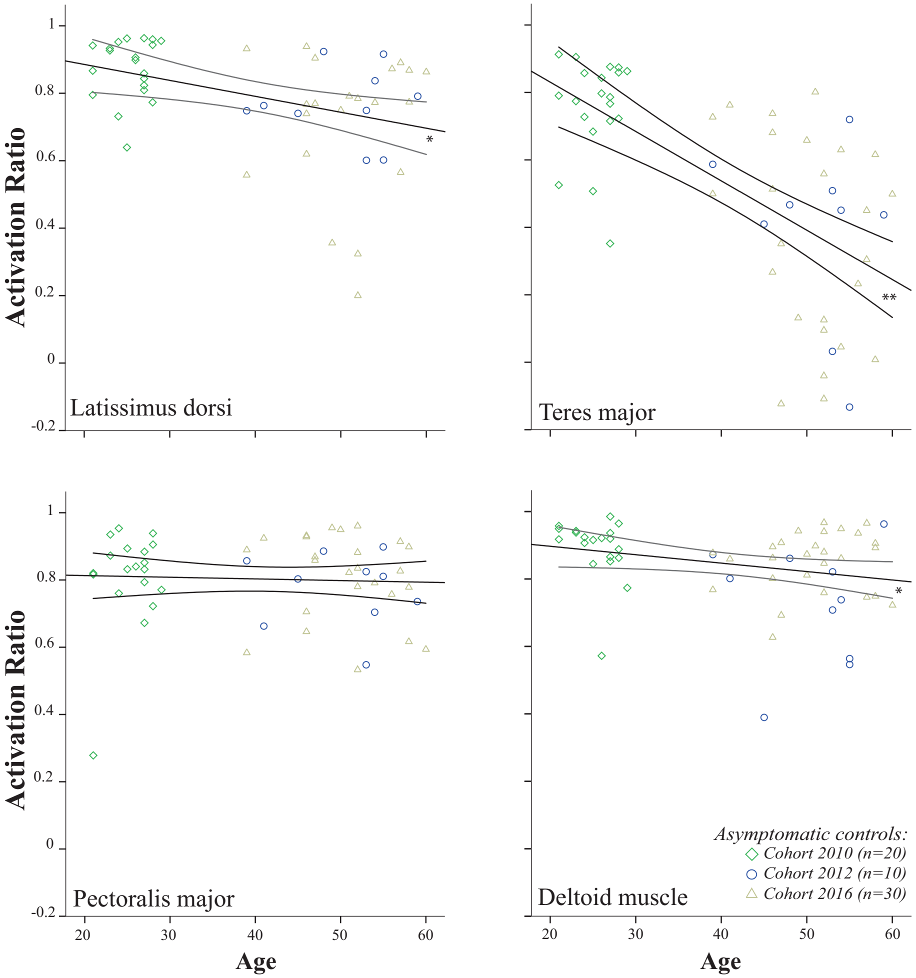

Figure 2 | Association between age and activation ratios in asymptomatic participants. Scatter plot with linear regression line and 95% confidence intervals.

* Significant at the level of alpha=0.05, ** Significant at the level of alpha=0.01

DISCUSSION

In this cross-sectional evaluation we found that during abduction young adults did not co-contract with arm adductors whereas middle-aged individuals did. This age-related increase in adductor co-contraction suggests that during ageing, counteraction of cranial deltoid forces and thus glenohumeral stabilisation, becomes more reliant on adductor co-contraction.

There have been no previous studies on the effect of ageing on adductor muscle activation during abduction. In biomechanical evaluations and a recent systematic review on the topic, it was shown that the arm adductors, specifically the latissimus dorsi, teres major, and, to a lesser extent, the pectoralis major, have the greatest contribution to humeral-head depression during arm abduction[13,17]. We suggest that the age-related increase in adductor co-contraction observed in our study may represent a compensation for reduced rotator cuff quality, loss of proprioception as well as altered bone morphology in the ageing shoulder, that is necessary for preserving shoulder stability and function[4,6,21-25].

Our study has some limitations. First, three previously recruited cohorts were combined for this study. Except for age, the selection criteria as well as measurement procedures were the same across these cohorts and therefore, we do not think bias was introduced by the design. This may also be interpreted from Figure 1 where no clustering by cohorts is recognisable. Second, 24 activation ratios were missing (10%), which was in 58% (14 activation ratios) due to a technical problem with the amplifier. There was also missing data (7 in total, 29%), because the mean agonistic EMG amplitude did not exceed the signal to noise ratio. In order to avoid bias and use all available data in the analyses, these missing values were imputed using multiple imputation[19]. The conclusions obtained from the dataset with missing values and the imputed dataset were similar although the p-value associated with the effect of age on the activation ratio of the LD was no longer significant in the dataset with missing values, possibly because of reduced power. Lastly, we only evaluated a selection of muscles that affect the craniocaudal position of the humerus the most[13,17,26]. Our conclusion may be supported by adding an analysis of other adductors, for example, the teres minor and lower parts of the infraspinatus and subscapularis.

Previously, it has been shown that patients with the age-related shoulder condition SAPS have reduced activation of the latissimus dorsi and teres major during abduction[12]. As these adductors are crucial for depressing the humerus (away from the acromion), this finding explained overloading of subacromial tissues and thereby pain in patients with SAPS[12,27]. Following this line of reasoning, our finding of increased adductor co-contraction during ageing in asymptomatic participants, could explain the age-related character of SAPS.

CONCLUSION

In this cross-sectional evaluation of muscles that directly act on the position of the humerus relative to the scapula, we found that in contrast to young individuals, middle-aged individuals have a high degree of teres major and latissimus dorsi activity during abduction. It was previously suggested that next to the rotator cuff, these two adductor muscles have a crucial contribution to counteracting deltoid forces, depressing the humerus and ensuring free passage of subacromial tissues underneath the acromion during abduction[13]. The age-related increase in adductor co-contraction observed in our study, suggests a shift in muscle activation patterns during ageing, that may be crucial for maintaining pain-free shoulder function. In a future study it should be tested whether inability to make this shift may contribute to the onset of age-related shoulder conditions like SAPS.

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Appendix

Appendix 1 | Association between age and activation ratios in asymptomatic participants examined in original dataset

	Activation Ratio			
Independent variables	*Estimate*	*95% CI*	*p-value*	*Adjusted R^2*
LD				
Intercept	0.94	(0.74 – 1.1)	–	
Age (years)	-0.003	(-0.007 – 0.000)	0.064	
Force task (N)	-0.051	(-0.22 – 0.12)	0.544	0.14
Sex (female is ref.)	0.091	(-0.013 – 0.20)	0.085	
Assessment of dominant arm (yes is ref.)	-0.045	(-0.16 – 0.066)	0.421	
TM				
Intercept	1.2	(0.89 – 1.4)	–	
Age (years)	-0.014	(-0.019 – -0.009)	**<0.001**	
Force task (N)	-0.18	(-0.41 – 0.044)	0.112	0.43
Sex (female is ref.)	0.15	(-0.0 – 0.31)	0.051	
Assessment of dominant arm (yes is ref.)	0.11	(-0.052 – 0.27)	0.183	
PM				
Intercept	0.74	(0.58 – 0.90)	–	
Age (years)	-0.001	(-0.004 – 0.002)	0.560	
Force task (N)	0.092	(-0.042 – 0.23)	0.174	-0.018
Sex (female is ref.)	-0.0	(-0.089 – 0.090)	0.991	
Assessment of dominant arm (yes is ref.)	0.027	(-0.062 – 0.12)	0.547	
DM				
Intercept	0.98	(0.84 – 1.1)	–	
Age (years)	-0.003	(-0.006 – 0.00)	**0.041**	
Force task (N)	-0.028	(-0.15 – 0.090)	0.632	0.028
Sex (female is ref.)	0.003	(-0.076 – 0.082)	0.940	
Assessment of dominant arm (yes is ref.)	0.041	(-0.038 – 0.12)	0.303	

Multivariable regression analysis with dependent variable *activation ratio* and independent variables *age*, *force task*, *sex* and *assessment of the dominant arm* on the original dataset without imputed values. LD, latissimus dorsi; TM, teres major; PM, pectoralis major; DM, deltoid muscle. Significant values at the level of alpha=0.05 are in bold.

2

Altered Co-contraction Patterns of Humeral Head Depressors in Patients with Subacromial Pain Syndrome: A Cross-sectional Electromyography Analysis.

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ABSTRACT

Background

In approximately 29% to 34% of all patients with subacromial pain syndrome (SAPS) there is no anatomic explanation for symptoms, and behavioural aspects and/or central pain mechanisms may play a more important role than previously assumed. A possible behavioural explanation for pain in patients with SAPS is insufficient active depression of the humerus during abduction by the adductor muscles. Although the adductor muscles, specifically the teres major, have the most important contribution to depression of the humerus during abduction, these muscles have not been well studied in patients with SAPS.

Questions/purposes

Do patients with SAPS have altered contraction patterns of the arm adductors during abduction compared with asymptomatic people?

Methods

SAPS was defined as nonspecific shoulder pain lasting for longer than 3 months that could not be explained by specific conditions such as calcific tendinitis, full-thickness rotator cuff tears, or symptomatic acromioclavicular arthritis, as assessed with clinical examination, radiographs, and magnetic resonance arthrography. Of 85 patients with SAPS who met the prespecified inclusion criteria, 40 were eligible and agreed to participate in this study. Thirty asymptomatic spouses of patients with musculoskeletal complaints, aged 35 to 60 years, were included; the SAPS and control groups were not different with respect to age, sex, and hand dominance. With electromyography, we assessed the contraction patterns of selected muscles that directly act on the position of the humerus relative to the scapula (the latissimus dorsi, teres major, pectoralis major, and deltoid muscles). Co-contraction was quantified through the activation ratio ([AR]; range -1 to 1). The AR indicates the task-related degree of antagonist activation relative to the same muscle's degree of agonist activation, equalling 1 in case of sole agonist muscle activation and equalling -1 in case of sole antagonistic activation (co-contraction). We compared the AR between patients with SAPS and asymptomatic controls using linear mixed-model analyses. An effect size of $0.10<AR<0.20$ was subjectively considered to be a modest effect size.

Results

Patients with SAPS had a 0.11 higher AR of the teres major (95% CI, 0.01 to 0.21; $p = 0.038$), a 0.11 lower AR of the pectoralis major (95% CI, -0.18 to -0.04; $p = 0.003$), and a 0.12 lower AR of the deltoid muscle (95% CI, -0.17 to -0.06; $p < 0.001$) than control participants did. These differences were considered to be modest. With the numbers available, we

found no difference in the AR of the latissimus dorsi between patients with SAPS and controls (difference = 0.05; 95% CI, -0.01 to 0.12; $p = 0.120$).

Conclusions

Patients with SAPS showed an altered adductor co-contraction pattern with reduced teres major activation during abduction. The consequent reduction of caudally directed forces on the humerus may lead to repetitive overloading of the subacromial tissues and perpetuate symptoms in patients with SAPS. Physical therapy programs are frequently effective in patients with SAPS, but targeted approaches are lacking. Clinicians and scientists may use the findings of this study to assess if actively training adductor co-contraction in patients with SAPS to unload the subacromial tissues is clinically effective. The efficacy of training protocols may be enhanced by using electromyography monitoring.

INTRODUCTION

Chronic shoulder pain is the second most common musculoskeletal disorder in the general population, with prevalence rates ranging between 15% and 22%[1-3]. A specific anatomic basis for perceived symptoms, such as full-thickness rotator cuff tears or calcific tendinitis, is observed in many patients[4]. However, in approximately 29% to 34% of all patients with chronic shoulder pain, referred to here as subacromial pain syndrome (SAPS), the subacromial (suprahumeral) tissues are inflamed, but there is no structural anatomic cause that could explain persisting symptoms[5,6]. The fact that altering bony shapes with surgical interventions yields unsatisfactory results comparable to those of physical therapy also suggests that behavioural and/or central pain mechanisms may play a more important role than previously assumed[7,8].

In patients with SAPS, pain is frequently exacerbated during abduction, suggesting that motion-related (kinematic) factors contribute to the perpetuation of symptoms[4,5]. Open MRI and radiographic studies have attributed this particular pain pattern, the painful arc, to insufficient humeral-head depression during abduction[9,10]. We believe that patients with SAPS could benefit from mechanical unloading of the subacromial tissues during abduction by the active contribution of shoulder muscles that act as humeral-head depressors[11-13]. The craniocaudal position of the humerus relative to the scapula is directly determined by a balance of cranial forces generated by the shoulder abductors and caudal forces generated by co-contraction of the rotator cuff and arm adductors[14,15]. In both research and clinical practice, there has been a focus on the rotator cuff, while the arm adductors, specifically the teres major, contribute the most to depression of the humerus during abduction[11,14,15].

Because of this, studying co-contraction of the arm adductors in patients with SAPS seems to be worthwhile; if adductor co-contraction is altered in patients with SAPS, this could indicate a treatable imbalance between the abductors and adductors. Accordingly, we asked: Do patients with SAPS have altered contraction patterns of the arm adductors during abduction compared with asymptomatic people?

PATIENTS AND METHODS

In this study, we defined SAPS as shoulder pain lasting for longer than 3 months with no specific anatomic abnormalities that could explain the pain and could benefit from specific treatment (such as acromioclavicular osteoarthritis, calcific tendinitis, or full-thickness rotator cuff tears)[4]. Between April 2010 and September 2016, consecutive patients with a clinical diagnosis of SAPS who were referred to the outpatient clinics of the Leiden University Medical Centre, Haaglanden Medical Centre, or Alrijne Hospital were evaluated for inclusion in this cross-sectional cohort study (Trial registry number NTR2283)[16]. Patients were selected through clinical examination, radiographs, and MR arthrography.

The inclusion criteria were unilateral shoulder pain for at least 3 months, positive results of a Hawkins-Kennedy test (passive anteflexion of the shoulder to 90° with subsequent internal rotation of the shoulder to provoke subacromial pain) and Neer lidocaine impingement test (examining for immediate relief of pain after subacromial infiltration with lidocaine), and at least one of the following symptoms: pain during daily life activities with arm abduction, extension, and/or internal rotation; pain at night or incapability of lying on the shoulder; painful arc; diffuse pain during palpation of the greater tuberosity; scapular dyskinesis; and a positive full-can test, empty-can test, or Yocum test result[16]. Exclusion criteria were insufficient Dutch-language skills, age younger than 35 years or older than 60 years, inflammatory arthritis of the shoulder, clinical signs of glenohumeral or acromioclavicular osteoarthritis, previous fracture, dislocation or surgery of the shoulder, cervical radiculopathy, glenohumeral instability, decreased passive function (frozen shoulder), malignancy, full-thickness rotator cuff tears, calcific tendinitis, labrum or ligament pathology, pulley lesion, biceps tendinopathy, os acromiale, cartilage lesion, or a bony cyst[16]. All MR arthrography studies were evaluated by an experienced independent radiologist[5]. Of 85 patients who were referred with the clinical diagnosis of SAPS, 45 were excluded, leaving 40 patients for evaluation in this study (**Figure 1**).

To select control participants, we recruited the spouses of patients with musculoskeletal complaints at the outpatient clinic of Leiden University Medical Centre between January 2016 and November 2016. Inclusion criteria were age between 35 and 60 years, no current or past shoulder concerns, no visit to a physician for shoulder related concerns, and no past shoulder discomfort for more than 1 week. Exclusion criteria were impaired passive and active shoulder function during clinical examination, insufficient Dutch-language skills, prior shoulder surgery, injections, shoulder fracture or dislocation, radiculopathy, frozen shoulder, osteoarthritis or rheumatoid arthritis, and neurologic or muscle disease. No additional imaging was performed in the control group, because we only used imaging in the SAPS group to exclude specific anatomic conditions that would have explained a patient's symptoms.

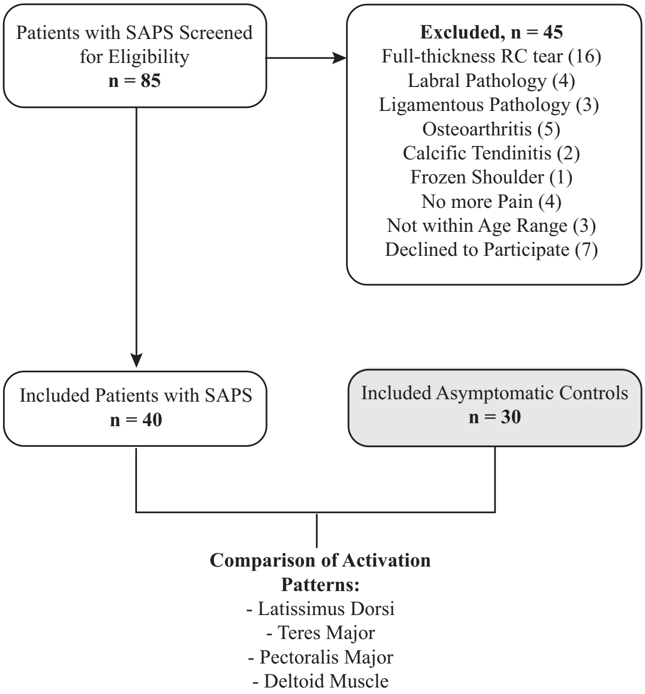

Figure 1 | A flow diagram of the participant inclusion process is shown.

Forty patients with SAPS and 30 asymptomatic controls were compared. The SAPS and control groups were not different with respect to age, sex, and hand dominance (**Table 1**).

The research was conducted according to the principles of the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013) and in accordance with the Medical Research Involving Human Subjects Act. The review board of our institutional ethical medical commission approved this study (P09.227 & P15.046) and all participants provided written informed consent.

Table 1 | Baseline characteristics of patients with SAPS and controls

	SAPS	**Controls**	
Demographics	*n=40*	*n=30*	*p-value*
Age, yrs (mean, SD)	50 (6)	51 (5.7)	0.740
Female (n, %)	23 (58)	17 (57)	0.944
Right side dominance (n, %)	35 (88)	25 (83)	0.622
Dominant side measured/affected (n, %)	25 (63)	17 (57)	0.622
Complaints duration in months (median, percentiles)	18 (12-29)	N/A	N/A

We used a standardised testing protocol[17]. In this study, we were interested in evaluating the activation patterns of muscles that directly act on the craniocaudal position of the humerus with respect to the scapula during abduction. In biomechanical evaluations and a recent systematic review on the topic, it has been shown that the deltoid muscle contributes the most to upward migration of the humerus during abduction[14,15]. The arm adductors, specifically the latissimus dorsi, teres major, and, to a lesser extent, the pectoralis major, are the strongest humeral-head depressors during abduction[14,15]. Other muscles that may contribute to humeral depression are the teres minor and the lower parts of the infraspinatus and subscapular muscles[14]. Because evaluating these muscles with EMG requires indwelling (fine wire) electrodes, we limited our evaluation to the deltoid, latissimus dorsi, teres major, and pectoralis major muscles.

With the target arm in external rotation at the side and attached to a one-dimensional force transducer at the wrist, we recorded activation of the latissimus dorsi, teres major, pectoralis major (clavicular part), and deltoid muscles (medial part) with surface EMG during rest and isometric abduction and adduction tasks (DelSys system Bagnoli-16, Boston, MA, USA; inter-electrode distance, 10 mm; bandwidth 20-450 Hz)[17].

The EMG and force signals were analog-digitally converted and recorded simultaneously at a sample rate of 2500 Hz. Offline, the EMG signals were subtracted from the mean EMG signals for offset removal, rectified, and combined with the moving average over intervals of 0.1 seconds, using custom-made software in Matlab (Math-Works Inc., R2018b, Natick, MA, USA).

Participants first performed maximal abduction and adduction tasks to determine the maximum voluntary force. The maximum voluntary force was set as the lowest value of either the maximum voluntary force during isometric adduction or abduction. Subsequently, a target force of 60% with a tolerance of ± 3.75% of the maximum voluntary force was presented to the participants on a computer screen[17]. Finally, participants performed a 15-second isometric force task in abduction and adduction at equal target force levels for the purpose of computing a standardised measure of the degree of antagonistic versus agonistic activation. Measurements were performed twice, and both assessments were used in this study to reduce variability[16]. We quantified muscle activation with the AR using the following equation:

$$AR_{muscle} = \frac{mEMG^{IP} - mEMG^{OP}}{mEMG^{IP} + mEMG^{OP}}$$ [17]

"Muscle" represents either the latissimus dorsi, teres major, pectoralis major, or deltoid muscle, and ^{IP} and ^{OP} indicate "in-phase" agonist activation and "out-phase" antagonist muscle activation, respectively, relative to the force task in abduction or adduction.

The AR ranges between -1 and 1 and indicates the task related degree of antagonist activation relative to the same muscle's degree of agonist activation. The AR equals 1 in case of sole agonist muscle activation and decreases with increasing co-contraction. An AR of -1 indicates sole antagonistic activation and no agonistic activation. Based on this AR, we assessed the difference in muscle activation patterns between patients with SAPS and asymptomatic controls. We also assessed the influence of the target force level on the activation ratio in the statistical analysis.

To prevent overestimation of the degree of co-contraction as assessed with the AR, the mean EMG amplitude during the agonistic task (the activity of the deltoid muscle during abduction and the activity of adductors during adduction) was verified to be twice the mean EMG amplitude of the 10% lowest EMG signals during the relative rest, abduction, and adduction tasks (a signal-to-noise ratio of 2.0). If this condition was not met or if EMG data were corrupt (because of loose electrodes or other technical problems), the ARs were excluded. In the SAPS group, one of 40 ARs of the latissimus dorsi (2.5%), one AR of the teres major (2.5%), one AR of the pectoralis major (2.5%), and one AR of the deltoid muscle (2.5%) had to be excluded because the twofold signal-to-noise ratio was not reached. For the same reason, four of 30 ARs of the latissimus dorsi (13%) and two ARs of the teres major (6.7%) had to be excluded in the control group. Furthermore, because of a disconnected EMG amplifier, three of 30 ARs of the deltoid muscle (10%), four ARs of the latissimus dorsi (13%), four ARs of the pectoralis major (13%) and three ARs of the teres major (10%) could not be used in the control group. Additionally, in the control group, one out of 30 ARs of the latissimus dorsi (3%) and one AR of the pectoralis major (3%) could not be used because of a broken electrode.

Categorical data are described with numbers and percentages and continuous parameters are described with means and either 95% CIs, SDs, or medians with the 25th and 75th percentiles, depending on data distributions. Demographic data were compared using independent-samples t-tests or Mann-Whitney's U test depending on the distribution of data. Linear mixed-model analyses assessed the differences in activation ratios between patients with SAPS and asymptomatic controls. There were separate analyses for each assessed muscle. The dependent variable was AR_{muscle} and the measurement moment was the repeated factor. Independent variables were the patient groups (SAPS or asymptomatic controls) and the target force level (60% maximum voluntary force). An effect size of $0.10<AR<0.20$ was subjectively considered to be a modest effect size.

The patient and control populations were recruited in two different studies, and no a priori sample size analysis was performed for the AR. The statistical analysis was performed using SPSS® version 23 (IBM® Corp., Armonk, NY, USA). The results of the linear mixed-model analyses are presented as estimated regression coefficients, 95% CIs, and p values. A two-sided p value of 0.05 or less was considered statistically significant.

RESULTS

Patients with SAPS showed less co-contraction of the teres major and more co-contraction of the pectoralis major than controls did. Patients with SAPS had a 0.11 higher AR of the teres major (95% CI, 0.01 to 0.21; p = 0.038), a 0.11 lower AR of the pectoralis major (95% CI, -0.18 to -0.04; p = 0.003), and a 0.12 lower AR of the deltoid muscle (95% CI, -0.17 to -0.06; p < 0.001) than controls did. In terms of effect size, these differences were considered to be modest. With the number of patients and controls available, there was no difference in the degree of latissimus dorsi co-contraction between the groups (difference = 0.05, 95% CI, -0.01 to 0.12; p = 0.120) (**Table 2**). The average activation ratios of the latissimus dorsi, teres major, pectoralis major and deltoid muscle were 0.78 (SD 0.14), 0.53 (SD 0.23), 0.68 (SD 0.23) and 0.73 (SD 0.18) in patients with SAPS, and 0.73 (SD 0.19), 0.41 (0.27), 0.82 (0.08) and 0.85 (0.10) in controls (**Figure 2**).

Table 1 | Difference in activation ratios between patients with SAPS and controls

	Activation Ratio		
Independent variables	*Estimate*	*95% CI*	*p-value*
Latissimus dorsi			
Intercept	0.67	(0.57 – 0.77)	–
SAPS patients vs. controls	0.05	(-0.01 – 0.12)	0.120
Force task	0.08	(-0.02 – 0.17)	0.108
Teres major			
Intercept	0.43	(0.28 – 0.59)	–
SAPS patients vs. controls	0.11	(0.01 – 0.21)	**0.038**
Force task	0.0	(-0.13 – 0.13)	0.994
Pectoralis major			
Intercept	0.73	(0.62 – 0.83)	–
SAPS patients vs. controls	-0.11	(-0.18 – -0.04)	**0.003**
Force task	0.09	(0.01 – 0.18)	**0.036**
Deltoid muscle			
Intercept	0.90	(0.81 – 0.98)	–
SAPS patients vs. controls	-0.12	(-0.17 – -0.06)	**<0.001**
Force task	-0.05	(-0.13 – 0.03)	0.200

DISCUSSION

In approximately 29% to 34% of all patients with SAPS there is no anatomic explanation for symptoms, and behavioural aspects and/or central pain mechanisms may play a more important role than previously assumed[5,6]. A possible behavioural explanation for pain in patients with SAPS is insufficient active depression of the humerus during abduction achieved by adductor co-contraction[11-13]. The adductor muscles, specifically the teres major, have the most important contribution to humeral depression; however, this subject hast not been studied well in patients with SAPS[12,15]. In the current study, we sought to determine whether patients with SAPS have altered co-contraction patterns of the arm adductors compared with asymptomatic controls, which could point towards a treatable imbalance between the abductor and adductor muscles. We found that patients with SAPS predominantly contracted with the pectoralis major, while controls did so with the teres major. To unload subacromial tissues, it may be more effective to co-contract with the teres major[11,15].

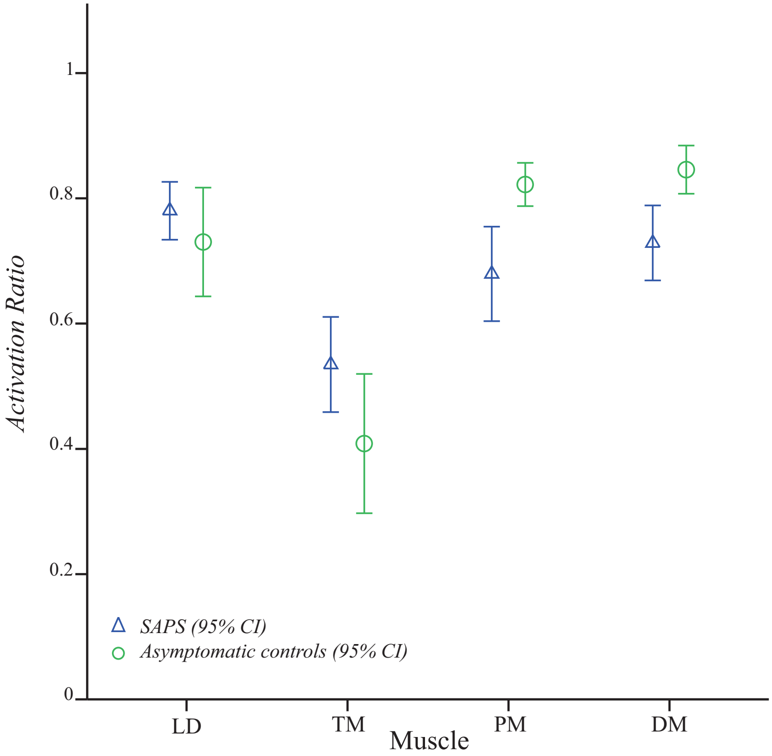

Figure 2 | The activation ratios of four shoulder muscles in patients with SAPS and controls are shown. LD = latissimus dorsi; TM = teres major; PM = pectoralis major; DM = deltoid muscle

Our study results have some limitations. First, the common chronic symptoms in the SAPS group were likely caused by a variety of anatomic factors. SAPS is a syndrome, not a specific anatomic diagnosis, and our conclusions need to be interpreted in light of this. A specific anatomic cause should be sought in patients presenting with shoulder pain, and treatment, other than nonsurgical therapies, should only be initiated when a specific, treatable anatomic basis is found for the symptoms[8]. Second, no a priori analysis was performed because the patient and control populations were recruited in two studies. Negative results may therefore have originated from underpowering. In light of the large amount of missing data for the latissimus dorsi in the control group (nine of 30 ARs; 30%), it plausible that there is a difference between patients with SAPS and controls in co-contraction of the latissimus dorsi, we may have been able to detect this difference due to underpowering. We do not consider it likely that missing data introduced a bias, because the predominant cause was failure of the EMG equipment (20 of 26 total missing values, 77%). Third, we did not control for potential confounding variables such as sports participation and BMI. Although we selected our control group from the patients' spouses, we cannot exclude the influence of these factors. Fourth, we only evaluated a selection of muscles that affect the craniocaudal position of the humerus the most[11,14,15]. Our conclusion may be supported by adding an analysis of other adductors, for example, the teres minor and lower parts of the infraspinatus and subscapularis.

Few studies have assessed the activation patterns of arm adductors during abduction tasks in patients with SAPS[18-20], and these studies contradicted one another, perhaps because of small sample sizes[18] or different testing positions[19]. In addition to altered adductor activation patterns, we observed a lower activation ratio of the deltoid muscle in patients with SAPS, originating from reduced activation during abduction. As suggested in previous studies[21,22], it seems that patients with SAPS attempt to avoid pain by reducing abductor activation at the cost of function (that is, reduced target force level). Co-contraction with the teres major, as we observed in the control group, may protect the patient from pain while preserving function.

Our EMG assessment of muscles that determine the craniocaudal position of the humerus during abduction provides new insight regarding the function of the teres major. Patients with SAPS predominantly co-contracted with the pectoralis major, whereas controls did so with the teres major (a glenohumeral muscle). Both muscles contribute to glenohumeral stabilisation. However, to reduce loading on subacromial tissues, it is more effective to use teres major co-contraction because this muscle is more capable of pulling the humerus downward (away from the acromion) than other muscles are[11,15].

Recently, it has been shown that surgical interventions commonly yield unsatisfactory results in treating patients with SAPS, and physical therapy is preferable[7,8,23]. We believe that such nonsurgical approaches can be improved with targeted approaches[23]. Supporting our findings, other clinical studies have suggested that increasing co-contraction of the arm adductors is a viable treatment option for patients with SAPS[12,13,24]. To improve targeted treatment approaches that enhance teres major (and latissimus dorsi) co-contraction in patients with SAPS, we suggest performing trials in which EMG is used[25-27].

In this cross-sectional EMG evaluation, we found decreased co-contraction of the teres major and increased co-contraction of the pectoralis major in patients with SAPS. We based our study on the rationale that insufficient humeral depression during abduction leads to perpetuation of SAPS, by overloading of the subacromial tissues[5,9,10]. For depressing the humerus, increasing teres major co-contraction as observed in the control group could be more effective[11,12,15]. Future studies using EMG monitoring should assess if actively training teres major (and latissimus dorsi) co-contraction could be a target for physical therapy protocols for patients with SAPS.

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3

Increased co-contraction of arm adductors is associated with a favorable course in subacromial pain syndrome.

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ABSTRACT

Background

Enhancement of arm adductor activity during abduction (i.e. adductor co-contraction), may be effective in the treatment of Subacromial Pain Syndrome (SAPS). We assessed whether an increase of adductor co-contraction is associated with a favourable course of SAPS.

Methods

At baseline and after nearly 4 years of follow-up, electromyography of the latissimus dorsi (LD), teres major (TM), pectoralis major and deltoid muscle was obtained during isometric abduction and adduction tasks in 26 patients with SAPS. Changes in co-contraction were assessed with change in the activation ratio (ΔAR). The AR ranges between -1 and 1, where lower values indicate more co-contraction. Clinical course was determined from an anchor question (*reduced, persistent* or *increased* complaints), the Visual Analogue Scale for pain (*VAS*), and the Western Ontario Rotator Cuff score (*WORC*).

Results

In patients indicating persistent complaints (31%), the *VAS* and *WORC* remained stable. In patients who indicated reduced complaints (69%), the *VAS* reduced (z score -3.4, $p=0.001$) and *WORC* increased (z score 3.6, $p<0.001$). Unchanged ARs associated with *complaints persistence*, whereas decreased AR of the LD (ΔAR_{LD}: -0.21, 95%CI: -0.36 to -0.06) and TM (ΔAR_{TM}: -0.17, 95% CI: -0.34 to -0.00) coincided with *reduced complaints*. There was a significant between-group difference in ΔAR_{LD} (-0.35, 95% CI: -0.60 to -0.10) and ΔAR_{TM} (-0.36, 95% CI: -0.66 to -0.05).

Conclusions

Increased co-contraction of the LD and TM is associated with a favourable course of SAPS. This may be explained by widening of the subacromial space accomplished by adductor co-contraction.

Level of evidence

Level I; Prospective Design; Prognostic Study

Key Words

Shoulder impingement syndrome; electromyography; biomechanical phenomena; co-contraction; teres major; latissimus dorsi

INTRODUCTION

During abduction of the arm, muscles that generate the moment for shoulder movement simultaneously generate a resultant force through the glenoid that stabilises the glenohumeral joint[1]. Studies have suggested that this active stabilisation is compromised in the Subacromial Pain Syndrome (SAPS), leading to painful upward migration of the humerus[2-6]. Model simulation and radiographic analyses show that humerus cranialisation may be counteracted with activation of arm adductors during abduction (i.e. adductor co-contraction)[7-9]. Therefore, increasing co-contraction of arm adductors like the latissimus dorsi (LD), teres major (TM) and pectoralis major (PM), may be beneficial for patients with SAPS.

Few studies have investigated arm adductor co-contraction in SAPS, and there is currently no evidence for alterations in activation patterns[10-12]. Moreover, longitudinal electromyography (EMG) assessments to support the theory that increasing adductor co-contraction is beneficial in SAPS, are yet lacking. In this study, we tested the hypothesis that increased arm adductor co-contraction would be associated with a favourable course of SAPS. In a prospective cohort with EMG assessment, changes in muscle activation of the LD, TM, PM and deltoid muscle (DM) were related to changes in complaints after nearly 4 years of follow-up.

MATERIALS AND METHODS

Between April 2010 and December 2012, 32 patients were recruited at the Leiden University Medical Center, Haaglanden Medical Center and Alrijne Hospital, under a previously registered and published study protocol (Netherlands Trial Register No. NTR2283)[13]. Patients with SAPS were selected using strict criteria on clinical examination and magnetic resonance arthrography[13]. Inclusion criteria were a positive Neer impingement test, a positive Hawkins test, and 1 or more additional criteria, including painful arc, shoulder complaints for longer than 3 months or diffuse pain during palpation of the greater tuberosity[13]. Exclusion criteria included, but were not limited to the presence of previous fracture or dislocation of the shoulder, frozen shoulder, comorbidities of the affected shoulder (e.g. tumor, instability), full-thickness rotator cuff tears or calcific tendinitis[13]. All patients gave written informed consent. After a period of usual care (e.g. physical therapy, subacromial injections), the 34 included patients were contacted for a follow-up visit between June 2014 and September 2015.

Measurement set- up

For EMG-measurements, participants were standing with the affected arm in external rotation at the side, facing a screen where the recorded force exertion was visualised (**Figure 1**). This testing position with the arm at the side was chosen so that all patients with SAPS could be evaluated, including those who could not abduct (fully) because of pain. We were also interested in typifying muscle activation strategies that patients use to generate an abduction moment, rather than in assessing the influence of pain on muscle activation patterns. In this position of relative rest and during abduction and adduction tasks against a 1-dimensional force transducer at the wrist, EMG of 3 shoulder adductors (LD, TM, PM, clavicular part) and the main shoulder abductor (DM, medial part) were recorded with bipolar surface EMG (DelSys system Bagnoli-16, Boston, MA, USA, interelectrode distance 10 mm, bandwidth 20 to 450 Hz) as previously described in detail[13]. EMG and force signals were analogue-digitally (AD) converted and recorded simultaneously at a sample rate of 2500 Hz. For offset removal, the mean was subtracted and the EMG-signals were rectified and enveloped (moving average) using custom made MATLAB software (MathWorks Inc., Natick, MA, USA). Corrupt EMG data or EMG signals that did not reach a 2-fold signal-to-noise ratio were excluded.

During the measurements, the maximal voluntary force (MVF) was first determined as the lowest absolute value of the *MVF* during isometric abduction and adduction. Second, participants performed an abduction and adduction force task at 60% ± 3.75% MVF. Muscle co-contraction was quantified using the activation ratio (AR), which is a reliable method to interpret EMG activity in a standardised manner and based on the muscles' principal action[14,15]. According to the principle action, muscle activation is expressed as agonistic "in-phase" activation (EMG^{IP}) and antagonistic "out-of-phase" activation (EMG^{OP})[15]. For example, activation of the DM, during the isometric abduction *force task* is called EMG^{IP} and activation during the adduction *force task* is called EMG^{OP}. These values were used to calculate ARs for the LD, TM, PM or DM (AR_{muscle}) using Eq. 1:

$$AR_{muscle} = \frac{EMG^{IP} - EMG^{OP}}{EMG^{IP} + EMG^{OP}} \qquad -1 \leq AR_{muscle} \leq 1 \qquad \textbf{Eq.1}$$

Outcome measures

Co-contraction

Changes in co-contraction were monitored using the AR (-1 to 1), where lower values indicate relatively more antagonistic activity (i.e. co-contraction)[14]. We also recorded the unstandardised group averages of the agonistic EMG^{IP} and antagonistic EMG^{OP} activity. Lastly, we used the magnitude of the *force task* to assess whether this mediated changes in AR.

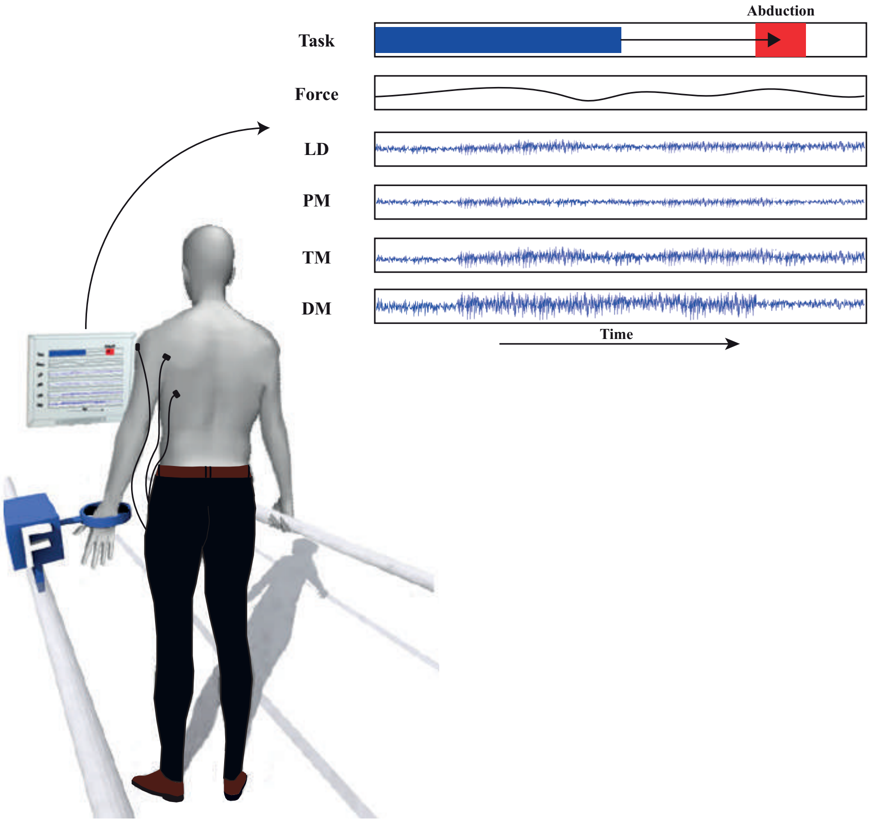

Figure 1 | Electromyography measurements during isometric force tasks. *LD*, latissimus dorsi; *PM*, pectoralis major; *TM*, teres major; *DM*, deltoid muscle.

Clinical course

- Anchor question for complaints persistence: The primary end point was an anchor question that assessed whether complaints had changed compared with the first visit, with 3 possible answers: *persistent complaints, reduced complaints* or *more complaints*. For the analyses of the association between ARs and the clinical course, patients were subgrouped according to their answers on the anchor uestion.
- Visual Analogue Scale for pain during motion *(VAS):* pain during arm movement was scored at baseline and follow-up using a 100mm *VAS* scale where 0 indicated no pain and 100 indicated maximal pain. We assessed whether changes in the *VAS* over time corresponded with answers on the anchor question and whether the change in the *VAS* score exceeded the minimal clinically important difference (MCID) of 14mm determined in patients with rotator cuff disease[16].
- Western Ontario Rotator Cuff score (*WORC):* The *WORC* is a clinical score focused at rotator cuff diseases assessing 5 domains in 21 items: physical symptoms, sports

and recreation, work, lifestyle and emotions[17]. The score ranges from 0 (worst possible) to 100 (best possible). We assessed whether changes in *WORC* over time corresponded with answers on the anchor question and whether the change in WORC score exceeded the MCID of 11.7 points determined in patients with rotator cuff disease[17,18].

Statistical analysis

Categoric data are described with numbers and percentages. Continuous data are described with means, standard deviation (SD) and 95% confidence intervals (95%CI) in case of normally distributed data or with medians and quartiles in case of nonparametric data (histograms).

We used Linear Mixed Models (LMM) to assess changes and intergroup differences in ARs over time (i.e. ΔAR_{muscle}). Dependent variables were the ARs of the LD, PM, TM or DM. In a fixed effects model, the clinical course was included as a factor and the measurement moment as a covariate. An interaction term between measurement moment and clinical course was included, to assess whether patients with a different clinical course (anchor question), differed in ΔAR_{muscle}. In addition, to rule out that the magnitude of *force task* during EMG tasks mediated possible changes in ARs, we conducted a simple LMM with fixed effect *force task* and dependent variable ARs[19]. Results from the LMM are presented as estimated group means, estimated group differences, 95% CI and p values. Depending on the distribution of data, changes in *VAS* and *WORC* scores over time were assessed by means of the paired samples t test or the Wilcoxon signed rank test. SPSS 20 software (IBM Corp, Armonk, NY, USA) was used for statistical analysis. A 2-sided p value of ≤ 0.05 was considered statistically significant.

RESULTS

Patient characteristics

At follow-up, 3 patients declined participation, 2 could not be contacted, and 1 had died, leaving a study cohort of 26 patients (76%) with baseline and follow-up data. Baseline characteristics of the included patients are described in **Table 1**. During the follow-up period of 3.8 (SD 0.48) years, patients reported to having received only exercise therapy (n=6, 23%), only subacromial infiltrations (n=3, 12%) or both (n=13, 50%), and a wait-and-see policy (n=4, 15%).

Table 1 | Baseline characteristics of patients with the Subacromial Pain Syndrome.

	Total group (n=32)	
	With follow-up	Loss to follow-up
	n=26	n=6
Demographics		
Age, mean (SD) yrs	50 (6.4)	53 (4.8)
Female, No. (%)	16 (62)	3 (50)
Right side dominance, No. (%)	23 (89)	5 (83)
Dominant side affected, No. (%)	16 (62)	4 (67)
Body Mass Index, mean (SD) kg/m^2	27 (4.5)	25 (1.5)
Duration of complaints, median (quartiles), mo	18 (12-29)	12 (10-30)

SD, standard deviation.

Clinical course of complaints

Compared with the first visit, none of the patients had *increased complaints* after the follow-up period, 8 patients (31%) had *persistent complaints*, and 18 (69%) had *reduced complaints*. Of the patients with *persistent complaints,* 1 (13%) reported to have only received subacromial infiltrations and 6 (75%) reported to have received exercise therapy and subacromial infiltrations. In patients with *persistent complaints*, the median *VAS* was 47 (quartiles 19 – 63) at baseline and 54 (quartiles 21 – 77) at follow-up (z score -0.35, p=0.726). Also the *WORC* showed no significant changes in these patients, with median scores of 57 (quartiles 51 – 68) at baseline and 44 (quartiles 34 – 67) at follow-up (Z-score -0.98, p=0.327). Conversely, in patients with *reduced complaints*, the *VAS* reduced from 32 (quartiles 17 – 62) at baseline to 5.9 (quartiles 2.0 – 34) at follow-up (Z-score -3.4, p=0.001), exceeding the MCID[16]. The *WORC* also showed clinical improvement exceeding the MCID with a median score of 60 (quartiles 43 – 74) at baseline and 92 (quartiles 75 – 95) at follow-up (Z-score -3.6, <0.001)[18].

Muscle activation in association with cli nical course

At baseline, there were no differences in ARs between patients who indicated *persistent* or *reduced complaints* at follow-up (**Figure 2**, **Table 2**). Over time, there were no significant changes in the AR of the LD in patients with *persistent complaints* (ΔAR_{LD}: 0.14, 95%CI: -0.06 to 0.34). However, in patients with *reduced complaints*, the AR of the LD significantly decreased (ΔAR_{LD}: -0.21, 95%CI: -0.36 to -0.06), indicating significantly increased co-contraction. The groups significantly differed in change in AR_{LD} over time (group difference in $\Delta AR_{LD:}$ -0.35, 95% CI: -0.60 to -0.10, p=0.009). Also regarding the TM, patients with *persistent complaints* had no significant changes in the AR (ΔAR_{TM}: 0.19, 95%CI: -0.07 to 0.44), whereas patients with *reduced complaints* had a significant decrease in AR of the TM (ΔAR_{TM}: -0.17, 95% CI: -0.34 to -0.00), indicating increased co-contraction. This resulted in a group-difference of -0.36 (95% CI: -0.66 to -0.05, p=0.023). There were no significant group differences in the ΔAR_{PM} (-0.08, 95% CI: -0.31 to 0.15) or ΔAR_{DM} (0.16, 95% CI: -0.01 to 0.32). Lastly, no association was found between the magnitude of force task during measurements and the AR of the LD (-0.07, 95%CI: -0.24 to 0.11, p=0.438), TM (-0.04, 95%CI: -0.28 to 0.20, p=0.724), PM (0.06, 95%CI: -0.09 to 0.21, p=0.417) or DM (-0.01, 95%CI: -0.11 to 0.10, p=0.886).

Unstandardised agonistic (EMG^{IP}) and antagonistic (EMG^{OP}) activity

In accordance with the presented ARs, the coinciding unstandardised EMG^{IP} and EMG^{OP} signals revealed increased antagonistic EMG^{OP} of the LD and TM in the group with *reduced complaints* at follow-up and decreased antagonistic EMG^{OP} of the LD and TM in the group with *persistent complaints* at follow-up (**Table 3**).

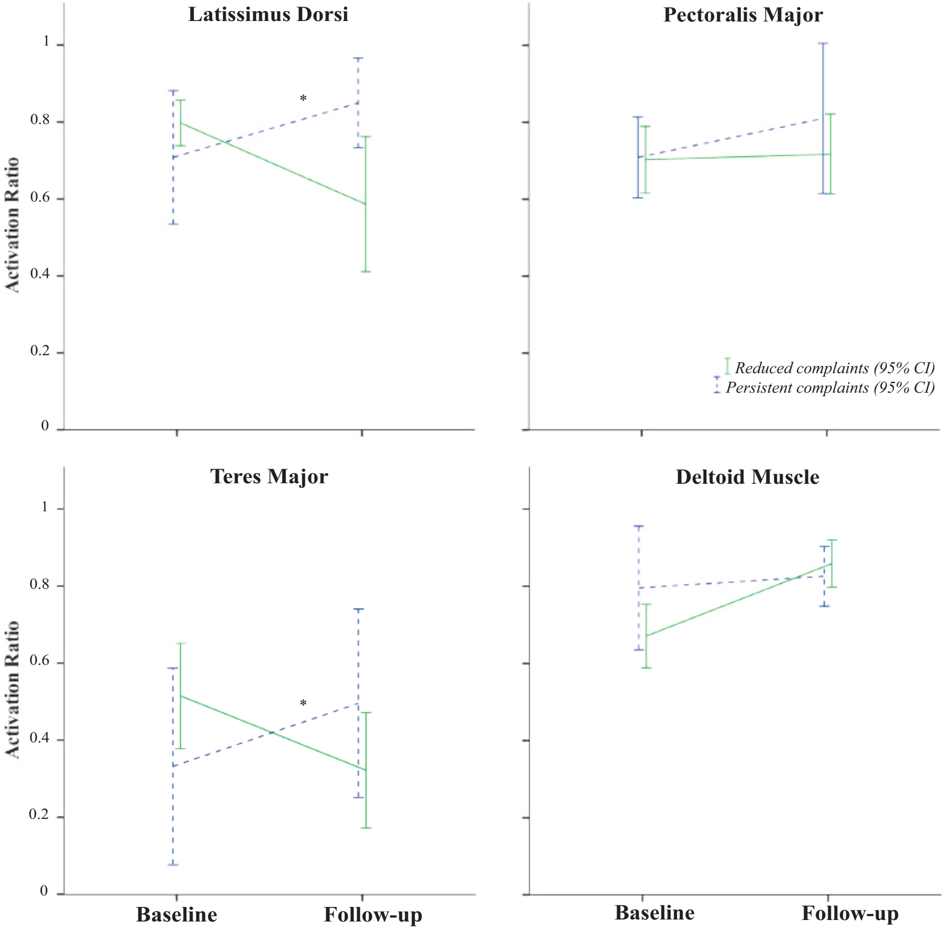

Figure 2 | Change in activation ratios over time stratified for shoulder complaints at follow-up. The whiskers represent the 95% Confidence Intervals (CI). Lower activation ratios indicate relatively more co-contraction. *Significant difference (α = 0.05) in activation ratio change between patients with persistent or reduced complaints at follow-up, based on Linear Mixed Model analysis.

Table 2 | Activation ratios (AR) associated with complaints at follow-up using Linear Mixed Model analysis.

	Persistent complaints		**Reduced complaints**		**Group difference**		
AR	Mean	95% CI	Mean	95% CI	Mean	95% CI	p-value
LD							
Baseline	0.71	(0.60 – 0.82)	0.80	(0.73 – 0.87)	0.09	(-0.04 – 0.22)	0.165
Follow-up	0.85	(0.66 – 1.0)	0.59	(0.45 – 0.73)	-0.26	(-0.50 – -0.03)	**0.031**
Delta (ΔAR)	0.14	(-0.06 – 0.34)	-0.21	(-0.36 – -0.06)	-0.35	(-0.60 – -0.10)	**0.009**
PM							
Baseline	0.71	(0.59 – 0.82)	0.70	(0.62 – 0.78)	-0.00	(-0.14 – 0.13)	0.944
Follow-up	0.80	(0.64 – 0.97)	0.72	(0.62 – 0.81)	-0.09	(-0.28 – 0.10)	0.350
Delta (ΔAR)	0.09	(-0.10 – 0.29)	0.01	(-0.11 – 0.13)	-0.08	(-0.31 – 0.15)	0.459
TM							
Baseline	0.32	(0.11 – 0.53)	0.52	(0.38 – 0.65)	0.20	(-0.05 – 0.44)	0.118
Follow-up	0.51	(0.30 – 0.71)	0.34	(0.20 – 0.48)	-0.16	(-0.41 – 0.09)	0.190
Delta (ΔAR)	0.19	(-0.07 – 0.44)	-0.17	(-0.34 – -0.00)	-0.36	(-0.66 – -0.05)	**0.023**
DM							
Baseline	0.80	(0.67 – 0.92)	0.67	(0.59 – 0.76)	-0.13	(-0.28 – 0.03)	0.100
Follow-up	0.83	(0.75 – 0.91)	0.86	(0.80 – 0.91)	0.03	(-0.07 – 0.13)	0.528
Delta (ΔAR)	0.03	(-0.11 – 0.17)	0.19	(0.09 – 0.28)	0.16	(-0.01 – 0.32)	0.066

CI, confidence interval; LD, latissimus dorsi; PM, pectoralis major; TM, teres major; DM, deltoid muscle. Fixed effects were complaints at follow-up (persistent/reduced complaints), moment (baseline/ FU), moment * complaints. P-values in bold are significant ($\alpha = 0.05$).

Table 3 | Mean agonistic (EMG_{IP}) and antagonistic (EMG_{OP}) activity at baseline and follow-up.

		Baseline		**Follow-up**	
Complaints after follow-up		Mean (µV)	SD	Mean (µV)	SD
Persistent complaints					
LD	EMG^{IP}	14	7.2	15	6.2
	EMG^{OP}	2.0	0.93	0.92	0.39
TM	EMG^{IP}	17	8.7	14	12
	EMG^{OP}	9.0	6.1	4.0	1.9
PM	EMG^{IP}	32	22	24	17
	EMG^{OP}	5.2	4.6	1.6	1.1
DM	EMG^{IP}	44	52	17	15
	EMG^{OP}	3.1	2.4	1.7	1.7
Reduced complaints					
LD	EMG^{IP}	17	13	14	13
	EMG^{OP}	1.7	1.0	3.4	4.3
TM	EMG^{IP}	18	9.2	22	16
	EMG^{OP}	5.7	3.9	12	8.5
PM	EMG^{IP}	27	16	29	22
	EMG^{OP}	4.7	3.7	4.0	4.1
DM	EMG^{IP}	36	22	42	60
	EMG^{OP}	6.3	3.6	1.9	1.7

SD, standard deviation; LD, latissimus dorsi; EMG^{IP}, electromyograph agonistic in-phase activation; EMG^{OP}, electromyograph antagonistic out-of-phase activation; TM, teres major; PM, pectoralis major; DM, deltoid muscle.

DISCUSSION

In this cohort nearing 4 years of follow-up, we found that decreased ARs of the LD and TM were associated with patient-reported *reduced complaints*, significantly decreased pain (*VAS*), and significantly increased quality of life (*WORC*)[16]. These improvements exceeded threshold values for a MCID, thus indicating a clinically relevant improvement[16,18]. A favorable course of SAPS was associated with increased co-contraction of the LD and TM. Conversely, unchanged activation patterns of these adductors were associated with persistent complaints.

Activation patterns of scapular muscles, e.g. upper trapezius, and glenohumeral muscles, e.g. the infraspinatus, have been commonly assessed in the context of SAPS[20]. In contrast, only few studies reported on activity of arm adductors in SAPS, representing a gap in knowledge[10-12]. No differences in adductor activity between patients with SAPS and controls were found in two cross-sectional studies, except for a higher LD activation between 45° and 60° of concentric abduction[10,12]. In another cross-sectional comparison of the affected and unaffected shoulder in SAPS, unaltered activation patterns of amongst others the LD and PM were found[11]. Our study is the first to longitudinally assess adductor activation patterns in association with complaints in SAPS.

The observed association between increased adductor co-contraction and a favourable clinical course may suggest different underlying mechanisms. First, adductor co-contraction may be an adaptation to pain. In the presence of pain, agonistic activity may be reduced and antagonistic activity increased, in an attempt to prevent (further) tissue damage.[21] This theory is supported by several studies that observed acute altered muscle activation patterns, including reduced agonistic deltoid activity, after inducing subacromial pain.[22-24] In our study, EMG was assessed with the arm at the side where patients did not experience complaints; therefore, an acute adaptation to pain is not likely. Furthermore, patients with SAPS had more pain at baseline than at follow-up (*VAS* scores) and complaints at baseline had already lasted for a median of 17 months. Given this state of symptoms and that patients had less adductor co-contraction at baseline than at follow-up, the observed increased adductor co-contraction was unlikely to be an adaptation to pain.

Alternatively, the association between increased adductor co-contraction and a favourable course of SAPS may indicate preceding insufficient adductor co-contraction. In other joints than the shoulder, increased co-contraction has been associated with normal ageing.[25-27] This finding is generally explained as a means to enhance joint stability under the influence of degeneration, e.g. declining proprioception[25-27]. Possibly, patients with SAPS develop complaints because they adapt insufficiently to such age-related changes in the shoulder. The consequences hereof may be even greater considering previous studies that showed an exaggerated loss of proprioception in SAPS[28-30].

No association was found between co-contraction of the PM and the clinical course of SAPS. Due to the more medially directed force vector of the PM, it may be that the PM is less effective in counteracting cranially directed forces when the arm is hold at the side[7]. In higher regions of abduction, partially also due to presence of pain, co-contraction of the PM may arguably be more effective. Skolimowski and colleagues tested activation of the PM during abduction (whole trajectory) and accordingly suggested development of compensatory activation during this movement.[11]

Our study had some limitations. First, the comparison of ARs between patients with persistent or reduced complaints at follow-up was performed on relatively low numbers of patients. Despite the small sample size, we observed a convincing association between (increased) adductor co-contraction and the reduction of complaints. In the context of these findings and the current tendency toward personalised medicine, we believe that positive results in small study populations are of specific interest. A potential drawback is that findings may not be generalisable due to selection bias. We applied and described strict eligibility criteria to enhance the interpretation and reproduction of our findings. Second, 39 ARs (17%) were missing because EMG-data did not reach the 2-fold signal-to-noise ratio (12%) or was corrupt (5%, e.g. problem with the amplifier). Third, patients were treated according to current clinical practice and we did not control for this. The type of treatment may influence whether or not patients develop adductor co-contraction. However, because it was not our goal to prove causal relationships between adductor co-contraction and complaints persistence, possible confounding by received therapy is not an issue.

To explore whether adductor co-contraction and complaints in SAPS are causally related, we suggest a placebo-controlled intervention study, with, for example EMG-guided exercise of adductors (e.g. humeral depressor exercise)[31]. Furthermore, to gain insight into the underlying mechanism, the association between adductor co-contraction and proprioception may be assessed, as well as the association between adductor co-contraction and ageing.

CONCLUSIONS

The current prospective cohort comparing patients with SAPS at baseline and after nearly 4 years of follow-up, showed that increased co-contraction of the LD and TM is associated with a favourable clinical course of SAPS. This finding may be explained by the beneficial effect of adductor co-contraction in widening of the subacromial space[7,9]. These results could open a window for research into muscle-specific physical therapy in SAPS.

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4

Pain does not explain reduced teres major co-contraction during abduction in patients with Subacromial Pain Syndrome.

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ABSTRACT

Background

Patients with Subacromial Pain Syndrome show reduced co-contraction of the teres major during abduction. Consequent insufficient humeral depressor function may contribute to painful irritation of subacromial tissues and offers a potential target for therapy. A crucial gap in knowledge is whether the degree of teres major co-contraction in these patients is influenced by pain itself. To gain insight into this matter, we assessed whether relief of subacromial pain with local analgesics leads to increased adductor co-contraction in 34 patients with subacromial pain.

Methods

In a single-arm interventional study with 34 patients, electromyographic activity of the latissimus dorsi, pectoralis major, teres major and deltoid was assessed during isometric force tasks in 24 directions before and after subacromial Lidocaine injection. Co-contraction was quantified using the activation ratio; range [-1 (sole antagonistic activation, i.e., co-contraction) to 1 (sole agonistic activation)].

Findings

There were no changes in activation ratio of the teres major after the intervention (Z-score: -0.6, p=0.569). The activation ratio of the latissimus dorsi increased to 0.38 (quartiles: 0.13 – 0.76), indicating decreased co-contraction (Z-score: -2.0, p=0.045).

Interpretation

Subacromial analgesics led to a decrease in co-contraction of the latissimus dorsi, whereas no change in the degree of teres major co-contraction was observed. This study shows that decreased teres major co-contraction in patients with subacromial pain, likely is not the consequence of pain itself, opening a window for physical therapy with training of teres major co-contraction to reduce subacromial irritation and pain.

INTRODUCTION

Compared to age-matched controls, patients with Subacromial Pain Syndrome (SAPS) show reduced co-contraction of the teres major during abduction[1]. While the rotator cuff muscles are regarded as the major humeral head depressors during abduction, teres major co-contraction may also play a role in humeral head depression during this movement[2]. Hence, observed reduction of teres major contraction during abduction in patients with SAPS may explain painful irritation of subacromial tissues and represent a target for therapy[3-5]. However, it has not yet been made clear whether decreased teres major co-contraction in patients with SAPS is owing to pain or underlying pathology, which is crucial information for the direction of treatment[1,6].

From studies involving asymptomatic individuals it is known that older individuals demonstrate increased contraction of the teres major and latissimus dorsi during abduction, compared to younger individuals[6]. This trend is associated with ageing and explained as a compensation mechanism for age-related degeneration of shoulder tissues (in particular the rotator cuff). The increased co-contraction enhances glenohumeral stability and protection of subacromial tissues by producing a caudally directed force counter-balancing the cranially directed force of the deltoid during abduction[2,6]. These findings suggest that changes in teres major co-contraction relate to biomechanical demands and not particularly to pain.

Therefore, the goal of this study was to assess whether reducing the degree of pain in patients with SAPS, results in increased teres major activation during abduction, i.e., co-contraction. In a single-arm interventional study, contraction of the deltoid muscle and simultaneous co-contraction of the latissimus dorsi, pectoralis major and teres major is measured before and after injection of subacromial anesthetics.

METHODS

Thirty-four patients were recruited between April 2010 and December 2012 at the Leiden University Medical Centre, Haaglanden Medical Centre and Alrijne Hospital, under a previously registered and published study protocol (Trial register no. NTR2283).[7] Consecutive patients with SAPS were screened using physical examination, shoulder radiographs and magnetic resonance arthrography by dedicated shoulder surgeons. In this study, we defined SAPS as shoulder pain lasting for longer than 3 months with no specific anatomic abnormalities that could explain complaints and require specific treatment (e.g., acromioclavicular osteoarthritis, calcific tendinitis, full thickness rotator cuff tears). The inclusion criteria were patients who were aged

35-60 years, who had unilateral shoulder complaints for >3 months and who received a clinical diagnosis of SAPS based on a positive Hawkins test and Neer impingement test with lidocaine.[7] The exclusion criteria were insufficient language skills, inflammatory glenohumeral (GH) arthritis, clinical signs of GH or acromioclavicular osteoarthritis, previous shoulder surgery, fracture or dislocation, cervical radiculopathy, GH instability, decreased passive GH mobility (e.g. frozen shoulder), and presence of electronic implants (e.g. pacemaker). Additionally, patients were excluded in case other specific conditions were diagnosed on radiographs or magnetic resonance arthrography such as calcific tendinitis, full-thickness rotator cuff tear, and labral or ligament pathology.[7] The review board of the institutional medical ethical committee approved this study (P09.227) and all patients gave written informed consent.

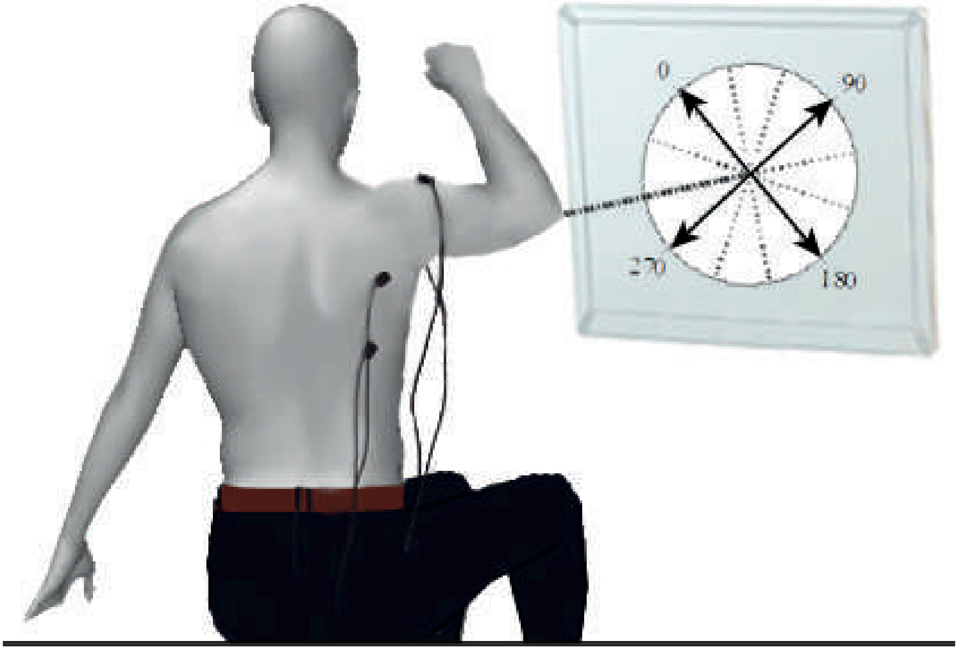

Figure 1 | Measurement set-up

Subjects were in seated position with the arm in a splint attached to a 3D force transducer such that the upper arm was in 60° of anteflexion, in 30° adduction, and 45° internal rotation, and the elbow 90° flexed (splint depicted in manuscript by De Witte and co-authors[8]). The exerted force was visualised through a cursor on a video screen to help subjects to control both force direction and magnitude. Subjects performed 24 submaximal (75% MVF) force tasks in 24 equidistant directions, 15° apart, ranging from pressing arm straight up (0°) to pushing the arm sideward (90°, 270°) or downward (180°). During these tasks, electromyography was obtained from the latissimus dorsi, pectoralis major, teres major and deltoid using bipolar surface electrodes.

Intervention

Using a 50 mm 21-gauge needle, 5ml 1% Lidocaine was injected in the subacromial space. The needle was inserted 1 to 2 cm inferior and medial to the posterolateral corner of the acromion, directing to the anterolateral corner of the acromion (soft spot). Patients were then given a 30 minutes adjustment period and were asked to move their arm in order to disperse the drug within the subacromial bursa. Following subacromial analgesics, all patients verbally reported reduced pain.

Electromyography (EMG) measurement set-up

Before and 30 minutes after subacromial analgesics, muscle activation patterns of the latissimus dorsi, teres major, pectoralis major (pars clavicularis) and deltoid (pars medialis) were assessed with EMG during isometric force tasks[9]. Bipolar surface electrodes (inter-electrode distance 10 mm) were adhered to abraded and ethanol cleaned skin overlying the middle of the muscle belly of the latissimus dorsi, pectoralis major (clavicular part), teres major and the middle part of the deltoid muscle (**Table 1**). The EMG was band pass filtered (20–500 Hz) before recording. Force and EMG signals were Analogue-Digitally converted and recorded simultaneously at a sample rate of 2000 Hz.

Subjects were in seated position with the arm in a splint such that the upper arm was in 60° of anteflexion, in 30° adduction, and 45° internal rotation (**Figure 1**)[8]. The elbow was 90° flexed. The force transducer was mounted on a sled and all gravitational forces and GH moments were neutralised by contra-weights, to ensure that participants only exerted forces perpendicular to the humeral longitudinal axis and prevent subjects from generating supplementary moments. The exerted force was visualised through a cursor on a video screen to help subjects to control both force direction and magnitude.

Before and after the injection of subacromial anesthetics, the following procedure was carried out. First, the Maximum Voluntary Force (MVF) was determined by asking subjects to perform 24 tasks in a range from 0-360° with 15° increments, in a random sequence, at the highest level of force wherein patients could comfortably fulfill the tasks for 2 seconds. Then, subjects were asked to perform 2 seconds force tasks visualised by a cursor on the video screen in the same 24 randomly sequenced directions at 75% of the lowest MVF. The raw EMG signal during two seconds of rest and raw EMG signals during the 75% MVF force tasks were rectified and averaged. The offset was removed by subtracting the rectified EMG signal during the rest task from the rectified EMG signals during the force tasks. These EMG-values were used for the calculation of the degree of co-contraction (below).

Table 1 | Shoulder muscles and localisation of the electrodes

Muscle	Location electrode
M. latissimus dorsi (LD)	6 cm below angulus inferior scapulae
M. pectoralis major, pars clavicularis (PM)	1/2 clavicula, 1cm caudally
M. teres major (TM)	4cm cranial to angulus inferior and 2cm lateral to LD
M. deltoideus, pars medialis (DM)	Middle muscle belly, 2-4cm below acromion, lateral

Calculation of co-contraction

The degree of adductor co-contraction was expressed using the activation ratio (AR), which represents the degree of antagonistic activation respective to the same muscle's agonistic activation. The AR ranges from -1 to 1, equaling 1 in case of pure agonistic muscle activation and -1 in case of pure antagonistic activation[9-11]. Calculation of the AR is based on the muscle's principal action as previously determined in young healthy participants[9,12]. These values were used to indicate in which direction of movement the muscle is supposed to be maximally active[9,12]. For instance, the deltoid muscle is expected to have maximum activation during arm abduction, i.e., the principal action[12]. Based on these principal actions, muscle activation can be expressed as the agonistic 'in-phase' activation (EMG^{IP}), and in the opposite direction as antagonistic 'out-of-phase' activation (EMG^{OP}) as depicted in **Figure 2** [9,12]. For the calculation of the mean EMG^{IP}, EMG magnitudes were averaged over seven force tasks, including the force task corresponding to the muscle's principal action and 3 adjacent force tasks on each side. Conversely, for the calculation of EMG^{OP}, EMG was averaged over 7 targets in targets in the exact opposite direction of the EMG^{IP} directions. Subsequently, based on these values the activation ratio (AR) was calculated using Eq. 1. In order to prevent overestimation of the degree of co-contraction as assessed with the AR, the maximum EMG-amplitude was verified to be twice the minimum EMG-amplitude (a signal-to-noise ratio of SNR ≥2.0). In case this condition was not met or in case EMG-data was corrupt (e.g., loose electrode), the ARs were excluded.

$$AR_{muscle} = \frac{EMG^{IP} - EMG^{OP}}{EMG^{IP} - EMG^{OP}} \qquad -1 \leq \mathrm{AR}_{\mathrm{muscle}} \leq 1 \tag{1}$$

Statistical analysis

Categorical data were described with numbers and percentages. Continuous parameters were described with means and either 95%-confidence intervals (95%

CI) or standard deviations (SD), or medians with the 25th and 75th percentiles, depending on data distributions. The changes in activation ratios and unstandardised EMG amplitudes (EMG^{IP} and EMG^{OP}) before and after intervention were assessed by means of paired T-tests or Mann Whitney U-test. The statistical analysis was performed using the Statistical Package of Social Sciences (SPSS®) version 23 (IBM® Corp, Armonk, NY, USA). A two-sided p-value of 0.05 or less was considered statistically significant.

Table 2 | Patient characteristics

Patient characteristics		**SAPS (n=36)**
Age	years (SD)	50 (6.5)
Female	n (%)	22 (61)
Length, cm	mean (SD)	173 (12)
Weight, kg	mean (SD)	78 (16)
BMI	mean (SD)	26 (4.4)
Duration of complaints, months	median (percentiles)	17 (12 – 24)
Right side dominance	n (%)	31 (86)
Right side affected	n (%)	21 (58)
Dominant side affected	n (%)	22 (61)
VAS in rest, mm	median (percentiles)	11 (2.0 – 25)
VAS during movement, mm	median (percentiles)	39 (18 – 59)
Constant Score	mean (SD)	71 (13)
WORC score	mean (SD)	58 (18)

SAPS, Subacromial Pain Syndrome; SD, Standard Deviation; n, number; VAS, Visual Analogue Scale; WORC, Western Ontario Rotator Cuff score[13,14].

RESULTS

Thirty-four patients with SAPS, with a mean age of 50 years (SD 6.5) were included in this study (**Table 2**). In four patients post-intervention assessments could not be performed due to a vasovagal syncope (n=1), allergy to lidocaine (n=1) or refusal to undergo the intervention (n=2). There was no loss of EMG signals. The EMG-measurements were performed at a mean force level of 35 N (SD 8.8) and 35 N (SD 8.0), before and after the intervention respectively.

Before the intervention, the activation ratios of the pectoralis major and the deltoid were around 0.8, indicating predominant agonistic activity (**Table 3**). In contrast, the median pre-intervention activation ratios of the teres major and latissimus dorsi were 0.48 (quartiles: 0.36 – 0.63) and 0.26 (quartiles: 0.09 – 0.66), indicating presence of antagonistic activity.

After intervention, the teres major showed no statistically significant change in activation ratio (Z-score: -0.6, p=0.569). The median activation ratio of the latissimus dorsi increased to 0.38 (quartiles: 0.13 – 0.76), which represented a significant change (Z-score: -2.0, p=0.045). The increase in activation ratio of the latissimus dorsi was explained by a relative decrease of activation during the antagonistic tasks (EMG^{OP}) and an increase in in activation during agonistic tasks (EMG^{IP}) as described in **Table 3**.

Table 3 | Activation Ratios and Unstandardised EMG amplitudes before and after Lidocaine injection

	SAPS (n=34)		**Paired difference**	
Muscle activity	Before intervention (median, quartiles)	After intervention (median, quartiles)	Z-score	p-value
Activation Ratio				
Latissimus dorsi	0.26 (0.09 – 0.66)	0.38 (0.13 – 0.76)	-2.0	**0.045**
Pectoralis major	0.83 (0.72 – 0.89)	0.78 (0.64 – 0.88)	-1.2	0.229
Teres major	0.48 (0.36 – 0.63)	0.51 (0.32 – 0.68)	-0.6	0.569
Deltoid	0.81 (0.74 – 0.94)	0.87 (0.79 – 0.94)	-1.1	0.254
Unstandardised agonistic EMG (µV)				
Latissimus dorsi	2.3 (1.5 – 4.3)	2.8 (1.3 – 4.2)	-0.32	0.750
Pectoralis major	14 (9.3 – 26)	17 (7.5 – 25)	-1.9	0.057
Teres major	7.7 (4.6 – 11)	7.9 (5.2 – 13)	-0.32	0.750
Deltoid	15 (8.0 – 27)	18 (11 – 30)	-0.03	0.975
Standardised antagonistic EMG (µV)				
Latissimus dorsi	1.0 (0.4 – 2.2)	0.8 (0.4 – 1.5)	-1.9	0.057
Pectoralis major	1.3 (0.7 – 3.0)	1.5 (0.8 – 3.8	-0.09	0.926
Teres major	2.6 (1.3 – 3.7)	2.8 (1.0 – 4.4)	-0.48	0.633
Deltoid	1.1 (0.5 – 2.9)	1.1 (0.7 – 2.6)	-0.42	0.673

Muscle activation patterns assessed using electromyography and expressed as the Activation Ratio (AR) are compared before and after lidocaine infiltration with paired t-tests or Wilcoxon Signed Rank test depending on the distribution of data. SAPS, Subacromial Pain Syndrome. Statistically significant differences are presented in bold.

DISCUSSION

In this single-arm interventional study, we found that co-contraction of the teres major did not change after the administration of subacromial analgesics, while a statistically significant increase in latissimus dorsi activation ratio after subacromial infiltration was observed, implying a decrease in co-contraction. Thus, pain does seem to affect latissimus dorsi co-contraction but has no direct influence on the degree of teres major co-contraction, suggesting different pathophysiological pathways.

The degree of co-contraction of the latissimus dorsi decreased after local administration of Lidocaine, while the degree of agonistic activation increased, resulting in a significant increase in activation ratio (suggesting relatively reduced antagonistic activation). It has been shown in previous studies that in the presence of pain, one may react with decreasing agonistic muscle activity and increasing antagonistic muscle activity, to protect damaged tissue[15]. Our finding regarding the latissimus dorsi, may be in line with this protective mechanism to pain; due to the reduction of pain after Lidocaine infiltration, co-contraction of the latissimus dorsi may no longer be necessary[15].

A different pattern was observed regarding the teres major where there was no difference in co-contraction before and after administration of subacromial analgesics. There are currently no studies to compare our results with, however, our finding may be explained in light of previous findings using the activation ratio. First, in a study showing that patients with SAPS exhibit decreased teres major co-contraction during abduction, the theory was raised that painful irritation of subacromial tissues in SAPS may (in part) be explained by insufficient humeral head depression during abduction by the teres major[1,2]. In a second study, increased teres major co-contraction in patients with SAPS towards the degree observed in asymptomatic controls, was associated with reduction of pain, again suggesting that teres major co-contraction is a physiologic finding that may protect from pain[1,4,16]. Thus, assuming that teres major co-contraction is physiologic and not a consequence of pain, it seems plausible that the degree of teres major co-contraction in this study did not change after subacromial Lidocaine infiltration.

Lastly, regarding the pectoralis major, no changes in activation ratio were observed after the intervention. Although biomechanical evaluations have subscribed a role to the pectoralis major muscle as a potential humeral head depressor, no clinical evidence is present yet in patients with SAPS[2,17]. In our study, this may partly be explained by the positioning of the arm during measurements in anteflexion, adduction and internal rotation.

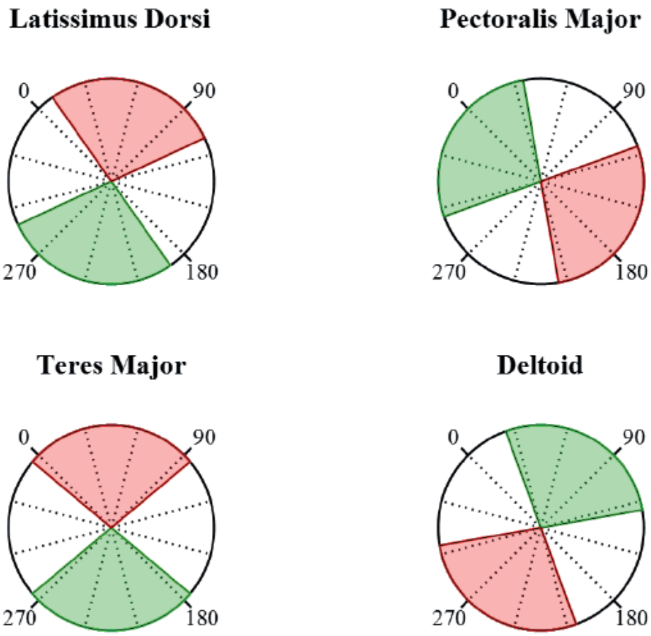

Figure 2 | In-phase and out-phase activation areas for calculation of the activation ratio
The principal action indicates in which direction of movement the muscle is supposed to be maximally active[9,12]. Based on the muscle's principal action, activation was expressed as agonistic 'in-phase' activation (*green*), and in the opposite direction, antagonistic 'out-of-phase' activation (*red*). Based on averaged EMG-values within these ranges, the activation ratio was calculated (Eq. 1).

This study has several limitations. First, although all patients verbally reported reduced subacromial pain after intervention, it is well likely that the responsiveness to subacromial injections varied per patient (e.g., due to uncontrolled administration) reducing the power to find differences in activation patterns after intervention. The fact that the level of latissimus dorsi co-contraction did change after the intervention suggests that the decrease in pain was sufficient to elicit changes in muscle activation patterns. Second, in this study we assumed that if reduced adductor co-contraction in patients with SAPS is a reaction to pain, it would increase right after administration of local analgesics. The fact that the activation pattern of the latissimus dorsi indeed changed after the intervention (in the expected direction) suggests that this is rightful assumption, however it should be noted that a more gradual reaction is possible. Thirdly, we did not perform an a-priori sample size calculation as this study was part of a larger project, and therefore effect sizes may have been underestimated[7]. Fourthly, we used surface electrodes for measurement of EMG-activity, and cannot exclude crosstalk from nearby muscles. Lastly, we evaluated a selection of muscles that affect the craniocaudal position of the humerus relative to the scapula[3,17,18]. The conclusions of this study may be further put in perspective by adding an analysis of other glenohumeral stabilisers, for example, the teres minor and the infraspinatus and subscapularis.

To conclude, we found that during an abduction movement, pain affects latissimus dorsi co-contraction but has no direct influence on the degree of teres major co-contraction in a group of 34 patients with SAPS. It has been previously shown that patients with SAPS exhibit decreased teres major co-contraction and that increasing co-contraction towards the degrees of observed in asymptomatic age-matched controls, is associated with reduction of pain [1,4,16]. The present study confirms that the deficit in teres major co-contraction observed in patients with SAPS is not the consequence of pain, and may represent a target for therapy to overcome perpetuating irritation of subacromial tissues during abduction by increasing humeral head depression.

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PART II |

Factors that may determine adaptation of adductor activation patterns and perception of pain in SAPS.

5

Shoulder movement complexity in the aging shoulder: A cross-sectional analysis and reliability assessment

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ABSTRACT

Healthy individuals perform a task such as hitting the head of a nail with an infinite coordination spectrum. This motor redundancy is healthy and allows for learning through exploration and uniform load distribution across muscles. Assessing movement complexity within repetitive movement trajectories may provide insight into the available motor redundancy during ageing. We quantified complexity of repetitive arm elevation trajectories in the ageing shoulder and assessed test-retest reliability of this quantification. In a cross-sectional study using 3D-electromagnetic tracking, 120 asymptomatic subjects, aged between 18 and 70 years performed repetitive abduction and forward/anteflexion movements. Movement complexity was calculated using the Approximate Entropy (ApEn-value): [0,2], where lower values indicate reduced complexity. Thirty-three participants performed the protocol twice, to determine reliability (intraclass correlation coefficient, ICC). The association between age and ApEn was corrected for task characteristics (e.g., sample length) with multiple linear regression analysis. Reproducibility was determined using scatter plots and ICC's. Higher age was associated with lower ApEn-values during abduction (unstandardised estimate: -0.003.year -1, 95%-CI [0.005;-0.002], $p<0.001$). ICC's revealed poor to good reliability depending on differences in sample length between repeated measurements. The results may imply more stereotype movement during abduction in the ageing shoulder, making this movement prone to the development of shoulder complaints. Future studies may investigate the pathophysiology and clinical course of shoulder complaints by assessment of movement complexity. To this end, the ApEn-value calculated over repetitive movement trajectories may be used, although biasing factors such as sample length should be taken into account.

INTRODUCTION

In the upper limb, disorders that develop during ageing, like rotator cuff pathology, are very common[1]. The pathophysiology of these disorders is considered multifactorial and due to cascading events, such as degeneration and overuse, but the true cause for shoulder region complaints is still not understood[2-4]. We theorise that at some point in the degenerative process, people may be no longer able to find effective movement strategies, eventually leading to complaints[2,5].

The young and healthy human body has a redundant number of ways to execute a specific task, enabling learning through trial and error, quick adaptation to change and uniform distribution of load across contractile tissues[5-8]. The complexity of repetitive movement trajectories (e.g., gait) has been interpreted as a characteristic of this motor redundancy, and thereby the healthiness of the underlying motor system[9-12]. A decreased complexity of movement during ageing may suggest a person to move in a rigid and predictable way as the result of muscular and sensory degeneration and be the cause for slow decline in functioning and frailty[8,13].

In the shoulder, there is a marked degeneration of predominantly rotator cuff muscles during ageing, requiring adaptation of the motor system to accomplish a task using different less affected muscles[3,4]. If motor redundancy becomes critical, this may predispose to the development of symptomatic disorders in the shoulder. The primary aim of this study was to determine shoulder movement complexity during abduction and anteflexion in 120 asymptomatic participants between 18 and 70 years old, to provide insight into the available motor redundancy during ageing. Since measurement of movement complexity in the shoulder is still in its infancy, we also performed a comprehensive reliability assessment as a base for future studies.

PARTICIPANTS AND METHODS

This was a level II prognostic study in which the complexity of repetitive arm elevation trajectories in the ageing shoulder was quantified and the test-retest reliability of this quantification was determined.

Participants

A prospective cohort study of asymptomatic participants, aged between 18 and 70 years was recruited through advertisements in public areas of the Leiden University Medical Centre and via word-of-mouth between May 2018 and January 2019 (**Figure 1**). Exclusion criteria were previous shoulder complaints that lasted longer than a week or for which a general practitioner was consulted, previous shoulder fractures, previous shoulder surgery, tumours in the breast or shoulder region, radiation therapy in the shoulder region (including breast), no full range of motion, electronic implants, pregnancy or insufficient Dutch language skills. Eligible participants were analysed at the laboratory of Kinematics and Neuromechanics (Leiden University Medical Centre, Leiden, the Netherlands). The study was approved by the Medical Research Ethics Committee (MREC). Participation was voluntary and all participants gave informed consent.

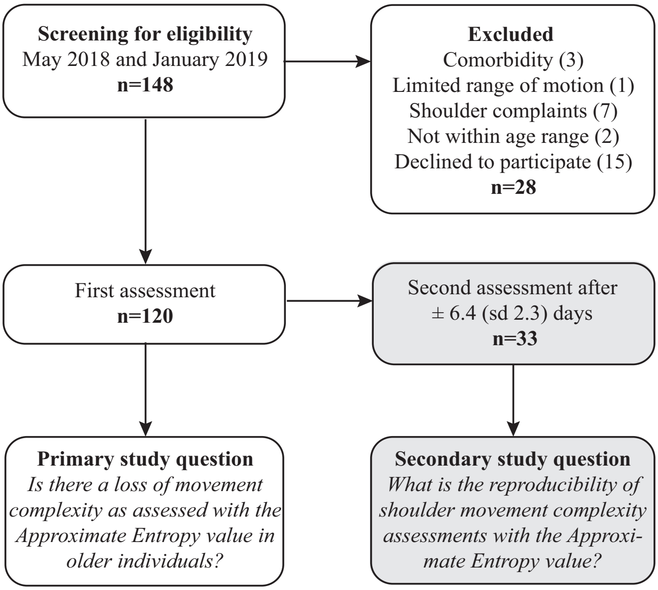

Figure 1 | Flow diagram of participant enrolment

Measurement set-up

The measurements were performed using a 3D-electromagnetic movement registration system with a sampling frequency of approximately 17Hz (Flock of Birds, FoB, Ascension Technology Inc., Milton, Vermont, USA). This validated device is frequently used in shoulder motion measurement and can accurately (margin of error of 2°) determine the position of both arms in space[14,15]. During all measurements, participants were seated in the FoB with their trunk upright. According to instructions on a computer monitor, the investigator placed seven sensors in a standardised way. One sensor was placed on the skin overlying the manubrium sterni with Fixomull self-adhesive bandage (Beiersdorf AG, Hamburg, Germany). Two sensors were adhered to the flat surface of the acromion just cranially to the acromial angle. Finally, using Velcro straps (Velcro Ltd, Middlewich, Cheshire, UK), bilateral humeral and forearm sensors were fastened around the distal part of the humerus and distal part of the forearm, respectively. Subsequently, twenty-four bony landmarks were palpated by the investigator, registered with an eighth sensor and digitised to construct a patient-specific 3D bone model relative to the 7 sensors[14]. The starting position was determined by asking the participant to sit up straight, with both arms in neutral position along the body. The participants were then asked to perform two movements, i.e., maximum abduction and maximum anteflexion, with either of both arms (chosen by flipping a coin), at a comfortable speed with the thumb up. Each movement was repeated five times during each registration. A sub-group of 33 volunteers repeated the procedure after approximately one week, to determine the test-retest reliability.

Signal processing

The angular position of the humerus with respect to the thorax (thus capturing shoulder dynamics) was used for the analysis[11,16,17]. The angular humerus elevation data vector per individual arm used for the analysis started from humerus first exceeding an elevation of 50° and ended when the humerus finally passed below 50° humerus elevation (**Figure 2**). The kinematic data was high-pass filtered at a frequency of 1.25 Hz to filter the 'static' components of movement control with custom-made MATLAB software as depicted in **Figure 2** (2018b release; The MathWorks, MA, USA).

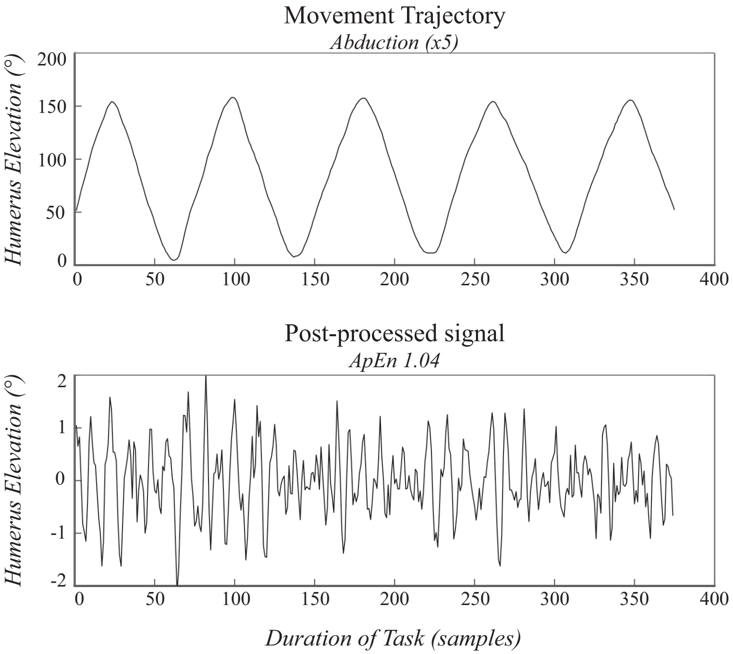

Figure 2 | Example of abduction movement trajectories. Example of the humerus elevation trajectory during abduction (degrees) before (upper panel) and after 1.25Hz High-Pass filtering (lower panel).

Outcome measures

For the assessment of movement complexity, the Approximate Entropy value (ApEn-value) was calculated using the function "ApproximateEntropy.m" in Matlab (2018b release; The MathWorks, MA, USA). The formula has been carefully described by Bruhn and co-workers[18]. The ApEn-value has been used in a wide range of pathologies and describes whether a system operates in a predictive, stereotype way or in a more chaotic, dynamic way, using many degrees of freedom[5,7]. Conceptually, the ApEn-value describes the logarithmic likelihood that a repetition of m consecutive data points, will not be followed by another (m+1) repeating data point[18,19]. The ApEn-value ranges between 0 and (about) 2, where lower values represent great regularity in data (e.g. in a sine wave), whereas values close to 2 represent irregular complex data structures (e.g. gaussian noise)[20]. In accordance with the literature, m (the number of samples to be matched) was set at 2 and r (the criterium for assessing whether two samples are a match) at 0.2 SD[19,21]. As the ApEn-value may depend on the data-length and arm dominance, we controlled for this in our statistical analysis[21]. The plane of elevation (degrees) and the maximum elevation height (degrees) were included in the statistical model to test whether these had an influence on the ApEn-value.

Statistical analysis

Version 23 of Statistical package of social sciences (SPSS, IBM Corp, Armonk, NY, USA) was used for statistical analysis. Subjects were distributed in four age categories [18-31, 32-45, 46-58, 59-70] years of age. Normality of data distribution was checked with histograms. Baseline characteristics were described with numbers and percentages, means and 95% confidence intervals (95%CI) or SD, as appropriate.

The association between independent variable age and dependent variable ApEn-value was analysed by means of multiple linear regression analysis using a block-enter method with controlling for task characteristics (duration of the task, plane of elevation and maximal elevation), gender and assessment of the dominant arm or not. The first block included age, gender, dominant side assessed, maximal elevation, the plane of elevation and a linear factor of the task duration. In subsequent blocks, it was tested whether entering a quadratic and cubic form of the task duration resulted in a significant greater explanation of variance in ApEn-value as based on an R square change of <0.10). Results of the regression analyses were presented using the standardised and unstandardised regression estimates with confidence intervals and p-values. A p-value <0.05 was considered to be statistically significant.

Reproducibility of the ApEn-value was depicted in scatter plots and quantified using the average measures Intraclass Correlation Coefficient (ICC), calculated in a two-way mixed model with absolute agreement[22]. To interpret the degree of reliability, the categorisation by Cicchetti et al. was used: 0.00–0.40—poor agreement; 0.40–0.59—fair agreement; 0.60–0.74—good agreement; 0.75–1.0—excellent agreement[23].

Power analysis

Based on a power of 95% and an alpha of 0.05, it was anticipated that 111 participants would be required for an effect size of 0.3 with regression analysis (G*Power version 3.0.10). Accounting for approximately 10% loss of data, 120 participants were recruited. For reliability analyses, it is advised to at least recruit 30 participants[24]. Again, to account for 10% loss of data, 33 out of 120 participants (28%), performed a second analysis.

RESULTS

Baseline characteristics are described in **Table 1**.

For abduction, the ApEn-value declined from 1.01 (SD 0.16) in the age-category of 18-31 years old, to 0.84 (SD 0.16) in the age-category of 59-70 years old (**Figure 3**). Accordingly, higher age was associated with lower ApEn values (estimate: -0.003 per year, 95% CI [-0.005 ; -0.002], $p<0.001$) during the abduction task (**Table 2**). The only factor further associated with the ApEn-value was sample length (**Table 2**).

For anteflexion, the ApEn-value declined slightly from 0.98 (SD 0.23) in the age-category of 18-31 years old, to 0.94 (SD 0.20) in the age-category of 59-70 years old (**Figure 3**). Age was not associated with the ApEn value (estimate: -0.001 per year, 95% CI [-0.003 ; 0.000], $p=0.090$) during the anteflexion task (**Table 2**).

A total of 33 (28%) participants with a mean age of 48 years (SD 14 years), 46% women and right-side dominance 94%, performed a second assessment after a mean of 6.4 days (SD 2.3). The ICCs for the overall group were: 0.417 (95% CI [0.084 ; 0.664) during abduction, and 0.297 (95% CI [-0.028 ; 0.571) during forward flexion. We observed that the difference in ApEn-values (ΔApEn) between both assessments strongly depended on the difference in duration (i.e., the number of samples) of the task between both assessments (ΔSamples). **Figure 4** exemplifies the association between ApEn-values of the first and second assessment and the difference in number of samples between those assessments. In case of small differences in duration of the task between both assessments (i.e., ΔSamples < 25), the agreement was good (**Figure 4**)[23].

Table 1 | Participant characteristics

	Asymptomatic participants n=120	
Demographics		
Age, yrs (mean, sd)	43.6 (14.9)	
Female (n, %)	67 (56)	
Right side dominance (n, %)	110 (92)	
Dominant side assessed (n, %)	60 (50)	
BMI (mean, sd)	24.0 (3.7)	
Profession (n, %)		
Unemployed (n, %)	12 (10)	
Seated (n, %)	99 (82.5)	
With upper limb activity above head (n, %)	9 (7.5)	
Sports		
No sports (n, %)	15 (12.5)	
Sports with upper limb activity below head (n, %)	55 (44.2)	
Sports with upper limb activity above head (n, %)	52 (43.3)	
Hours/ week	3.8 (2.8)	
Clinical score		
Self reported general health	18 (12-29)	
Excellent (n, %)	31 (25.8)	
Very good (n,%)	49 (40.8)	
Good (n,%)	39 (32.5)	
Fair (n,%)	1 (0.8)	
Bad (n,%)	0 (0)	
Constant Shoulder score dominant arm (median, qrtls)	96 (93 ; 100)	
Constant Shoulder score non-dominant arm (median, qrtls)	95 (92 ; 100)	
VAS for pain in rest (median, qrtls)	0 (0 ; 3)	
VAS for pain during movement (median, qrtls)	1 (0 ; 3)	
VAS for daily functioning (median, qrtls)	0 (0 ; 3)	
Measurement characteristics		
Assessment of dominant arm		
18-31 yrs (n, %)	17 (50)	
32-45 yrs (n, %)	14 (47)	Chi-square: 0.501 P-value: 0.919
46-58 yrs (n, %)	14 (48)	
59-70 yrs (n, %)	15 (56)	
Samples during abduction (n, SD)		
18-31 yrs (n, SD)	308 (113)	
32-45 yrs (n, SD)	271 (99)	F-statistic: 1.566 P-value: 0.201
46-58 yrs (n, SD)	263 (72)	
59-70 yrs (n, SD)	271 (66)	
Samples during anteflexion (n, SD)		
18-31 yrs (n, SD)	311 (120)	
32-45 yrs (n, SD)	309 (135)	F-statistic: 0.045 P-value: 0.987
46-58 yrs (n, SD)	302 (91)	
59-70 yrs (n, SD)	303 (83)	

BMI, body mass index; N, number; SD, standard deviation; VAS, Visual Analogue Scale; yrs, years.

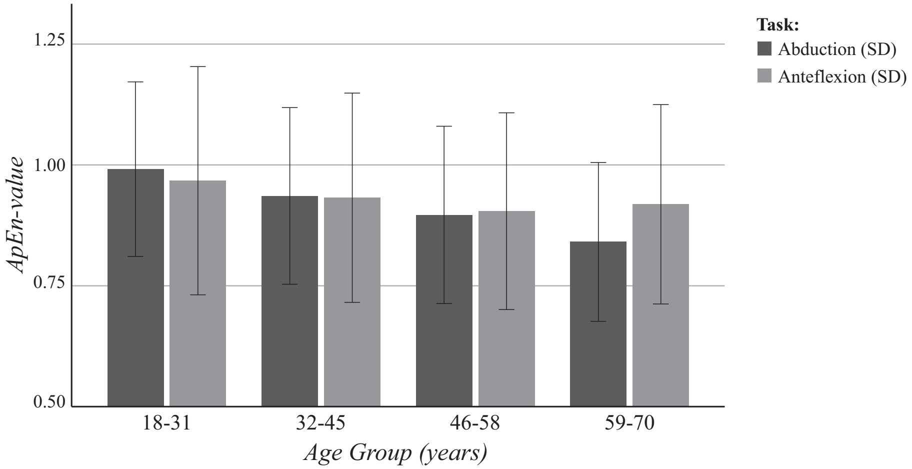

Figure 3 | Bar chart of ApEn-values during Abduction and Anteflexion

SD, standard deviation

Table 2 | Approximate Entropy value in asymptomatic participants as predicted by Age and potential covariates for the repeated Abduction and Anteflexion movements.

	Approximate Entropy value				
	Standardised coefficient	*Unstandardised coefficient*	*95% CI with unstandardised coefficient*	*p-value*	*Adj. R2*
Abduction					
Intercept		.449	[.038 ; .860]	NA	0.651
Age	-0.252	-.003	[-.005 ; -.002]	**<0.001**	
Sex (female is ref.)	0.101	.037	[-.003 ; .076]	0.070	
Dominant side assesed (no is ref.)	-0.029	-.011	[-.051 ; .030]	0.611	
Plane of elevation°	-0.019	.000	[-.003 ; .002]	0.935	
Maximal elevation°	-0.005	.000	[-.003 ; .002]	0.758	
Sample length (linear)	1.651	.003	[.002 ; .004]	**<0.001**	
Sample length (quadratic)	-0.944	-2.9x10-6	[-5.0x10-6 ; -1.0x10-6]	**0.001**	
Anteflexion					
Intercept		.327	[-.074 ; .728]	NA	0.636
Age	-0.100	-.001	[-.003 ; .000]	0.090	
Sex (female is ref.)	-0.009	-.004	[-.053 ; .045]	0.870	
Dominant side assesed (no is ref.)	0.102	.043	[-.004 ; .091]	0.072	
Plane of elevation°	0.033	-.002	[-.005 ; .000]	0.101	
Maximal elevation°	-0.104	.001	[-.002 ; .003]	0.587	
Sample length (linear)	1.527	.003	[.002 ; 0.004]	**<0.001**	
Sample length (quadratic)	-0.748	-2.0x10-6	[-3.0x10-6 ; -8.0x10-7]	**0.001**	

Multivariate regression analysis. Significant values at the alpha=0.05 in bold.

DISCUSSION

In the current study, we determined shoulder movement complexity during abduction and anteflexion in 120 asymptomatic participants between 18 and 70 years old, to provide insight into the available motor redundancy during ageing. Since measurement of movement complexity in the shoulder is still in its infancy, we also performed a comprehensive reliability assessment as a base for future studies. In line with the common loss-of-complexity hypothesis, we found a significant age-related decline in movement complexity during abduction, which may imply more stereotype movements and less ability to adapt to stresses during ageing, making the movement prone for development of complaints[5-8]. Assessing the complexity of repetitive movement trajectories proved reliable, although severely dependent on the length of data.

The decline in movement complexity we found in older individuals during abduction may be due to a loss of functional components (e.g., muscle atrophy) and/or altered coupling between those components (e.g., central degeneration)[25]. Several factors could explain why the decline in movement complexity was present during abduction and not during anteflexion. In contrast to the abduction task, the movement trajectory of the anteflexion task is nearly completely within the visual field, which may allow for compensation of functional loss[26]. In addition, participants might be more skilled in the execution of anteflexion rather than abduction tasks as fine motor skills are most commonly performed in front of the body[27-29]. It could be that during "less-challenging" tasks, movement complexity might be similar in elderly and young people, and that more "challenging" tasks are required to detect changes in movement complexity during ageing[5,9,11].

Age-associated decline in complexity of motor output has been observed in various regions of the musculoskeletal system, including gait and postural control[30-32]. Reduced movement complexity in walking patterns of elderly has been associated with risk of frailty and a consequent risk for falling[33-35]. Furthermore, individuals who have to make repetitive movements with little variability (e.g., wheelchair users, assembly line workers, butchers) have been shown to be more likely of developing overuse disorders when they have reduced movement complexity on beforehand[28,29,36-40]. For that matter, movement complexity may be an interesting and easy to access prognostic factor for shoulder pathologies[33-38,41-43].

The prospective design and relatively large number of participants were strong points of our study, but some limitations should be acknowledged. First, we cannot rule out the presence of a selection bias due to the fact that participants were recruited via advertisements, which may result in inclusion of participants with a specific interest for shoulder (dis-)functioning. However, since the outcome of interest is an objective measure, we do consider it unlikely that selection bias hampered generalisability in this study. Secondly, our outcome measure, the ApEn-value has not been extensively validated in the assessment of shoulder movement complexity[21]. Hampering the comparability of our data, we found a strong association between the ApEn-value and the duration of the motor task, although this did not affect conclusions regarding the association between age and ApEn-values, since the distribution of sample length was equal across the age-groups and controlled for in the regression analyses. Thirdly, we included participants based on a clinical assessment and did not rule out asymptomatic pathologies through radiological examination. Hence, participants with asymptomatic shoulder pathology may have been included in this study. It has been previously shown that reduction in movement complexity is multi-factorial and between-patient variance in movement complexity exists in the presence of comparable local pathology[43,44]. Therefore, while participants with asymptomatic shoulder pathology may have been included in this study, we do not think that this affects the possible clinical implication of our finding that there is reduced movement complexity during abduction in elderly, which may indicate vulnerability to developing complaints. Fourthly, we performed the measurements during only abduction ($p < 0.001$) and anteflexion ($p = 0.09$) tasks and therefore, we cannot conclude whether a loss of movement complexity during ageing is isolated or diffuse. On itself, the finding of reduced movement complexity manifesting predominantly during abduction is interesting considering the fact that shoulder pathology is associated with this movement[45]. However, in future assessments it may be interesting to investigate whether the reduction in movement complexity is indeed isolated to the abduction movement (and possibly asymptomatic pathology) or diffuse by assessing movement complexity during other movements, for example axial humeral rotation. Finally, while this study was initiated to provide a base for research in symptomatic patients, findings related to reduction of movement complexity during abduction in elderly, as well as findings related to reliability, may not be extrapolatable to symptomatic patients.

Shoulder complaints are highly prevalent in western societies and have a great impact on an individual's ability to perform daily activities and quality of life[45-47]. Currently, the pathophysiology of common shoulder complaints is not clear, but there is increasing evidence that behavioural/dynamic factors play a crucial role[2,48,49]. We theorise that movement complexity may contribute to whether one is able to maintain symptomless function in case of functional decline and stress on (contractile) tissues in the shoulder[46]. To further study this theory, we suggest to quantify shoulder movement complexity[44].

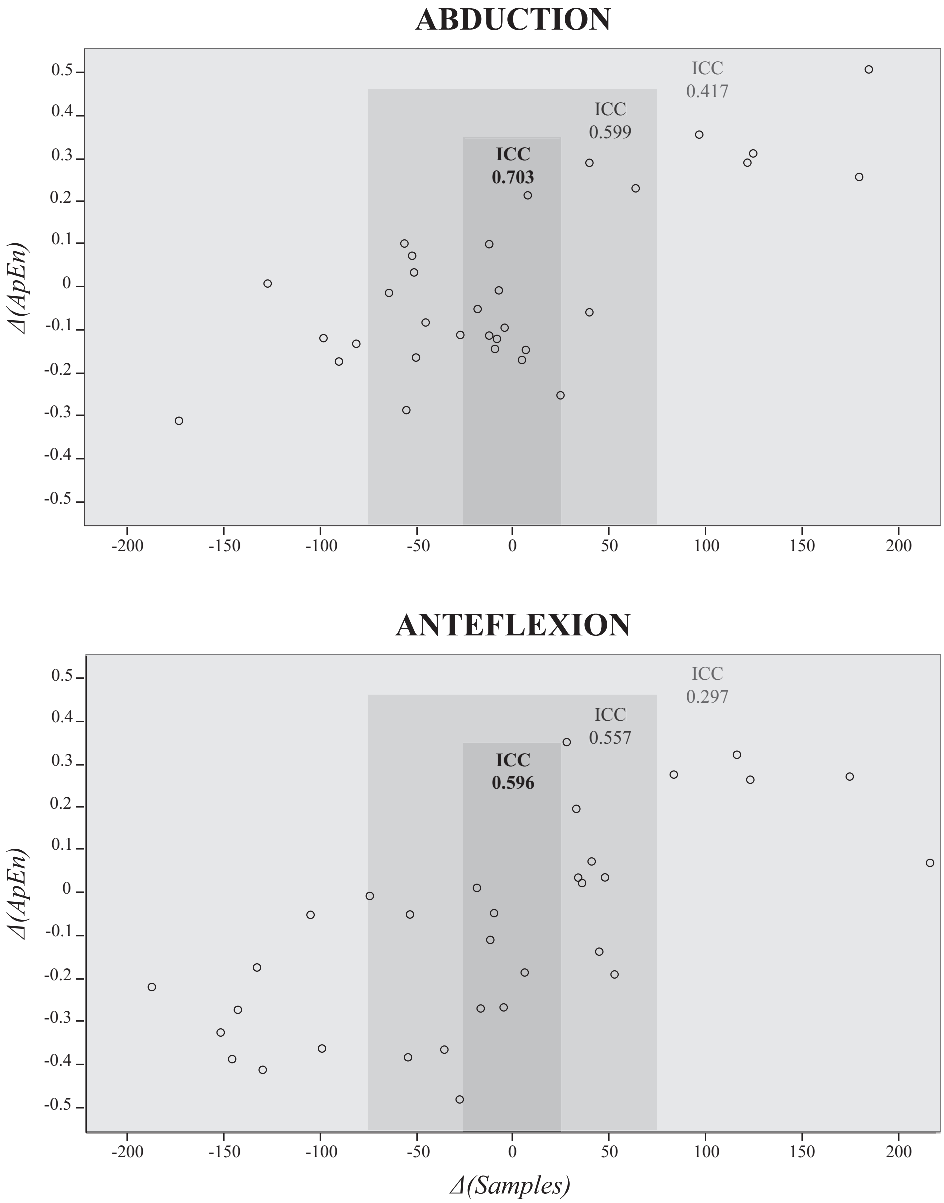

Figure 4 | Reproducibility of assessment of motor complexity using the Approximate Entropy value. The difference in sample length between the first and second assessment Δ(Samples) is plotted against the difference in Approximate Entropy value between the first and second assessments Δ(ApEn). The reproducibility of the ApEn value was calculated with the Intraclass Correlation Coefficient (ICC) for the data vectors differing < 25 samples (abduction: n=10, anteflexion: n=6), <75 (abduction: n=22, anteflexion: n=19) samples and <200 samples (n=33) between the first and second assessment.

We designed a method for measuring movement complexity in the shoulder, applying criteria (*m* and *r*) for the calculation of the ApEn-value in accordance with the literature, to enhance statistical reproducibility and comparability[22]. As has been described earlier, we found a strong association between the ApEn-value and the duration of the motor task[21]. This became clear during the main regression analysis, but even more so in the reliability assessment. Therefore, duration of motor task recording has to be taken into account when assessing shoulder movement complexity[21]. In future studies, this problem can be avoided by extending measurement time up to the level where the ApEn-value reaches a plateau phase (in our case > 400 samples)[21].

In this prospective cross-sectional cohort study with assessment of shoulder movement complexity in 120 participants between the age of 18 to 70 years old, we found that higher age was associated with a decline in movement complexity during abduction, indicating reduced motor redundancy during this movement. If the redundancy of ways to execute a specific task becomes critical, adapting to change and distributing load equally across tissues may become difficult[5-8]. Therefore, our finding of reduced motor redundancy during abduction in older individuals could play a role in the frequent onset of abduction-related shoulder (overuse) complaints in this population[45-47]. In future studies, movement complexity may be assessed to study the pathophysiology and clinical course of shoulder complaints. To this end, the Approximate Entropy value calculated over repetitive movement trajectories may be used, although biasing factors such as data length should be taken into account.

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Reduced force entropy in Subacromial Pain Syndrome: a cross-sectional analysis.

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ABSTRACT

Background

Generating a force at the hand requires moments about multiple joints by a theoretically infinite number of arm and shoulder muscle force combinations. This allows for learning and adaptation and can possibly be captured using the complexity (entropy) of an isometrically generated force curve. Patients with Subacromial Pain Syndrome have difficulty to explore alternative, pain-avoiding, motor strategies and we questioned whether loss of motor complexity may contribute to this. We assessed whether patients with Subacromial Pain Syndrome have reduced entropy of an isometrically generated abduction and adduction force curve.

Methods

Forty patients and thirty controls generated submaximal isometric ab- and adduction force at the wrist. The force curve was characterized by the magnitude of force variability [standard deviation and coefficient of variation], and the entropy (complexity) of force variability [approximate entropy].

Findings

Patients showed reduced entropy both during the abduction (-0.16, confidence interval: [-0.33 ; -0.00], *p*: 0.048) and adduction task (-0.20, confidence interval: [-0.37 ; -0.03], *p*: 0.024) and reduced force variability during abduction (standard deviation: -0.006, confidence interval: [-0.011 ; -0.001], *p*: 0.013 and coefficient of variation: -0.51, confidence interval: [-0.93 ; -0. 10], *p*: 0.016).

Conclusions

Isometric force curves of patients with Subacromial Pain Syndrome show reduced complexity compared to asymptomatic controls, which may indicate more narrow and stereotype use of motor options. In future studies, it should be investigated whether the finding of reduced force (motor) entropy indicates functional decline, contributing to decreased ability to acquire and optimise motor strategies in Subacromial Pain Syndrome.

INTRODUCTION

Healthy physiological systems have an infinite number of solutions for a given task, resulting in a measurable complexity of the system's output[1,2]. This output complexity (entropy) reflects the spectrum of motor solutions available, which is fundamental for the acquisition of skills, adaptation to changing environments and equal distribution of load among tissues[3-6]. Loss of complexity has been interpreted as one of the driving principles for functional decline and measuring output complexity has been proven useful in identifying pre-clinical changes in aging, pain and disease[1,2,7,8]. In the musculoskeletal system, loss of complexity manifests by declined ability to generate precise levels of force, declined walking ability, disrupted (balance) control and frailty[1,2,7,9-11]. Loss of motor output complexity has been associated with the clinical course of pain conditions involving amongst others, the low back[7,9-14]. We questioned whether the most common chronic pain condition of the shoulder (Subacromial Pain Syndrome, SAPS), is associated with reduced motor output complexity.

In SAPS, there are no specific anatomic abnormalities that could explain complaints (e.g., acromioclavicular osteoarthritis, calcific tendinitis, full thickness rotator cuff tears), but movement factors including scapular dyskinesia and reduced humerus depression during abduction relate to pain[15-19]. Physical therapy for SAPS in which these factors are targeted have been shown effective, however, patients report persisting complaints in up to 40%[20-23]. We propose that loss of motor output complexity may contribute to the perpetuation of pain in patients with SAPS, as patients may not have the possibility to explore alternative motor strategies and avoid subacromial pain[24]. Few studies have looked into this aspect of motor control in SAPS by analysing the dispersion of force output using measures like the standard deviation (SD) or coefficient of variation (CV)[25-28]. These studies showed unaltered force steadiness (i.e., the degree of variability of force variability) in patients with SAPS, leading to the conclusion that force control is preserved[25-28]. However, information on a different, potentially important, aspect of motor control lying in the entropy (i.e., structure) of force variability, was disregarded in these studies and may provide further insight[1,2,25-29].

In this paper, we extend the analyses of variability by quantifying the complexity of isometric force curves using Approximate Entropy (ApEn) in patients with SAPS and controls[30]. We hypothesise that compared to asymptomatic controls, patients with SAPS have reduced force entropy in the shoulder indicated by lower ApEn values. Force entropy will be determined during an isometric abduction task, because the resulting movement is associated with pain in SAPS. We will furthermore determine force entropy during isometric adduction, to provide insight into whether a potential loss of force entropy is specific to the abduction movement, or more systemic for the arm.

PATIENTS AND METHODS

This was a level II prognostic study in which the entropy of force curves was compared between patients with SAPS and asymptomatic controls.

Participants with SAPS

SAPS was defined as shoulder pain of subacromial origin, lasting for longer than 3 months with no other specific anatomic abnormalities that could explain complaints and require specific treatment (e.g., acromioclavicular osteoarthritis, calcific tendinitis, full thickness rotator cuff tears)[15]. From April 2010 through September 2016, 40 patients with SAPS were recruited at the Leiden University Medical Centre, Haaglanden Medical Centre and Alrijne Hospital, under a registered and published protocol (Trial register no. NTR2283)[31]. Patients were selected through a medical interview, clinical examination, radiographs and a Magnetic Resonance Imaging Arthrogram (MRA). Inclusion criteria were unilateral shoulder complaints for at least three months, positive Hawkins-Kennedy test (passive anteflexion of the shoulder to 90° with subsequent internal rotation of the shoulder to provoke subacromial pain complaints) and Neer lidocaine impingement test (looking for immediate relieve of pain after subacromial infiltration with Lidocaine). Further, patients had to have at least one of the following symptoms: pain during daily life activities with arm abduction, extension, and/or internal rotation, pain at night or incapable of lying on the shoulder, painful arc, diffuse pain at palpation of the greater tuberosity, scapular dyskinesis, and positive full or empty can test or positive Yocum test[31]. Patients were excluded in case of insufficient language skills, age under 35 or over 60 years, no written informed consent, any form of inflammatory arthritis of the shoulder, clinical signs of glenohumeral (GH) or acromioclavicular osteoarthritis, GH instability, decreased passive GH mobility (e.g., frozen shoulder), history of shoulder surgery, fracture or dislocation of the affected shoulder, cervical radiculopathy, and presence of a pacemaker or other electronic implants. Additionally, patients were excluded in case of an alternative diagnosis on radiographs or MRA, e.g., calcific tendinitis, full-thickness rotator cuff tear, labrum or ligament pathology, pulley lesion, biceps tendinopathy, os acromiale, tumour, cartilage lesion, and a bony cyst. Notably, general findings associated with subacromial pain (bursitis and tendinopathy) were no exclusion criteria. All MRAs were evaluated by an independent radiologist[18]. Included patients with SAPS were allowed to have participated in earlier studies for varying purposes[17,18,32-35].

Asymptomatic controls

Under a separate protocol, asymptomatic controls were recruited at the Leiden University Medical Centre between January 2016 through November 2016. Spouses of patients with musculoskeletal complaints were invited to volunteer in case they were aged between 35-60 years and had no current or past shoulder complaints. We selected participants according to their age and sex to make sure that there were no differences between the SAPS and control groups in these characteristics. Exclusion criteria were impaired passive and active shoulder function during clinical examination, insufficient Dutch language skills, prior shoulder surgery, injections, shoulder fracture or dislocation, radiculopathy, frozen shoulder, osteoarthritis or rheumatoid arthritis and neurologic or muscle disease. No additional imaging was performed in the control group, as this was only of interest in the SAPS-group to exclude specific anatomic conditions that could give an alternative explanation for the symptoms.

The study was undertaken with the understanding and written consent of each subject, and that the study conforms with The Code of Ethics of the World Medical Association (Declaration of Helsinki), printed in the British Medical Journal (18 July 1964). The review board of the institutional ethical medical commission approved these study protocols (P09.227 & P15.046) and all participants provided written informed consent.

Measurement set-up

Force entropy is generally measured during isometric force tasks[29]. The movement associated with SAPS is abduction[15]. Because of the multiple joints (i.e., degrees of freedom) within the arm-shoulder complex, we postulate that if there exists a relation between SAPS and force entropy this would manifest at the hand (end point) and be observable during the abduction force direction which would result in the painful abduction motion. We also determined force entropy during isometric adduction to control for whether a potentially reduced force entropy is isolated for the pain related force or more systemic in the arm. During measurements, participants were in standing position facing a computer for force feedback, with the target arm in external rotation at the side attached to a one-dimensional force transducer at the wrist[31]. In this setup, participants performed isometric force tasks in ab- and adduction (figure of measurement set-up in[32]). The force task magnitude was similar for both abduction and adduction and equal to 60% of the maximal voluntary force (MVF), defined as the lowest absolute value of the MVF in abduction or adduction.

Signal processing

Post-processing of the (2500 Hz sampled) force signal had to result in a signal with a sample rate of at least 200 Hz, accounting for sufficient Motor Unit recruitment induced variance[36]. The sampled force signal was therefore low-pass filtered using a third order Butterworth filter with a cut-off frequency of 125 Hz and down-sampled to 250Hz using custom made software (Matlab 2018b, MathWorks inc., Natick, USA). The data-vector used for the analyses consisted of consecutive force data points within a tolerance of 10% below or above the force task level (60% MVF). To exclude initial overestimation and undershooting of the force task (i.e., steering), the first 17.5% and last 2.5% of data were removed from the data-vector[26]. To have sufficient data length for the ApEn-analysis (i.e., >1000 samples), selected data vectors shorter than 4 seconds were discarded[37].

Outcome measures

Magnitude of force variability

The magnitude of force variability was assessed by calculating the Standard Deviation (SD) and the Coefficient of Variation (SD/mean force x 100, CV). These measures respectively represent the absolute and relative variability of the force about the mean, indicating higher force variability with higher values[25-27].

Complexity of force variability

The complexity of force variability was assessed with the Approximate Entropy value (ApEn). ApEn has been used in a wide range of pathologies and describes whether a system operates in a predictive, stereotype way or in a more chaotic, dynamic way, using many degrees of freedom[1,2]. The ApEn-value ranges between 0 and (about) 2. In general, healthy systems would reveal high ApEn-values, whereas functional decline is associated with low ApEn-values[1,2]. The ApEn-value was calculated according to articles of Pincus et al. with the function ApproximateEntropy in Matlab (Matlab 2018b, MathWorks inc., Natick, USA) and parameters set at $m = 2$ and $r = 0.2*SD$[30,38].

Statistical analysis

The data was stored and analysed using the Statistical package of social sciences (SPSS®) version 23 (IBM® Corp, Armonk, NY, USA). Categorical data are described with numbers and percentages and continuous parameters with means and either 95%-confidence intervals (CIs), standard deviations (SDs), or medians with the 25th and 75th percentiles, depending on data distributions. Demographic data, force task characteristics (data length and exerted force level) and the magnitude of force variability (SD and CV) were compared with the chi-square test and independent samples t-tests or Mann-Whitney U test depending on the distribution of data. The structure of force variability (ApEn) was compared between patients with SAPS and controls in a multivariate regression analysis with controlling for the data length associated with the force task. Results are presented as mean differences, estimated regression coefficients, 95% CI's and *p*-values. A two-sided *p*-value of 0.05 or less was considered statistically significant.

RESULTS

Cohort and task characteristics

Forty patients with SAPS and 30 asymptomatic participants were included. There were no differences in baseline or task characteristics, except for the data length during the abduction task, which was 1.5 seconds (i.e., 375 samples) shorter (CI: [-2.76; -0.22], *p*: 0.022) in patients with SAPS (**Table 1**). Because of corrupt data (e.g., 50 Hz noise), the abduction data of 4 patients with SAPS and the adduction data of 5 patients with SAPS and two controls were unsuitable for the analysis.

Table 1 | Patient characteristics of patients with SAPS and asymptomatic controls

	SAPS	**Controls**	***Group difference***		
	n=40	*n=30*	*Mean*	*95% CI*	*p-value*
Age, yrs (mean, SD)	50 (6.38)	51 (5.71)	-0.49	[-3.43 ; 2.45]	0.740
Female (n, %)	23 (58)	17 (57)	Chi-square value: 0.005		0.944
Right side dominance (n, %)	35 (88)	25 (83)	Chi-square value: 0.243		0.622
Dominant side measured/affected (n, %)	25 (63)	17 (57)	Chi-square value: 0.243		0.622
Duration of complaints (median, IQR)	18 (12-29)	-	-	-	-
Abduction task					
Data length (sec.)	7.38 (2.32)	7.50 (2.80)	-0.12	[-1.38 ; 1.14]	0.850
Exerted force (N)	0.92 (0.35)	0.99 (0.31)	-0.07	[-0.23 ; 0.09]	0.400
Adduction task					
Data length (sec.)	7.38 (2.25)	8.87 (2.80)	-1.5	[-2.76 ; -0.22]	**0.022**
Exerted force (N)	0.93 (0.35)	1.0 (0.31)	-0.07	[-0.24 ; 0.10]	0.406

SAPS, Subacromial Pain Syndrome; n, number; N, Newton; SD, standard deviation.

Magnitude of force variability

Patients with SAPS had reduced magnitude of variability during the abduction task as assessed with the SD (group-difference: -0.006 N (CI: [-0.011; -0.001], *p*: 0.013) and CV (group-difference: -0.51 (CI: [-0.93; -0.10], *p*: 0.016). We did not observe differences in magnitude of variability during the adduction task (**Table 2**).

Complexity of force variability

Patients with SAPS had lower ApEn-values during the abduction task (-0.16, 95% CI: [-0.33 ; -0.00], *p*: 0.048) and adduction task (-0.20, 95% CI: [-0.37 ; -0.03], *p*: 0.024) (**Table 3, Figure 1**).

Table 2 | Difference in magnitude of force variability between patients with SAPS and controls

	SAPS	*Controls*	*Group difference*		
	Mean (SD)	*Mean (SD)*	*Mean*	*95% CI*	*p-value*
Abduction task					
SD (N)	0.019 (0.010)	0.026 (0.010)	-0.006	[-0.011 ; -0.001]	**0.013**
CV (%)	2.16 (0.76)	2.68 (0.92)	-0.51	[-0.93 ; -0.10]	**0.016**
Adduction task					
SD (N)	0.025 (0.013)	0.029 (0.011)	-0.004	[-0.010 ; 0.002]	0.229
CV (%)	2.62 (0.88)	2.93 (0.76)	-0.31	[-0.73 ; 0.11]	0.143

SAPS, Subacromial Pain Syndrome; n, number; N, Newton; SD, standard deviation.

Table 3 | Difference in structure of force variability between patients with SAPS and controls

	ApEn-value		
	Beta	*95% CI*	*p-value*
Abduction task			
Intercept	0.78	[0.52 ; 1.0]	NA
SAPS (ref. is control)	-0.16	[-0.33 ; -0.00]	**0.048**
Data length (seconds)	0.02	[-0.01 ; 0.05]	0.216
Adduction task			
Intercept	0.94	[0.67 ; 1.21]	NA
SAPS (ref. is control)	-0.20	[-0.37 ; -0.03]	**0.024**
Data length (seconds)	-0.01	[-0.05 ; 0.02]	0.392

Estimated group difference in Approximate Entropy value (ApEn) between patients with Subacromial Pain Syndrome (SAPS) and controls, adjusted for the data length associated with the task.

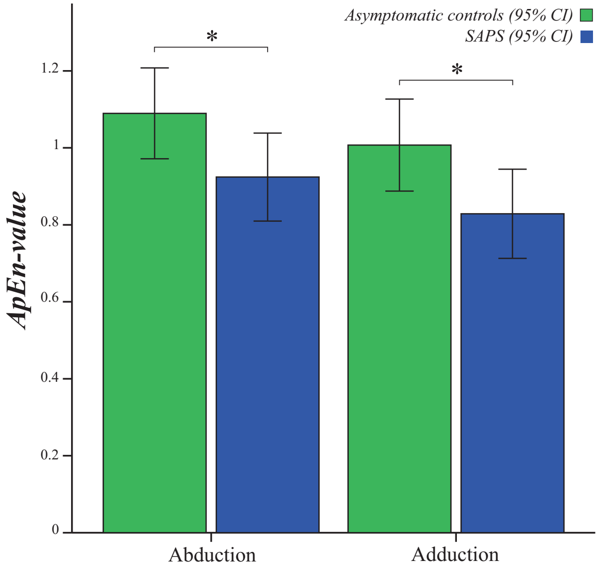

Figure 1 | Difference in force entropy between patients with SAPS and controls

Approximate Entropy values (ApEn) in patients with Subacromial Pain Syndrome (SAPS) and controls. Asterixis indicate significant adjusted estimated group differences in ApEn-values between patients with SAPS and controls, adjusted for the data length associated with the task

DISCUSSION

This cross-sectional evaluation showed that patients with SAPS have reduced motor output complexity during isometric abduction and adduction tasks, which may indicate functional decline. Furthermore, patients with SAPS showed reduced magnitude of force variability during isometric abduction.

In recent years, there has been an expansion of research on the subject of how musculoskeletal complaints can be discordant with observable pathology and become chronic. The focus has shifted from peripheral processes to factors as cognition, pain sensitisation and more recently, the adaptability of the motor system (e.g., assessed by the structure of motor control variability)[39-41]. The latter has already been investigated in various musculoskeletal disorders, and predominantly in low back pain there is a growing body of evidence suggesting that impaired adaptability of the motor system plays a role in the perpetuation of pain[12,14,41]. Furthermore, it has been shown that individuals who are involved in repetitive movements (e.g. butchers, assembly line workers) are more likely to develop overuse disorders if they have less complex variability between repetitions[12,14,42]. In SAPS, complaints become chronic in approximately 40% of patients, and reduced complexity of the motor system may contribute to the frequent perpetuation of complaints[40].

Only a few studies have investigated variability of force output in SAPS, with a focus on the magnitude hereof, discarding time-dependent characteristics[25-28]. In contrast to these previous studies that showed no alteration in magnitude of force variability and minor changes in control in SAPS, we did observe reduced magnitude of variability during isometric abduction. Our finding may be explained by a protective pain mechanism. It has been proposed that patients with pain minimise micro-movements at the painful joint by co-contracting with antagonists, to avoid damage and pain, resulting in a decrease of movement variability on a smaller scale[43-45]. In our study we measured force variability with the arm at the side, where patients experience least pain, to reduce direct pain interference. We assumed that the exertion of the abduction force that would lead to arm abduction elicits protective behaviour, because this movement is associated with pain exacerbation (painful arc)[15].

The main finding of our study was reduced motor complexity in patients with SAPS. There is yet no clarity on the nature of the association between pain and complexity of motor variability. In experiments with pain inducement, sudden alterations in motor complexity have been observed, suggesting that changes in motor output complexity are the consequence of pain[46]. On the contrary, reduced motor output complexity has been suggested as a cause of functional decline, overuse and pain[1,2,7,8]. To gain further insight into the cause-and-effect relationship and into the potential prognostic value of assessing motor output complexity in SAPS, future studies should assess whether patients with SAPS who have reduced motor output complexity, are less able to develop successful motor strategies and hence more at stake of developing chronic complaints[6,24,47].

In this study we acknowledge the following limitations. First, inherent to the definition of SAPS, the cause of symptoms present in the SAPS-group were not related to observable anatomic derivatives, and thus could have been heterogeneous[15]. Our findings may therefore not be applicable to every individual SAPS-patient. Second, this study was based on a comparison of two separate study-cohorts for which no *a-priori* power analysis was performed. Third, the results of this study are based on measurements performed in a single posture. Future assessments with varying postures may provide more insight into whether a loss of complexity is isolated or systemic. Lastly, due to our measurement set-up there were differences in data-length between the SAPS and control group. As the ApEn-value is sensitive to differences in signal length and the choice of parameters, we corrected for data length in the ApEn analysis and chose parameters in conjunction with the literature[37,38,48].

To conclude, this cross-sectional evaluation of isometric force output signals suggests that patients with SAPS have reduced complexity of isometric force curves than asymptomatic controls, which may indicate more narrow and stereotype use of motor options. In future studies, it should be investigated whether the finding of reduced force (motor) entropy indicates functional impairment and decreased ability to acquire and optimise motor strategies in patients with SAPS[3-6].

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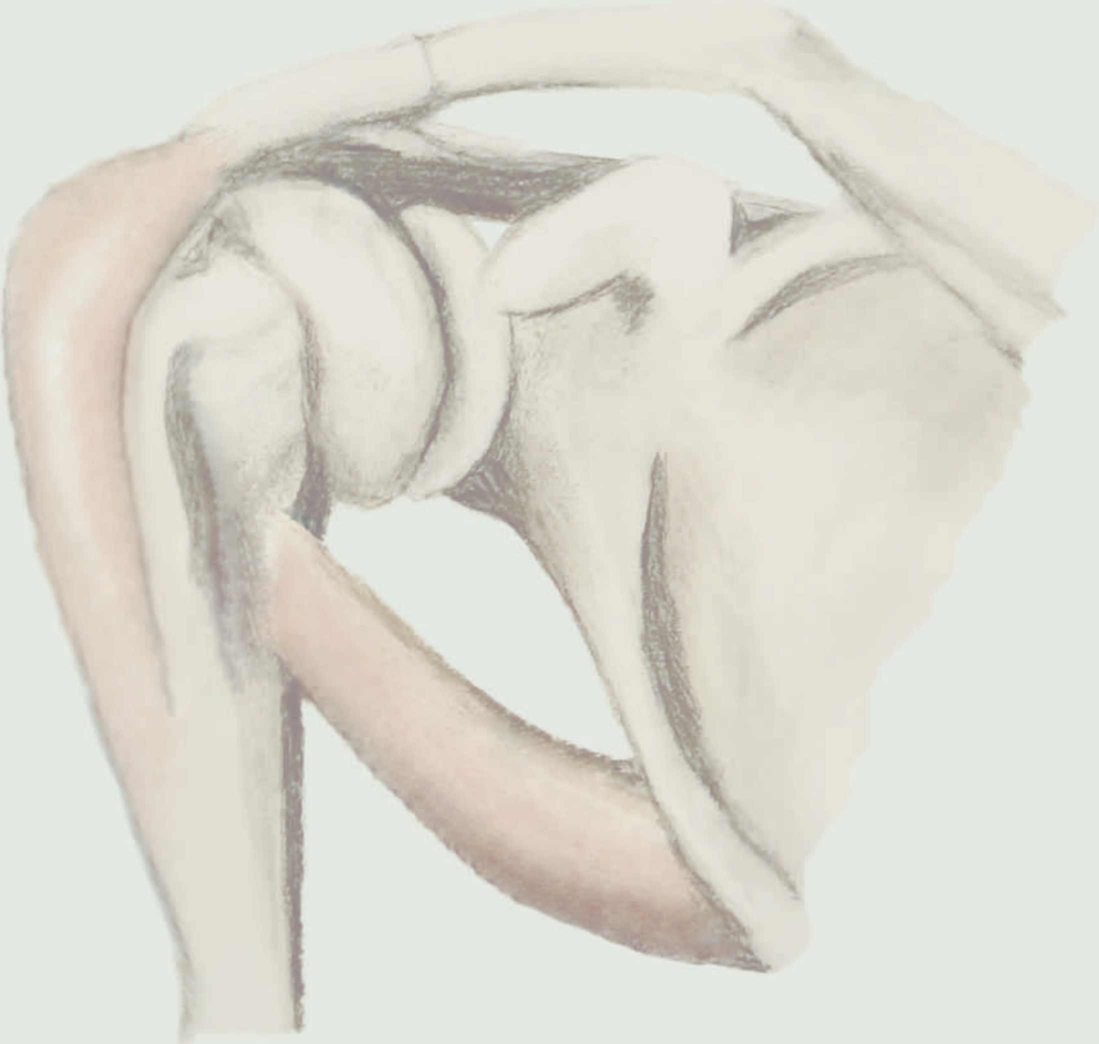

7

The effect of conservative therapies on proprioception in subacromial pain syndrome: a narrative synthesis

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ABSTRACT

Background

Physical exercises targeting proprioception are part of conservative therapy for Subacromial Pain Syndrome (SAPS). However, the effect of such exercises on proprioception itself has not been orderly established, hampering the advancement of treatment protocols and implementation. We summarised the evidence for a loss of proprioception in SAPS and defined the type of interventions that target and improve proprioception in SAPS.

Methods

Two reviewers independently analysed 12/761 articles that evaluated joint position, kinaesthetic or force sense in patients with SAPS.

Results

Patients with SAPS had reduced joint position sense during abduction. There was no evidence for a loss of kinesthetic sense or force sense. Stretching, strengthening and stabilisation exercises improved joint position and kinaesthetic sense in SAPS. Microcurrent electrical stimulation and kinesiotaping did not improve proprioception in SAPS.

Conclusions

The lack of evidence on proprioception in SAPS is striking. We found limited evidence for a loss of joint position sense in the higher ranges of abduction in SAPS. Active training programs including strengthening and stabilisation exercises showed superiority in terms of enhancing proprioception relative to passive methods like kinesiotaping. The results of this narrative synthesis should be used as a base for providing value-based and data-driven treatment solutions to SAPS.

PROSPERO

CRD42017055520

Key words

shoulder pain; position sense; physical therapy; rehabilitation; systematic review.

INTRODUCTION

Chronic shoulder pain is the second most common musculoskeletal disorder in the general population, with prevalence rates ranging between 15% and 22%[1-3]. In approximately 29% to 34% of all patients with chronic shoulder pain a specific anatomical explanation (e.g. acromioclavicular osteoarthritis, calcific tendinitis, or full-thickness rotator cuff tears) is not present, and the condition of these patients is described as Subacromial Pain Syndrome (SAPS)[4,5]. This prevalent condition becomes chronic frequently and the associated pain, sleep disturbance and restrictions in activities of daily living have a substantial impact on an individual's quality of life[6]. Recent studies suggest that surgical treatment provides no significant benefit over non-surgical intervention and while conservative management is effective, more targeted approaches are warranted[4,5,7-9].

A systematic review dating from 2015 showed evidence for a loss of proprioception in SAPS and studies have demonstrated a clinical benefit of exercises targeting proprioception in SAPS[10-12]. Hence, conservative management aimed at improving shoulder proprioception and active joint stabilisation is suggested as a viable targeted treatment approach in SAPS[13-15]. The effect of exercises on proprioception itself has however not been orderly established, which hampers the advancement of treatment protocols and clinical implementation.

We were interested in defining the type of interventions that target proprioception in patients with SAPS and assessing whether these interventions improve proprioception. Because there has been an expansion of research on the loss of proprioception in SAPS since a systematic review in 2015[10], we first re-evaluated the evidence for a loss of proprioception in SAPS[16-19]. Then, we summarised the effectiveness of different types of intervention on proprioception and symptoms in SAPS.

MATERIAL AND METHODS

Protocol and registration

We conducted this review following the published guidelines by the International Committee of Medical Journal Editors (ICMJE) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[20,21]. The protocol was published (PROSPERO: No. CRD42017055520, registered 10/02/2017) prior to conducting the search[22].

Information sources and search strategy

We performed the search with support from an expert librarian using PubMed, Embase, CINAHL, Web of Science, Cochrane Library, CENTRAL, Academic Search Premier, Emcare and ScienceDirect from inception to February 27th, 2019. Search terms included text words and controlled vocabulary i.e. Medical Subheadings (MeSH) and equivalents related to 1) subacromial pain syndrome and 2) proprioception[23]. These components were combined with the operator, "AND" and the search was performed without any limits (**Appendix 1**). We also included relevant articles from the reference lists of included articles and reference lists of systematic reviews on similar topics.

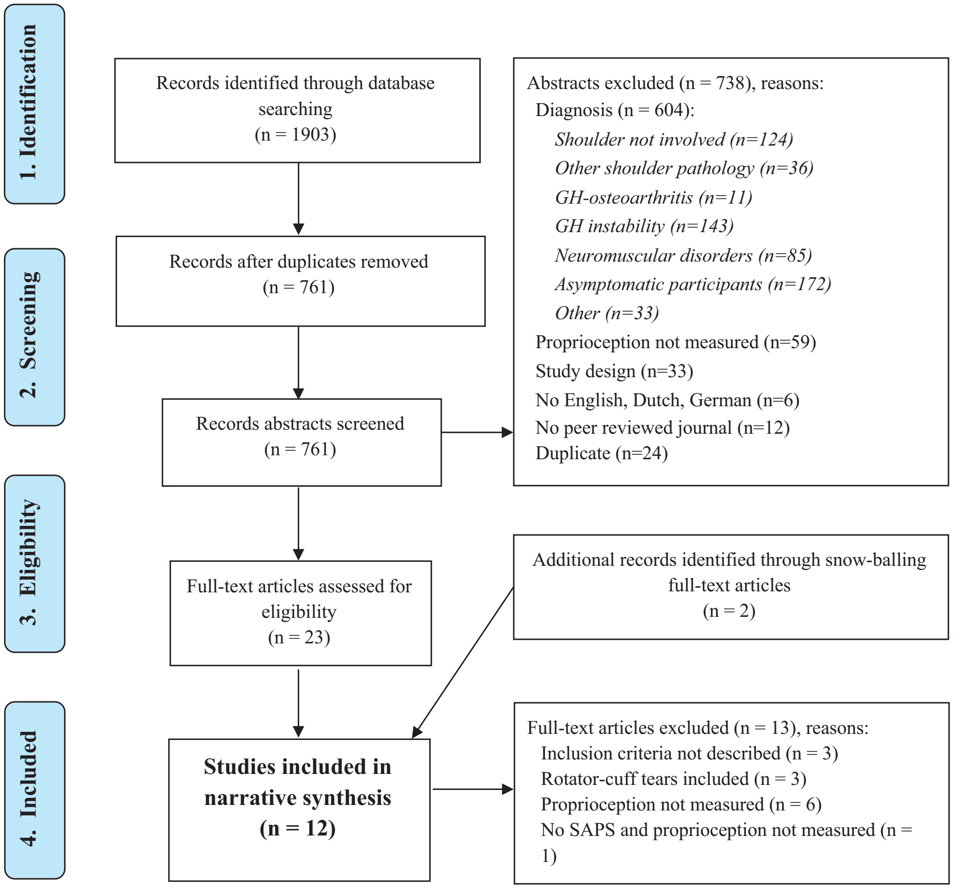

Figure 1 | Flowdiagram

Study selection

We managed search data using a reference manager (EndNote X7.7.1. 2016; Thomson

Reuters). Duplicates were removed and titles and abstracts were individually screened for eligibility by two researchers (C.L.O, MD, H.G., MD). SAPS was defined as shoulder pain that exacerbated by abduction, with at least one positive clinical test for SAPS (e.g. Neer test, Hawkins test, Jobe test)[24]. Articles had to furthermore measure aspects of proprioception, including joint position sense, kinaesthetic sense and force sense. These aspects of proprioception can be measured with good reliability using joint reproduction testing, measurement of the threshold to detection of passive movement and force steadiness testing, repsectively[14-16,22,23]. Exclusion criteria included signs of other shoulder pathology (e.g. acromioclavicular osteoarthritis, massive tears, isolated subscapularis tears, frozen shoulder), primary or secondary glenohumeral osteoarthritis, glenohumeral instability disorder, neuromuscular disorder (e.g. cerebral ischemic attack, muscular dystrophy), no measurement of proprioception, surgical intervention, inappropriate study design (e.g. systematic review, letters to the editor), non-peer reviewed articles in languages other than Dutch, German or English language. We accessed the full-text in cases of uncertainty regarding the eligibility of an article and disagreements were solved by means of discussion with a third reviewer (J.N., MD) until consensus was reached.

Assessment of methodological quality

The full-text of all included articles were assessed for methodological quality for each research question separately. We used the validated Effective Public Health Practice Project (EPHPP) instrument, which scores six components (i.e. selection bias, study design, confounders, blinding, data collection method and withdrawals/drop-outs) on an ordinal scale, i.e. 1) strong, 2) moderate and 3) weak[25,26]. This grading system allows for the assessment of both observational, non-randomised studies as well as interventional, randomised or clinical controlled trials[25]. An additional quality assessment of two components (intervention integrity and assessment of analyses) was performed for studies related to our second research question i.e. interventions targeting proprioception, using the same ordinal scale[25]. We then assigned a rating for overall methodological quality for each study (i.e. 1) strong, 2) moderate or 3) weak global rating[25]. A strong rating was given if there were no weak ratings in any components, moderate if there was one weak rating, and weak if there are two or more weak ratings[25]. Two researchers (C.L.O, H.G.) assessed the quality of the articles independently and disagreements were solved via discussion with a third reviewer (J.N.) and reaching consensus.

Data collection and abstraction

We extracted the following data using a standardised data-abstraction sheet: 1) author, year of publication and country; 2) study design, study populations, demographics (age/gender); 3) intervention, if applicable; 4) duration of follow-up, if applicable;

5) measurement method of joint position sense, kinaesthetic sense and force sense and; 6) other reported outcome measures: e.g. clinical symptoms, patient reported outcome measures, if applicable. Due to the heterogeneity of studies in terms of the outcome measures and measurement methods, statistical pooling was not considered feasible or appropriate and thus, our conclusions were based on a narrative synthesis of study results and methodological quality.

RESULTS

The search yielded 761 unique articles. After screening for eligibility, 738 studies were excluded, leaving 23 articles of which the full-text articles were screened for eligibility (flow diagram, **Figure 1**). Two additional articles were retrieved from the reference lists of included studies. Thirteen full-text articles were excluded, resulting in 12 articles for the final analysis (**Figure 1**)[16-18,27-35]. One study performed both a comparison of proprioception between patients with SAPS and controls and assessed the efficacy of an intervention in SAPS, and was therefore used for both study questions (**Table 1**)[36].

Loss of proprioception in SAPS

Joint Position Sense

Three studies compared Joint Position Sense between a total of 73 patients with SAPS and 92 controls (**Table 1**)[16,18,34]. Joint Position Sense was tested using Joint Position Reproduction tasks (JPR) in scapular plane abduction (scaption)[16] and axial humerus rotation[18,34]. Active JPR testing in scaption showed that patients with SAPS have a higher Degree of Mismatch (MM_{degree}) compared to controls at 100°, indicating reduced Joint Position Sense, which was not present during testing in 40° scaption (**Table 3**)[16]. During the testing in 100° scaption, patients experienced significantly more pain (3.4 cm on 10 cm Visual Analogue Scale) compared to testing in 40° scaption (1.8 cm on 10 cm Visual Analogue Scale), which may be associated with the observed reduction in Joint Position Sense[16]. The risk of bias in this study was low, and a reliability assessment showed that measurements were performed with good reliability during testing in 40° and moderate reliability during testing in 100° (**Table 2**)[16]. During both passive and active axial humerus rotation testing neither of the two studies found a difference in MM_{degree} between patients with SAPS and controls[18,34]. Thus, Joint Position Sense in patients with SAPS may be affected during high scaption[16], but seems to be preserved during axial humerus rotation[18,34]. It is yet unclear whether declined Joint Position Sense during high scaption is influenced by associated pain (or vice versa)[16].

Table 1 | Study characteristics

Author (year)	Country	1st question (case-control comparison)	2nd question (interventional study)	Populations	Selectioncriteria SAPS	Age±SD	M/F
Anderson et al. (2011)[16]	Australia	X		26 patients	- Positive Neer test. - Pain >3months, >3/10 on VAS, exacerbated by abduction or external rotation.	56±11	15/11
				30 matched controls		56±4.5	17/13
Atya (2012)[27]	Egypt		X	19 patients with intervention	- Symptoms >3 months. - Shoulder pain >5/10 VAS. - 2/4 positive tests: e.g. Neer test, Hawkins test, painful arc. - Pain during 1/4 resistance test.	49±6	10/9
				21 patients without intervention		49±3.3	9/12
Bandholm et al. (2006)[28]	Denmark	X		9 patients	- Recurrent unilateral shoulder pain in dominant shoulder > 2 months. - Positive painful arc, Hawkins test.	28±5.3	NA
				9 matched asymptomatic controls		28±4.2	NA
Baskurt et al. (2011)[29]	Turkey		X	20 patients with intervention	- Positive Neer, Hawkins, and Jobe test. - Consistent radio- and ultrasonography.	52±8.4	13/27[e]
				20 patients without intervention		51±12	13/27[e]
Camargo et al. (2009)[31]	Brazil	X		27 patients	- At least 3 positive tests: e.g. Neer, Hawkins, Jobe test. - Consistent ultrasonography.	33±9.9	18/9
				23 matched asymptomatic controls		32±9.0	15/8
De Oliviera (2019)[35]	Canada		X	22 patients	- Painful arc - Positive Neer or Hawkins test - Resistence tests painful (e.g. empty can test).	29±6.7	14-sep
Gomes et al. (2019)[34]	Brazil	X		32 patients	- Unliateral pain during abduction, Hawkins, Neer and Drop Arm test.	33±6.9	22/10
				32 matched asymptomatic controls		33±6.9	22/10
Haik et al. (2013)[18]	Brazil	X		15 patients (ALW)	- At least 3 positive tests: e.g. Neer, Hawkins, Jobe test. - Consistent ultrasonography.	36±5.8	0/15
				15 matched asymptomatic controls (ALW)		34±5.5	0/15
				15 matched asymptomatic controls (no ALW)		33±6.2	0/15

Table 1 | Continued

Author (year)	Country	1st question (case-control comparison)	2nd question (interventional study)	Populations	Selectioncriteria SAPS	Age±SD	M/F
Jerosch and Wüstner (2002)[33]	Germany		X	32 patients	- Symptoms >3 months. - Positive Jobe, painful arc, Neer test and pain during palpation of tuberculum majus. - Consistent radio- and ultrasonography.	37 (range 25-56)	NA
Keenan et al. (2017)[32]	USA	X	X	10 patients with intervention	- Pain ≥ 2 weeks. - Positive Neer, Hawkins and Painful Arc Test.	25±5.1	5/5
				10 patients without intervention		24±3.2	8/2
				10 asymptomatic controls		26±3.8	3/7
Maenhout et al. (2012)[17]	Belgium	X		36 patients	- Unilateral pain ≥ 3 months (≥3 VAS). - Painful arc, 2/3 positive tests (Hawkins, Jobe, Neer), 2/4 resistance tests painful (e.g. full can test). - Palpation pain at SSP/ISP insertion. - Consistent ultrasonography or MRI.	43±14	14/22
				30 matched asymptomatic controls		41±13	15/15
Zanca et al. (2010)[30]	Brazil	X		14 patients (ALW)	- At least three positive test: e.g. Neer, Hawkins, Jobe test.	37±5.2	0/14
				15 matched asymptomatic controls (ALW)		36±5.5	0/15

1st study question: Is there a loss of proprioception in paitnets with Subacromial Pain Syndrome (SAPS)?
2nd study question: What is the effect of conservative interventions on proprioception in SAPS?
ALW, Assembly Line Workers; NA, not available in original article.[a] Originally referred to as chronic rotator cuff pathology (CRCP). [b] Originally referred to as subacromial impingement, subacromial impingement syndrome, impingement syndrome, shoulder impingement syndrome. [c]Originally referred to as rotator cuff tendinopathy. [d] Originally referred to as unspecific shoulder pain. [e] Not described per group.

Table 2| Quality assessment of included full-text articles

Author (year)	Selection bias	Study design	Confounders	Data collection method	Blinding	Withdrawals and dropout	Intervention integrity	Assessment of analyses	Global rating 1st study question	Global rating 2nd study question
Anderson et al. (2011)[16]	2	2	1	2	2	-	-	-	Strong	NA
Atya et al. (2012)[27]	2	1	2	3	1	3	2	1	NA	Weak
Bandholm et al. (2006)[28]	2	2	1	3	2	-	-	-	Moderate	NA
Baskurt et al. (2011)[29]	2	1	2	3	3	1	2	1	Moderate	Weak
Camargo et al. (2009)[31]	2	2	1	2	2	-	-	-	Strong	NA
De Oliviera et al. (2019)[35]	2	2	1	2	2	1	2	1	NA	Strong
Gomes et al. (2019)[34]	3	2	1	2	2	-	-	-	Moderate	NA
Haik et al. (2013)[18]	3	2	1	2	2	-	-	-	Moderate	NA
Jerosch and Wüstner (2002)[33]	2	2	1	2	2	3	2	1	Moderate	Moderate
Keenan et al. (2017)[32]	2	1	1	2	2	1	2	1	Strong	Strong
Maenhout et al. (2012)[17]	2	2	1	2	2	-	-	-	Strong	NA
Zanca et al. (2010)[30]	3	2	1	3	2	-	-	-	Weak	NA

1st study question: Is there a loss of proprioception in paitnets with Subacromial Pain Syndrome (SAPS)?
2nd study question: What is the effect of conservative interventions on proprioception in SAPS?
Assessment of methodological quality using the validated Effective Public Health Practice Project (EPHPP) tool (Deeks et al., 2003; Thomas et al., 2004)[25,26]. Each component was scored as strong (1), moderate (2) or weak (3). The global rating of an article is strong if there are no components rated as weak, moderate if there is one weak rating and weak if there are two or more weak ratings.

Kinaesthetic sense

Using the Threshold to Detection of Passive Motion (TTDPM) testing method, the two case-control comparisons, which were of moderate[34] and strong[32] methodological quality (**Table 2**), showed no differences in MM_{degree} between patients with SAPS and controls in adduction and 60° scaption, thus Kinaesthetic Sense seems preserved in patients with SAPS (**Table 3**).

Force sense

Only one of four studies found a deficit in Force Sense[28], and this was only in one of three tasks (concentric contraction, **Table 3**), which suggests that Force Sense is not affected in patients with SAPS[17,28,30,31].

Table 3 | Summary of results – loss of proprioception in SAPS

Author (year)	JPS	Kinaesthetic sense	Force sense	Device	Outcome measure	Task	Statistic	SAPS ± SD	Controls ± SD	Proprioception reduced in SAPS?	p-value
Anderson et al. (2011)[16]	X			Optic 3D motion tracker	Active JPR	Scaption 40°	MM_{degree}	4.2 ± 3.1	3.4 ± 1.8		0.289
						Scaption 100°	MM_{degree}	5.2 ± 3.7	2.8 ± 1.7	X	**0.003**
Gomes et al. (2019)[34]	X	X		Dynamometer	Active and passive JPR	IR from 50° to 0°, in 60° scaption	$MM_{\text{degree (passive)}}$	3.8 ± 3.6	3.8 ± 5.1		0.75
							$MM_{\text{degree (active)}}$	2.6 ± 2.1	2.8 ± 1.8		0.93
						ER from 0° to 50°, in 60° scaption	$MM_{\text{degree (passive)}}$	7.9 ± 7.3	8.1 ± 7.7		0.88
							$MM_{\text{degree (active)}}$	7.7 ± 7.3	9.5 ± 7.3		0.96
					TTDPM	IR in 60° scaption	MM_{degree}	2.5 ± 2.8	2.1 ± 2.0		0.38
						ER in 60° scaption	MM_{degree}	2.8 ± 3.4	2.1 ± 3.2		0.27
Haik et al. (2013)[18]	X			Dynamometer	Active and passive JPR	IR from 90° to 30°, in 90° scaption	$MM_{\text{degree (passive)}}$[a]	8.4 ± 4.9	8.4 ± 5.7[b]		>0.05
							$MM_{\text{degree (active)}}$[a]	9.9 ± 7.4	13 ± 8.6[b]		>0.05
						ER from 0° to 75°, in 90° scaption	$MM_{\text{degree (passive)}}$[a]	9.8 ± 6.5	9.9 ± 6.1[b]		>0.05
							$MM_{\text{degree (active)}}$[a]	15 ± 11	14 ± 11[b]		>0.05
Keenan et al. (2017)[32]		X		Dynamometer	TTDPM	IR	MM_{degree}	2.9 ± 1.5[c]	3.9 ± 4.9		0.315
						ER	MM_{degree}	2.0 ± 1.0[c]	3.7 ± 5.1		0.436
Bandholm et al. (2006)[28]			X	Dynamometer	Force steadiness	Abduction 90°	SD	NA	NA		>0.05
							CV	NA	NA		>0.05
						Abduction from 120° to 30°	SD	NA	NA		>0.05
							CV	NA	NA		>0.05
						Abduction from 30° to 120°	SD	3.6 ± 0.86	2.7 ± 1.1	X	**0.05**
							CV	6.7 ± 2.3	4.5 ± 1.3	X	**0.03**
Camargo et al. (2009)[31]			X	Dynamometer	Force steadiness	Scaption 80°	SD	1.6 ± 0.68[d]	1.4 ± 0.40[d]		>0.05
							CV	4.3 ± 1.4[d]	4.1 ± 1.2[d]		>0.05

Table 3 | Continued

Author (year)	JPS	Kinaesthetic sense	Force sense	Device	Outcome measure	Task	Statistic	SAPS ± SD	Controls ± SD	Proprioception reduced in SAPS?	p-value
Maenhout et al. (2012)[17]			X	Dynamometer	Force reproduction	IR	MM_{degree}	15	13		0.17[e]
						ER	MM_{degree}	21	15		
					Force steadiness	IR	CV	6.4	10		0.478[e]
						ER	CV	12	11		
Zanca et al. (2010)[30]			X	Dynamometer	Force steadiness	IR at 45° and 75° ER in 90° scaption	SD	NA	NA		>0.05
							CV	NA	NA		>0.05
						ER at 45° and 75° ER in 90° scaption	SD	NA	NA		>0.05
							CV	NA	NA		>0.05

JPS, Joint Position Sense; JPR, Joint Position Reproduction; TTDPM, Threshold to Detection of Passive Motion; IR, Internal Rotation; ER, External Rotation; $MM_{degree,}$ Degree of Mismatch between target and reproduced position (JPR) or between start of motion and perception of motion (TTDPM); SD, standard deviation; CV, Coefficient of Variation, i.e. (SD/mean force) * 100; NA, not available in original article.

[a] Standard errors converted to standard deviations following [$SD = SE \times \sqrt{n}$]. [b] Data from one of both control-groups presented (assymbly line workers without SAPS). [c] Data from one of both SAPS-groups presented (flexible foil group). [d] Data from one of both SAPS-groups presented (kinesiotape). [e] Values averaged over dominant and nondominant sides, for SD with formula [$\sqrt{((SD_1^2+SD_2^2)/2)}$]. [f] Test for group-difference in MM_{degree}, not taking task direction (IR/ER) into account

The effect of conservative interventions on proprioception in SAPS

There were five studies that assessed the effect of an active (e.g. strengthening exercises)[29,33] or passive (e.g. kinesiotape or microcurrent electrical stimulation)[27,32,35] training program on proprioception in a total of 103 patients with SAPS (10 to 32 per study)[27,29,32,35,36].

Active training programs

The 6-weeks training program of Baskurt et al. consisted of standardised flexibility exercises, strengthening, Codman exercises and scapular stabilisation exercises[29]. Flexibility exercises focused on anterior, posterior and inferior capsule stretching, next to forward flexion, abduction and internal rotation stretching. The subscapularis, infraspinatus, supraspinatus, and anterior part of deltoid and posterior part of deltoid were strengthened. Scapular stabilisation exercises consisted of scapular proprioceptive neuromuscular facilitation (PNF) exercises, scapular clock exercise, standing weight shift, double arm balancing, scapular depression, wall push up, wall slide exercises[29].

The 4-weeks training program of Jerosch and Wüstner consisted of standardised sensorimotor training for the glenohumeral joint, using proprioceptive exercise tools (body-blade, BOING), next to Tai Chi and aquatic gymnastic[33].

Both studies showed that the active training programs improved Joint Position Sense (and Kinaesthetic Sense[33]) with a moderate[33] and large[29] risk of bias (**Table 4**). These studies also showed significant reduced pain (assessed with the Visual Analogue Scale[29], Constant Score[33] and University of California Los Angeles score[33]) and reduced impairment or disability (assessed with the Constant Score[33], Western Ontario Rotator Cuff index[29] and University of California Los Angeles score[33]) after intervention.

Passive training programs

No improvement in proprioception was observed using micro-current electrical stimulation, while symptoms did improve (weak methodological quality)[27]. Both studies assessing the effect of kinesiotaping on proprioception, used the taping methods suggested by Kase et al. with slight differences[37]. Next to a Y-strip covering the deltoid and a I-strip horizontally crossing the glenohumeral joint, De Oliveira applied a I-strip crossing the glenohumeral joint vertically[35], while Keenan et al.[32] applied a Y-strip from the insertion to the origin of the supraspinatus. Both studies showed no effect of kinesiotaping on proprioception (both strong methodological quality)[32,35]. The effect of these taping methods on symptoms was not assessed[32,35]. Altogether, passive methods including micro-current electrical stimulation[27] or kinesiotaping[32,35] had no effect on proprioception.

Table 4 | Summary of results – effect of intervention

Author (year)	JPS	Kinaesthetic sense	Outcome measure	Follow up	Device	Task	Intervention	MM$_{degree}$ at baseline	MM$_{degree}$ at follow-up	Sensory feedback improved?	p-value
Atya (2012)[27]	X		Active JPR	6 weeks	Dynamometer	IR/ER in 90° scaption, averaged	Microcurrent electrical stimulation	11 (SD 0.65)	10 (SD 1.3)		0.067
							Placebo microcurrent stimulation	11 (SD 0.95)	10 (SD 1.1)		0.231
Baskurt et al. (2011)[29]	X		Passive JPR	6 weeks	Inclinometer	IR in 90° abduction	Stretching, strengthening & scapular stabilisation	4.5 (SD 2.9)	1.5 (SD 1.3)	X	**<0.05**
						ER in 90° abduction		4.7 (SD 2.6)	2.1 (SD 1.5)	X	**<0.05**
						IR in 90° abduction	Stretching, strengthening	4.6 (SD 2.8)	3.3 (SD 1.4)	X	**<0.05**
						ER in 90° abduction		4.3 (SD 2.2)	3.3 (SD 1.4)	X	**<0.05**
De Oliviera (2019)[35]	X		Active JPR	Immediate	Inertial measurement unit sensor	Anteversion (45°-65°)	Kinesiotape	3.48 (SD 2.2)	3.0 (SD 2.6)		0.427
						Anteversion (80°-100°)		2.9 (SD 2.2)	3.3 (SD 2.1)		0.448
						Abduction (45°-65°)		2.7 (SD 2.4)	3.2 (SD 3.2)		0.497
						Abduction (80°-100°)		2.0 (SD 1.3)	2.8 (SD 1.8)		0.140
Jerosch and Wüstner (2002)[33]	X		Active JPR	4 weeks	Optic 3D motion tracker	Anteversion (50°)	Proprioceptive exercises, glenohumeral stabilisation, tai-chi, aqua-gymnastics	8.4^{a}	7.0^{a}	X	**<0.05**
						Anteversion (100°)		5.4^{a}	4.9^{a}		>0.05
						Abduction (50°)		7.1^{a}	5.9^{a}		>0.05
						Abduction (100°)		5.2^{a}	3.6^{a}	X	**<0.05**
						IR in 90° abduction		5^{a}	4.6^{a}		>0.05
						ER in 90° abduction		4.2^{a}	4^{a}		>0.05
		X	TTDPM	4 weeks	Dynamometer	Abduction	Proprioceptive exercises, glenohumeral stabilisation, tai-chi, aqua-gymnastics	12^{a}	6.4^{a}	X	**<0.05**
						Adduction		9.8^{a}	5.6^{a}	X	**<0.05**
						IR		12^{a}	9.2^{a}	X	**<0.05**
						ER		12^{a}	8.9^{a}	X	**<0.05**

Table 4 | Continued

Author (year)	JPS	Kinaesthetic sense	Outcome measure	Follow up	Device	Task	Intervention	MM_{degree} at baseline	MM_{degree} at follow-up	Sensory feedback improved?	p-value
Keenan et al. (2017)[32]		X	TTDPM	Immediate	Dynamometer	IR	Kinesiotape in SAPS	2.9 (SD 1.5)	2.2 (SD 1.9)		0.333
						ER		2.0 (SD 1.0)	1.9 (SD 1.1)		0.444
						IR	Placebo Tape in SAPS	1.3 (SD 0.84)	1.4 (SD 0.81)		0.721
						ER		3.0 (SD 2.7)	2.1 (SD 1.0)		0.333
						IR	Kinesiotape in controls	3.9 (SD 4.9)	4.4 (SD 6.0)		0.767
						ER		3.7 (SD 5.1)	3.9 (SD 4.3)		0.721

JPS, Joint Position Sense; JPR, Joint Position Reproduction; TTDPM, Treshold to Detection of Passive Motion; IR, Internal Rotation; ER, External Rotation; SAPS, subacromial pain syndrome; $MM_{degree,}$ Degree of Mismatch between target and reproduced position (JPR) or between start of motion and perception of motion (TTDPM).

[a] Interpreted from figure 1 in the concerning article(Machner et al., 2003). [b] Dispersion measures not described in original article.

DISCUSSION

We included twelve studies in a narrative analysis on the loss of proprioception in SAPS and the effect of interventions targeting proprioception in SAPS. Although two components of proprioception (kinaesthetic sense and force sense) seem to remain intact in SAPS, joint position sense in higher angles of scapular plane elevation may be compromised. Passive therapeutic strategies, such as kinesiotape, did not yield an improvement in proprioception, whereas active training with strengthening and stabilisation exercises improved proprioception in SAPS.

Loss of proprioception in SAPS

We found no evidence for a loss of kinaesthetic or force sense in patients with SAPS[17,28,30,31,36]. The well-powered, strong methodological quality study by Anderson and Wee[16] suggests that patients with SAPS do have a loss of joint position sense manifesting at higher scapular plane elevation angles, but not during axial humerus rotation.

It has been suggested that impaired joint position sense present in patients with SAPS during abduction, but not during axial humerus rotation, means that glenohumeral proprioception is preserved and pain is the explanation for observed deficits during abduction[34]. This explanation is contradicted by two experimental studies that showed reduced joint position sense and increased asymmetry of scapular kinematics in response to pain relief with subacromial anaesthetics in patients with SAPS[38,39]. We therefore suggest an alternative line of reasoning. Electromyography studies have shown that patients with SAPS exhibit reduced co-contraction of shoulder girdle muscles during abduction, which is also related to excessive upward migration of the humerus during this movement[40-42]. Subsequent reduced muscle tonus of antagonists (e.g. infraspinatus and teres major) results in reduced excitability of muscle spindles and this may explain impaired joint position sense in patients with SAPS during abduction[43].

Effect of interventions targeting proprioception

Based on consistent findings in two studies of moderate and weak methodological quality, it may be suggested that proprioception (joint position sense[29,33] and kinaesthetic sense[33]) in SAPS can be improved with exercise therapy aimed at enhancing shoulder stability[29,33] and strength[29], either or not also aimed at enhancing range of motion[29]. Additional well designed studies are warranted to confirm these findings.

Previous studies have suggested impaired active joint stabilisation as a causal factor in SAPS [40-42] and the goal of exercises targeting proprioception would be to enhance joint stability[40-42,44,45]. We suggest that effective exercises may accomplish enhanced joint stability in two ways. First, exercises may result in increased co-contraction of agonists and antagonists at the glenohumeral and scapulothoracal joint, which directly results in increased active stabilisation[40-42]. Second, consequent increased tonus of antagonistic muscles may lower the excitation threshold of muscle spindles, enhancing joint position sense, and thus active joint stabilisation[43]. Considering also that muscle spindle information is the main source of input for joint position sense, this would explain why passive strategies such as kinesiotape are less effective in improving joint position sense in patients with SAPS[27,35,36,46].

This study had a number of limitations. First, we found only few relevant articles on the topic and therefore our conclusions should only serve as guidance for future studies and not for direct clinical interpretation. Second, due to inconsistency in diagnostic criteria for SAPS, variability in population characteristics may have occurred[47]. In order to enhance the generalisability of our findings, we handled strict inclusion criteria. Third, sample sizes were low in five studies (≤20 participants per group). Four of these studies had negative results, and it cannot be made sure that there indeed was no effect, or that negative results may be explained by underpowering. Nevertheless, the findings of studies with low power were consistent with other higher powered studies and therefore we do not think that underpowering affected our conclusions. Fourth, regarding our second study question, the studies that showed a positive effect of active training programs on proprioception did not include control groups without therapy and thereby did not account for a bias of time or natural regression to the mean[29,33]. In one of these, the follow-up duration was 4 weeks, while the pre-existent duration of complaints was minimal 3 months (mean 6.2 months)[37]. Considering this pre-existent duration of complaints it seems unlikely that the observed improvement in proprioception would have also occurred without the intervention.

In patients with SAPS, it has been shown that surgical treatment provides no significant benefit over non-surgical intervention and physical therapy is preferable[7-9]. We believe that physical therapy programs can be improved with targeted approaches[7]. Generally, the goal of these programs is to enhance proprioception and active joint stabilisation[40-42] through stability[29,33] and strength exercises[29]. It has been suggested that increasing cocontraction of the arm adductors (teres major and latissimus dorsi) is a viable treatment option for patients with SAPS to enhance stability[41,48,49]. In future clinical assessments, it may be assessed whether enhancing proprioception and stability in patients with SAPS, for instance by training adductor co-contraction is effective. To gain insight into causal relationships, EMG monitoring, kinematic assessments to monitor excessive upward migration of the humerus during abduction and clinical evaluations may be used[50-52].

CONCLUSION

For the prevalent condition SAPS, physical treatment is the treatment of choice, with exercise therapy focusing on proprioception and stability being cornerstone[4,5,7-9]. In this narrative review we found a striking lack of evidence on proprioception in patients with SAPS. There was limited evidence for a reduction of joint position sense during arm elevation (not during axial humerus rotation) in patients with SAPS[16]. No evidence was found for a loss of kinaesthetic sense or force sense in patients with SAPS[17,28,30,31,33,36]. It showed that active treatment programs targeting proprioception, such as stability[29,33] and strength exercises [29], enhance joint position and kinaesthetic sense, while passive strategies, such as kinesiotaping, do not improve proprioception in patients with SAPS[27,35,36]. Providing value-based and data driven solutions to common shoulder problems such as SAPS should be the goal of practicing orthopaedic surgeons, general practitioners and physical therapists. The findings of this review may serve as a base for further studies into the development of targeted conservative treatment approaches in SAPS.

DISCLOSURE OF INTEREST

The authors report no conflict of interest.

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SUPPLEMENTARY MATERIAL | SEARCH STRATEGY

The search strategy was built up from two components, i.e. one component describing sensory feedback and one component describing SAPS, combined with “AND”. This search was altered to match the search engines of several databases:

Component 1 *Subacromial Pain Syndrome*	(“Shoulder Impingement Syndrome”[Mesh] OR “Subacromial Impingement Syndrome”[tw] OR “Subacromial pain syndrome”[tw] OR “Subacromial Impingement”[tw] OR “Subacromial pain”[tw] OR “Sub-acromial Impingement”[tw] OR “Sub-acromial pain”[tw] OR “SAIS”[tw] OR “SAPS”[tw] OR “SIS”[tw] OR “shoulder pain”[tw] OR ((“Rotator Cuff”[mesh] OR “rotator cuff”[tw]) AND (“Tendinopathy”[mesh] OR “tendinopathy”[tw] OR tendinopath*[tw] OR tendin*[tw] OR partial tear*[tw] OR degenerat*[tw])) OR “tendinitis calcarea”[tw] OR calcific tend*[tw] OR calcified tend*[tw] OR “supraspinatus tendinopathy”[tw] OR “subacromial bursitis”[tw] OR ((“Bursitis”[mesh] OR “bursitis”[tw]) AND (subacromial*[tw] OR subdeltoid*[tw])) OR “subacromial bursitis”[tw] OR “tendinosis calcarea”[tw] OR “biceps tendinitis”[tw] OR “shoulder injury”[tw] OR “shoulder injuries”[tw] OR “Shoulder Joint/injuries”[mesh] OR “chronic rotator cuff pathology”[tw] OR “Rotator Cuff Injuries”[Mesh] OR “rotator cuff injury”[tw] OR “rotator cuff injuries”[tw] OR “rotator cuff pain”[tw] OR “rotator cuff disease”[tw] OR “rotator cuff diseases”[tw])
Component 2 *Sensory feedback*	(“Proprioception”[Mesh] OR propriocep*[tw] OR “joint sense”[tw] OR “position sense”[tw] OR kinesthe*[tw] OR kinaesthe*[tw] OR “Postural Balance”[tw] OR “Position Senses”[tw] OR “Sense of Position”[tw] OR “Sensorimotor alteration”[tw] OR “Sensorimotor factor”[tw] OR “Sensorimotor alterations”[tw] OR “Sensorimotor factors”[tw] OR “neuromuscular control”[tw] OR “sensorimotor control”[tw] OR “sense of effort”[tw] OR “sense of balance”[tw] OR “sense of tension”[tw] OR “sense of resistance”[tw] OR “sense of strength”[tw] OR “joint position sense”[tw] OR “movement sense”[tw] OR “sensory motor control”[tw] OR “time-to-peak torque”[tw] OR “force sensation”[tw] OR “sensory-motor control”[tw] OR “force sense”[tw] OR “force steadiness”[tw] OR “torque steadiness”[tw] OR “force reproduction”[tw] OR “joint position reproduction”[tw] OR (“joint position”[tw] AND “reproduction”[tw]) OR “Treshold to detect passive movement”[tw] OR (threshold*[tw] AND detect*[tw] AND “passive movement”[tw]))
Combined search strategy *(component 1+2)*	(((“Shoulder Impingement Syndrome”[Mesh] OR “Subacromial Impingement Syndrome”[tw] OR “Subacromial pain syndrome”[tw] OR “Subacromial Impingement”[tw] OR “Subacromial pain”[tw] OR “Sub-acromial Impingement”[tw] OR “Sub-acromial pain”[tw] OR “SAIS”[tw] OR “SAPS”[tw] OR “SIS”[tw] OR “shoulder pain”[tw] OR ((“Rotator Cuff”[mesh] OR “rotator cuff”[tw]) AND (“Tendinopathy”[mesh] OR “tendinopathy”[tw] OR tendinopath*[tw] OR tendin*[tw] OR partial tear*[tw] OR degenerat*[tw])) OR “tendinitis calcarea”[tw] OR calcific tend*[tw] OR calcified tend*[tw] OR “supraspinatus tendinopathy”[tw] OR “subacromial bursitis”[tw] OR ((“Bursitis”[mesh] OR “bursitis”[tw]) AND (subacromial*[tw] OR subdeltoid*[tw])) OR “subacromial bursitis”[tw] OR “tendinosis calcarea”[tw] OR “biceps tendinitis”[tw] OR “shoulder injury”[tw] OR “shoulder injuries”[tw] OR “Shoulder Joint/injuries”[mesh] OR “chronic rotator cuff pathology”[tw] OR “Rotator Cuff Injuries”[Mesh] OR “rotator cuff injury”[tw] OR “rotator cuff injuries”[tw] OR “rotator cuff pain”[tw] OR “rotator cuff disease”[tw] OR “rotator cuff diseases”[tw]) AND (“Proprioception”[Mesh] OR propriocep*[tw] OR “joint sense”[tw] OR “position sense”[tw] OR kinesthe*[tw] OR kinaesthe*[tw] OR “Postural Balance”[tw] OR “Position Senses”[tw] OR “Sense of Position”[tw] OR “Sensorimotor alteration”[tw] OR “Sensorimotor factor”[tw] OR “Sensorimotor alterations”[tw] OR “Sensorimotor factors”[tw] OR “neuromuscular control”[tw] OR “sensorimotor control”[tw] OR “sense of effort”[tw] OR “sense of balance”[tw] OR “sense of tension”[tw] OR “sense of resistance”[tw] OR “sense of strength”[tw] OR “joint position sense”[tw] OR “movement sense”[tw] OR “sensory motor control”[tw] OR “time-to-peak torque”[tw] OR “force sensation”[tw] OR “sensory-motor control”[tw] OR “force sense”[tw] OR “force steadiness”[tw] OR “torque steadiness”[tw] OR “force reproduction”[tw] OR “joint position reproduction”[tw] OR (“joint position”[tw] AND “reproduction”[tw]) OR “Treshold to detect passive movement”[tw] OR (threshold*[tw] AND detect*[tw] AND “passive movement”[tw]))) OR ((“Shoulder”[majr] OR “Shoulder Joint”[majr] OR Shoulder*[ti]) AND (“Proprioception”[majr] OR propriocep*[ti] OR “joint sense”[ti] OR “position sense”[ti] OR kinesthe*[ti] OR kinaesthe*[ti] OR “Postural Balance”[ti] OR “Position Senses”[ti] OR “Sense of Position”[ti] OR “Sensorimotor alteration”[ti] OR “Sensorimotor factor”[ti] OR “Sensorimotor alterations”[ti] OR “Sensorimotor factors”[ti] OR “neuromuscular control”[ti] OR “sensorimotor control”[ti] OR “sense of effort”[ti] OR “sense of balance”[ti] OR “sense of tension”[ti] OR “sense of resistance”[ti] OR “sense of strength”[ti] OR “joint position sense”[ti] OR “movement sense”[ti] OR “sensory motor control”[ti] OR “time-to-peak torque”[ti] OR “force sensation”[ti] OR “sensory-motor control”[ti] OR “force sense”[tw] OR “force steadiness”[tw] OR “torque steadiness”[tw] OR “force reproduction”[tw] OR “joint position reproduction”[tw] OR (“joint position”[tw] AND “reproduction”[tw]) OR “Treshold to detect passive movement”[tw] OR (threshold*[tw] AND detect*[tw] AND “passive movement”[tw]))))

8

Reduced psychosocial functioning in Subacromial Pain Syndrome is associated with persistence of complaints after 4 years.

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ABSTRACT

Background

Patients with Subacromial Pain Syndrome (SAPS) frequently present with co-existing psychosocial problems, however, whether this also associates with long-term outcome is currently unknown. We assessed whether psychosocial functioning in patients with SAPS is associated with persistence of complaints after 4 years of routine care.

Methods

In a longitudinal study, 34 patients with SAPS were selected after clinical and radiological evaluation and assessed at baseline and after 4 years. For the assessment of psychosocial functioning, the RAND-36 domains of social functioning, role limitations due to emotional problems, mental health, vitality and general health were evaluated. Complaints persistence at follow-up was assessed by (1) an anchor question (reduced, persistent or increased symptoms), (2) change in pain (change in visual analog scale), and (3) change in quality of life (change in Western Ontario Rotator Cuff index score).

Results

Lower baseline mental health (odds ratio [OR] 0.92, 95% CI: 0.85 – 0.98, p=0.013), vitality (OR 0.90, 95% CI: 0.83 – 0.98, p=0.011), and general health (OR 0.93, 95% CI: 0.88 – 0.98, p=0.009) were associated with persistent complaints as reported by the anchor question, change in visual analog scale score, and change in Western Ontario Rotator Cuff index score.

Conclusions

Evaluating psychosocial functioning parallel to physical complaints is currently not standard procedure in the treatment of SAPS. In this study, we showed that factors related to psychosocial functioning are associated with long-term persistence of complaints in SAPS. Future studies may investigate whether a multimodal treatment with assessment of psychosocial functioning may facilitate pain relief and recovery in SAPS.

INTRODUCTION

Shoulder pain affects 70% of the general population at some point in life[1]. Most frequently, shoulder pain is attributed to irritation of subacromial tissues and is accordingly called subacromial pain (or impingement) syndrome[2]. Subacromial Pain Syndrome (SAPS) is associated with significant individual and socioeconomic consequences as it compromises the ability to perform daily activities owing to related pain and disability[1-6]. Current treatments focus primarily on symptom relief of the shoulder. Such treatments include physical therapy to improve neuromuscular control and subacromial clearance, as well as the use of subacromial corticosteroid injections to reduce subacromial inflammation. Failure to respond to these usually reliable treatments suggest a nonorganic chronic condition in up to 40% of all patients with SAPS[1,2,7,8].

In various musculoskeletal pain disorders, a close relation between pain and psychosocial functioning (e.g. depression, anxiety or social support) is documented[9,10]. Impaired psychosocial functioning is frequently viewed to be a result of pain; however, it may also enhance the perception of pain[11]. In the knee and hip, it has repetitively been observed that patients who have depressive feelings tend to respond poorly to interventions targeting the painful joint[12,13]. Furthermore, treating concurrent depression in patients with chronic low back pain has been shown to result in pain-relief in nearly 25% of patients[14]. These studies show the importance of psychosocial functioning in the treatment of musculoskeletal pain[15].

Regarding research on SAPS, there has been a focus on peripheral pathology of the shoulder whereas psychosocial factors have received less attention[16-22]. It has been established that patients with SAPS frequently present with coexisting psychosocial problems; however, whether this also associates with long-term outcome is unknown[20-22]. Therefore, we assessed whether psychosocial functioning in patients with SAPS is associated with persistence of complaints after 4 years of routine care.

MATERIAL AND METHODS

For this longitudinal prognostic analysis, eligible patients were recruited between April 2010 and December 2012 at the Leiden University Medical Centre, Haaglanden Medical Centre and Alrijne Hospital, under a previously registered and published study protocol (Trial register no. NTR2283)[23]. Consecutive patients with SAPS were selected through physical examination, shoulder radiographs and magnetic resonance arthrography by dedicated shoulder surgeons. The inclusion criteria were patients who were aged 35-60 years, who had unilateral shoulder complaints for >3 months and who received a clinical diagnosis of SAPS based on a positive Hawkins test and Neer impingement test with lidocaine[23]. The exclusion criteria were insufficient language skills, inflammatory glenohumeral (GH) arthritis, clinical signs of GH or acromioclavicular osteoarthritis, previous shoulder surgery, fracture or dislocation, cervical radiculopathy, GH instability, decreased passive GH mobility (e.g. frozen shoulder), and presence of electronic implants (e.g. pacemaker). Additionally, patients were excluded in case other specific conditions were diagnosed on radiographs or magnetic resonance arthrography such as calcific tendinitis, full-thickness rotator cuff tear, and labral or ligament pathology[23]. Patients who provided written informed consent were included and contacted for a follow-up visit between June 2014 and September 2015 (i.e., 3-4 years later).

Psychosocial functioning

At baseline and follow-up, psychosocial functioning was assessed by means of the Research And Development questionnaire (RAND-36)[24-26]. The RAND-36 questionnaire is a widely used and validated survey for the evaluation of health-related quality of life in 8 domains: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, vitality, bodily pain and general health[24-26]. The reliability of these individual domains ranges between an α of 0.78 and an α of 0.93[27]. Each domain is separately scored by standardisation of scales, aggregation of scale scores and transformation to summary scores, ranging between 0 and 100. Higher scores represent better function[24-26]. The RAND-36 scores on the domains of social functioning, role limitations due to emotional problems, mental health, vitality and general health were evaluated to assess psychosocial functioning[26].

Persistence of complaints

- At follow-up, an anchor question was used to assess whether patients experienced persistent, reduced or increased complaints compared to the first visit.
- At baseline and follow-up, a visual analogue scale (VAS) for pain during movement was assessed using a 100mm VAS scale (on which 0 indicated no pain and 100 indicated maximal pain). Changes in pain over time were expressed as Δ VAS score.
- At baseline and follow-up, the Western Ontario Rotator Cuff (WORC) index was used to assess quality of life through 5 domains on a scale from 0 (worst possible) to 100 (best possible)[28,29]. Changes in WORC scores were expressed as Δ WORC index score.

Statistical analysis

We first determined whether there were baseline differences in psychosocial functioning (RAND-36 score) and other characteristics (e.g., age, sex, or treatment) between patients who had increased, persistent, and reduced complaints at follow-up by use of the independent samples t-test, Wilcoxon rank sum test or χ^2 test depending on the type and distribution of data. Subsequently, logistic and linear regression analyses were performed to assess whether baseline psychosocial functioning (RAND-36 score) was associated with complaint persistence (anchor question, Δ VAS score, and Δ WORC index score). For this, the dependent variables (Δ VAS score and Δ WORC index score) were checked for a normal distribution. Additionally, we determined from scatter plots that the relations between the RAND-36 domains and the Δ VAS score and Δ WORC index score were linear and the residual errors had a normal distribution. The analyses were also performed with inclusion of age and sex to assess the influence of these factors on the estimated groups differences[30]. Results from logistic and linear regression analyses were presented as odds ratios (ORs) and unstandardised β values, respectively.

The data was stored in a Microsoft Access 2010 database (version 14.0.7195.5000; Microsoft, Redmond, WA, USA) with SP2 MSO (Service Pack 2, Microsoft Office, version 14.0.7214.5000; Microsoft). For statistical analyses, SPSS software (version 20; IBM, Armonk, NY, USA) was used. A 2-sided p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Thirty-four patients fulfilled our eligibility criteria. After a follow-up period of 3.8 years (standard deviation [SD], 0.5 years), 3 patients declined to participate, 1 patient had died, and 2 patients could not to be contacted. The 6 patients lost to follow-up were aged 53 years (SD, 4.6 years), with 50% (n=3) being women; the median complaint duration was 12 months (25th quartile – 75th quartile, 12 – 30 months) at baseline. The eventual study cohort of 28 patients (82%) had a mean age of 50 years (SD, 6.5 years), with 61% (n=17) being women; the median complaint duration was 17 months (25th quartile – 75th quartile, 12-26 months). All these patients were treated conservatively with physical therapy (n=21, 75%) and/or subacromial infiltrations (n=17, 61%). Two patients were treated operatively after failed conservative management by Neer acromioplasty (n=1) and distal clavicle resection (n=1).

Table 1 | Baseline characteristics of patients with persistent or reduced shoulder complaints at follow-up

	SAPS-complaints at follow-up		**Group difference**	
	Persistent (n=9)	Reduced (n=19)	95% CI or statistic*	p-value
Demographic characteristics				
Age, mean (SD), yr	47 (4.7)	52 (6.8)	-0.3 to 10	0.063
Female, n (%)	6 (67)	11 (58)	0.2	0.657
Right side dominance, n (%)	9 (100)	15 (79)	2.2	0.137
Dominant side affected, n (%)	7 (78)	10 (53)	1.6	0.203
Duration of complaints, median (quartiles), mo	30 (20 to 69)	12 (9.3 to 24)	-2.6	0.009†
Therapy, n (%)				
Physiotherapy	7 (78)	14 (74)	0.1	0.815
Subacromial infiltration	7 (78)	10 (53)	1.6	0.203
Operation	1 (11)	1 (5.3)	0.3	0.575
Pain and disability				
VAS score during movement, median (quartiles)	44 (25 to 62)	32 (18 to 62)	-0.4	0.681
WORC index score, mean (SD)	59 (15)	58 (19)	-16 to 14	0.864
RAND-36 score				
Physical Functioning, median (quartiles)	75 (90 to 100)	80 (75 to 90)	-2.6 to 20	0.127
Social Functioning, median (quartiles)	75 (56 to 81)	88 (75 to 100)	-1.7	0.099
Role-Physical, median (quartiles)	0 (0 to 63)	75 (50 to 100)	-2.3	0.023†
Role-Emotional, median (quartiles)	100 (67 to 100)	100 (100 to 100)	-0.1	0.918
Mental Health, mean (SD)	65 (14)	82 (12)	5.9 to 27	0.003†
Vitality, median (quartiles)	50 (45 to 60)	70 (60 to 80)	-2.9	0.004†
Bodily Pain, mean (SD)	56 (15)	58 (16)	-11 to 14	0.793
General Health, median (quartiles)	45 (25 to 63)	75 (65 to 85)	-2.7	0.008†

Complaints persistence was assessed with an anchor question at 4 years' follow-up. Depending on the type and distribution of data (histograms), data were analysed with the independent samples t-test, Wilcoxon rank sum test or χ^2 test. SAPS, subacromial pain syndrome; CI, confidence interval; SD, standard deviation; VAS, visual analogue scale; WORC, Western Ontario Rotator Cuff.

* χ^2 Value or *z* score

† Statistically significant (P<0.05)

Compared with the first visit, none of the patients reported increased complaints on the anchor question at follow-up, whereas 9 patients (32%) reported persistent complaints and 19 (68%) reported reduced complaints. There were no differences in the received treatment between the 2 subgroups (**Table 1**). Patients with persistent complaints at follow-up had a significantly longer median duration of complaints at presentation (30 months; quartiles, 20 – 69 months), than patients with reduced complaints at follow-up (12 months; quartiles, 9 – 24 months). There were no baseline differences in physical functioning and pain (RAND-36, VAS score or WORC index score) between patients with persistent complaints and those with reduced complaints at follow-up (**Table 1**). The patients who reported persistent complaints at follow-up did have lower baseline scores on the psychosocial functioning domains of the RAND-36 (i.e., role limitations due to physical problems, mental health, vitality and general health) than patients who reported reduced complaints.

Table 2 | Baseline psychosocial functioning associated with complaints at follow-up

	Persistent complaints at follow-up		**Δ VAS score**		**Δ WORC index score**	
RAND-36	*OR (95% CI)*	*p-value*	*β (95% CI)*	*p-value*	*β (95% CI)*	*p-value*
Social Functioning	0.97 [0.93 to 1.01]	0.152	-0.39 [-0.99 to 0.20]	0.183	0.08 [-0.45 to 0.61]	0.755
Role limitations due to emotional problems	1.00 [0.98 to 1.02]	0.843	-0.11 [-0.46 to 0.24]	0.513	-0.07 [-0.38 to 0.24]	0.627
Mental Health	0.92 [0.85 to 0.98]	0.013*	-0.90 [-1.65 to -0.16]	0.020*	0.84 [0.19 to 1.48]	0.013*
Vitality	0.90 [0.83 to 0.98]	0.011*	-1.03 [-1.72 to -0.33]	0.006*	0.88 [0.26 to 1.50]	0.008*
General Health	0.93 [0.88 to 0.98]	0.009*	-0.79 [-1.27 to -0.31]	0.002*	0.57 [0.11 to 1.02]	0.017*

Logistic regression was performed with complaint persistence as the dependent variable (with reduced complaints as the reference value), whereas linear regression was performed with the following dependent variable: change in visual analogue scale for pain during movement over time (Δ VAS score) and change in WORC index score over time (Δ WORC index score). The independent variables are the RAND-36 domains related to psychosocial functioning. VAS, visual analogue scale; WORC, Western Ontario Rotator Cuff; OR, odds ratio; CI, confidence interval.
* Statistically significant (P<0.05)

Lower baseline levels of mental health (OR, 0.92; 95% confidence interval [CI], 0.85 to 0.98; p=0.013), vitality (OR, 0.90; 95% CI, 0.83 to 0.98; p=0.011) and general health (OR, 0.93; 95% CI, 0.88 to 0.98; p=0.009) were associated with persistence of complaints as indicated on the anchor question (**Table 2**). In accordance, baseline mental health (β, -0.90; 95% CI, -1.65 to -0.16), vitality (β, -1.03; 95% CI, -1.72 to -0.33) and general health (β, -0.79; 95% CI: -1.27 to -0.31) were negatively associated with Δ VAS score (**Table 2**). Moreover, baseline mental health (β, 0.84; 95% CI, 0.19 to 1.48), vitality (β, 0.88; 95% CI, 0.26 to 1.50), and general health (β, 0.57; 95% CI, 0.11 to 1.02) were associated with Δ WORC index score (**Table 2**). The association between baseline psychosocial functioning and persistence of complaints at follow-up was not affected by inclusion of sex and age in the analysis, as described in **Appendix 1**.

DISCUSSION

In this longitudinal study, we showed that lower baseline levels of mental health, vitality and general health (RAND-36) are associated with persistence of complaints after approximately 4 years of routine care in patients with SAPS. The baseline scores of patients with persistent complaints in these RAND-36 domains were 12, 17 and 24 points lower, respectively, than those in the Dutch population and comparable to those obtained from patients with depression[25,31,32].

In SAPS, few studies have been conducted on the association between shoulder complaints and psychosocial functioning[18,19]. In confirmation with our study, depressive symptoms have been associated with recurring shoulder symptoms in a community-based sample from the general population.[33] Furthermore, pain self-efficacy, expectations and pain catastrophising have been associated with chronic shoulder symptoms[8,19,34]. In this longitudinal study, we showed that there is an association between lower levels of mental health, vitality and general health and long-term persistence of complaints in SAPS, which emphasises the role of psychosocial factors in SAPS.

Our study has some limitations. First, the calculations were performed on a small sample size. Because of limited power, we could not control for various factors such as the type of treatment received. However, because there were no differences in received treatment between the 2 subgroups with persistent vs. reduced complaints, we do not think that this introduced bias. Second, we did not assess all psychosocial constructs that may determine the course of complaints. Baseline psychosocial variables such as anxiety or catastrophising may have an effect on long-term pain and function as well and should be evaluated in future studies[10,35]. Third, there was a longer baseline duration of complaints in patients with persistent complaints at follow-up than in those with reduced complaints at follow-up. We therefore could not clarify cause-and-effect relationships, but this was also out of the scope of this study.

In SAPS, complaints become chronic in up to 40% of all patients[1,2,7,8]. Clinicians generally focus on anatomical deformities and damaged subacromial tissues, whereas complaints do not correspond with magnetic resonance imaging pathologies in nearly half of all patients[36,37]. Conditions external to the shoulder, for example, psychosocial functioning, may contribute to the perception of pain as well, and studies in other pain conditions have shown that addressing these factors results in quicker relief of pain and recovery[14,37-40]. Future studies may investigate whether such a multimodal treatment may also benefit patients with SAPS[14].

CONCLUSION

In this prospective longitudinal study with nearly 4 years' follow-up, we showed that reduced psychosocial functioning in patients with SAPS is associated with long-term persistence of complaints. In other musculoskeletal pain conditions, it has been suggested that addressing coexisting psychosocial problems may enhance treatment outcome[14,38-40]. Future studies may investigate whether a multimodal treatment with assessment of psychosocial functioning may also facilitate pain relief and recovery in SAPS.

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Appendix

Appendix 1 | Baseline psychosocial functioning associated with complaints at follow-up, adjusted for sex and age.

	Persistent complaints at follow-up		**Δ VAS score**		**Δ WORC index score**	
RAND-36	*OR (95% CI)*	*p-value*	*β (95% CI)*	*p-value*	*β (95% CI)*	*p-value*
Social Functioning	0.97 [0.93 to 1.0]	0.179	-0.22 [-0.86 to 0.21]	0.223	0.023 [-0.49 to 0.55]	0.907
Role limitations due to emotional problems	1.0 [0.98 to 1.0]	0.782	0.043 [-0.31 to 0.38]	0.830	-0.21 [-0.48 to 0.15]	0.300
Mental Health	0.91 [0.84 to 0.99]	**0.020***	-0.39 [-1.5 to -0.090]	0.028*	0.42 [0.12 to 1.4]	0.022*
Vitality	0.90 [0.82 to 0.99]	**0.025***	-0.39 [-1.5 to -0.035]	0.041*	0.42 [0.065 to 1.4]	0.033*
General Health	0.90 [0.83 to 0.98]	**0.015***	-0.55 [-1.2 to -0.35]	0.001*	0.45 [0.12 to 1.0]	0.015*

Logistic regression was performed with complaint persistence as the dependent variable (with reduced complaints as the reference value), whereas linear regression was performed with the following dependent variable: change in visual analogue scale for pain during movement over time (Δ VAS score) and change in WORC index score over time (Δ WORC index score). The independent variables are the RAND-36 domains related to psychosocial functioning, sex and age. VAS, visual analogue scale; WORC, Western Ontario Rotator Cuff; OR, odds ratio; CI, confidence interval.

* Statistically significant ($P<0.05$)

GENERAL DISCUSSION

A painful shoulder has historically been viewed as the consequence of "impingement" by the coracoacromial arch on the rotator cuff tendons and other subacromial tissues[1,2]. As a solution for this "impingement", the surgical subacromial decompression was introduced, which has been the standard treatment for decades[1]. In recent years only, it has been shown that clinical outcome after subacromial decompression is similar to sham surgery; in which the arthroscope is introduced, or the bursa is resected without surgery to the acromion[3-5]. Based on these and other clinical studies, "impingement" is no longer regarded as the cause for shoulder pain, resulting also in a redefinition of the concept of shoulder pain where dynamic, behavioral and/or central pain mechanisms are supposed to be involved, but etiologic mechanisms are still undiscovered; the Subacromial Pain Syndrome or SAPS[3-5]. The Dutch "*Richtlijnendatabase*" now strongly recommends against subacromial decompression surgery for patients with SAPS[6].

THIS THESIS

PART I - Observations regarding adductor co-contraction in the (a)symptomatic ageing shoulder

We were the first to show that adductor co-contraction is not specific for symptomatic pathology of the shoulder, but instead a physiological finding associated with ageing. In *chapter 1*, we observed that in contrast to young individuals, middle-aged asymptomatic individuals have a high degree of teres major and latissimus dorsi activity during abduction[7]. We suggest that this age-related increase in adductor co-contraction may represent a compensation for degeneration of shoulder tissues, mainly the rotator cuff, that is necessary for preserving shoulder stability and function in two ways[8-14]. First, the degenerated upper parts of the rotator cuff will contribute less to the abduction movement, and therefore the deltoid has to compensate for the lost abduction moment, resulting in a more cranially, instead of mediocranially directed force on the humerus. Second, reduced stabilising force by the degenerative rotator cuff may jeopardise counteraction of cranial deltoid forces. Both require a compensatory force in the mediocaudal direction, to counteract humerus cranialisation. This may explain why older asymptomatic individuals show increased co-contraction of the teres major and latissimus dorsi during abduction.

In *chapter 2*, we sought to determine whether patients with SAPS have altered co-contraction patterns of the arm adductors compared with asymptomatic controls. We found that patients with SAPS predominantly co-contracted with the pectoralis major, while controls did so with the teres major[15]. To unload subacromial tissues, it may be more effective to co-contract with the teres major, given its more caudally directed force vector[16,17]. These results thus suggested that patients with SAPS are unable to adapt adequately to age-related changes in the shoulder and could point towards a treatable imbalance between the abductor and adductor muscles.

In *chapter 3*, we evaluated the potential clinical value of increased caudally directed forces during abduction, by studying the degree of co-contraction and perceived symptoms in patients with SAPS at baseline and after a period of approximately 4 years. We found that increased co-contraction of the latissimus dorsi and teres major was associated with patient-reported reduced complaints, decreased pain and increased quality of life[18]. A favorable course of SAPS was associated with increased co-contraction of the latissimus dorsi and teres major.

These results are promising, but may evoke a discussion on cause-and-effect relationships between pain and adductor co-contraction. Given the long duration of symptoms prior to the study and the fact that patients had less adductor co-contraction at the study baseline than at follow-up (when symptoms had severely reduced), the observed increased adductor co-contraction unlikely is an adaptation to pain[19,20]. However, whether the initial lack of adductor co-contraction in patients with SAPS was present due to pathology or due to pain remains subject for research.

In order to further elaborate on this relationship between pain and adductor co-contraction in patients with SAPS, the effect of subacromial lidocaine infiltration on adductor activation patterns was evaluated (*chapter 4)*. We found that co-contraction of the teres major did not change after the administration of subacromial anaesthetics, while the degree of latissimus dorsi co-contraction slightly decreased after lidocaine infiltration[21]. This study shows that decreased teres major co-contraction in patients with subacromial pain, likely is not the consequence of pain itself.

PART II - Factors that may determine adaptation of adductor activation patterns and perception of pain in SAPS.

In recent years, there has been an expansion of research on the subject of how musculoskeletal complaints can be discordant with observed musculoskeletal pathology and how symptoms become chronic. The focus has shifted from anatomical structures to central nervous factors as cognition, pain sensitisation and more recently, the adaptability of the motor system (assessed by motor complexity)[22-24].

Motor complexity

The young and healthy human body has a redundant number of ways to execute a specific task. The latter enables learning through trial and error, quick adaptation to change and uniform distribution of load across contractile tissues[25-28]. The complexity of repetitive movement trajectories (e.g., gait) has been interpreted as a characteristic of this motor redundancy, and thereby a reflection of the healthiness of the underlying motor system[29-32]. A decreased complexity of movement suggests a person to move in a rigid and predictable way, as the result of muscular and sensory degeneration. This could be the cause of frailty, decline in functionality and eventually symptomatic pathology[28,33].

In *chapter* 5, we sought to determine the motor complexity within repetitive shoulder abduction movement trajectories in 120 asymptomatic participants between 18 and 70 years old. Insight was provided into available motor redundancy in a cross-sectional study of different ages[34]. We found a significant age-related decline in motor complexity, suggestive for declined motor redundancy. If motor redundancy becomes critical this may imply more stereotype “rigid” movements and less ability to adapt to internal or external stresses and make the abduction movement prone for (overuse) complaints[25-28,34].

To further build on the hypothesis that reduced motor complexity may play a role in the inability to find effective motor strategies in patients with SAPS, we compared motor complexity of an isometric abduction force curve between patients with SAPS and asymptomatic controls (*chapter 6)*[35]. Patients with SAPS showed reduced motor output complexity during isometric abduction and adduction force tasks, which may indicate functional decline and play a role in the development or perpetuation of shoulder complaints[35].

Proprioception

In *chapter* 7, a narrative review on the loss of proprioception in SAPS patients and the effect of conservative interventions was done[36]. Very limited evidence for a loss of proprioception in SAPS is present; a single study suggested that joint position sense in higher angles of scapular plane elevation may be compromised[36,37]. Passive therapeutic strategies, such as kinesiotape, did not yield an improvement in proprioception, whereas active training with strengthening and stabilisation exercises improved proprioception in SAPS [36,38,39]. We suggest that these exercises are effective because they result in increased co-contraction of agonists and antagonists at the glenohumeral and scapulothoracic joint, increasing active stabilisation[15,40,41]. Furthermore, consequent increased tonus of antagonistic muscles may increase excitability of muscle spindles, leading to measurable enhanced joint position sense (proprioception)[42]. Considering that muscle spindle information is the main source of input for joint position sense, this would explain why passive strategies such as kinesiotape are less effective than active strategies[43-46].

Psychosocial functioning

In various musculoskeletal pain disorders, a close relation between pain and psychosocial functioning (e.g., depression, anxiety or social support) is documented[47,48]. It has become clear from systematic reviews that psychosocial factors also play a role in the perception of symptoms in musculoskeletal pain disorders of the shoulder. However, the association with poor clinical outcome remains obscure, and therefore longitudinal designs are needed[49-51]. In *chapter 8*, we performed a longitudinal study and showed that lower baseline levels of mental health, vitality and general health (RAND-36) are associated with persistence of complaints after approximately 4 years[52]. The baseline scores of patients with persistent complaints on these RAND-36 domains were respectively 12, 17 and 24 points lower than the Dutch population and comparable to those obtained from patients with depression[53-55]. This finding may imply that the effect of treatment may be influenced by the patient's psychosocial functioning. Both the direct influence of psychosocial functioning on symptom perception as well as the association between psychosocial functioning and motor complexity should be evaluated in patients with SAPS, both in clinical and in research setting[56].

VIEWPOINTS AND LIMITATIONS OF THIS THESIS

Patient population and generalisability

Despite recent advancements, there is still inconsistency in diagnostic criteria for SAPS and therefore our results may not simply be generalised[57]. Furthermore, we selected our samples from patients who presented to a secondary of tertiary referral centre.

Study design and causality

The conclusions in this thesis are predominantly based on cross-sectional observational studies, hence we cannot report on cause-and effect relationships. The purpose of this thesis is to provide an objective kinematic, biomechanical and neurophysiological hypothesis on the pathophysiology of SAPS and thus potential treatment modalities, which is fundamental for implementation studies.

Selection of muscles spanning the glenohumeral joint

Following the line of reasoning that SAPS is caused by dynamic irritation of subacromial tissues during motion, specifically abduction, we focused on muscles that directly act on the craniocaudal position of the humerus. In biomechanical evaluations and a recent systematic review on the topic, it has been shown that the deltoid muscle contributes the most to upward migration of the humerus during abduction[16,58]. The arm adductors, specifically the latissimus dorsi, teres major, and, to a lesser extent, the pectoralis major, are potent humeral-head depressors during abduction[16,58]. Other muscles that may contribute to humeral depression are the teres minor and the lower parts of the infraspinatus and subscapular muscles[58]. Since evaluating the latter muscles with EMG requires indwelling (fine wire) electrodes and the contribution of these muscles to the craniocaudal position of the humerus may be less (especially when degenerated), we limited our evaluation to the deltoid, latissimus dorsi, teres major, and pectoralis major muscles in this thesis[11,58,59].

Scapulothoracic muscle activation patterns and scapular kinematics

Contrary to the evaluation of muscles spanning the glenohumeral joint, several other research groups assign a more important role to scapulothoracic muscles, and these muscles were not evaluated in the current thesis[60-62]. As such, we also disregarded the position of the scapula and the possible contribution of scapular dyskinesis to symptoms in SAPS. It has been suggested that altered scapular muscle activation patterns and position of the scapula may compromise subacromial tissues and thus cause pain[60-62]. Based on that hypothesis, treatments focusing on normalising scapular kinematics have been widely introduced[63,64]. However, clinical studies have so far shown limited added value of these exercises over other physiotherapeutic modalities[64]. Furthermore, it has been observed that predominantly glenohumeral kinematics, and not scapulothoracic kinematics, affect the width of the subacromial space[16,65,66]. Finally, two recent studies showed that relief of pain with subacromial anaesthetics in patients with SAPS further increases scapular dyskinesis, illustrating that the role of scapulothoracic kinematics in SAPS has yet to be clarified[67,68].

Measurement set-up

Findings on adductor co-contraction in this thesis were based on measurements in an isometric measuring device with electromyography assessment[69]. The reliability of this assessment is moderate to good and due to the standardisation method results can be extrapolated to other patient groups[69]. Measurements were all performed during isometric abduction with the arm next to the body, and we did not assess adductor co-contraction during the rest of the abduction trajectory. The latter is challenging and potentially flawed due to limitations in the validity and standardizing methods of EMG during free movement (e.g. due to electrode shifting, signal non-stationarity, change in conductivity)[70]. We hypothesise that muscle activation patterns that initiate the movement (isometric abduction force exerted with the arm next to the body), will remain the same during the first trajectory of abduction, during which subacromial narrowing generally occurs[65]. Given the limitations of measuring EMG during free motion, we suggest to study adductor co-contraction in a clinical setting instead, for further insight and possible future clinical implementation[70].

FUTURE PERSPECTIVES

Surgical treatment has long been the cornerstone of treatment for SAPS, despite low success rates[3]. In response to the latter, several studies into conservative treatment have been performed, resulting in physiotherapy taking over the role of cornerstone treatment[3-5]. Strikingly, evidence based guidelines for physiotherapists are still lacking, jeopardising clinical outcome and education[71]. It is commonly acknowledged that shoulder strengthening and stabilisation exercises are important in the treatment of SAPS, however there is no consensus on which muscles to train, because the cause for complaints is still largely unknown. In this thesis, we explored and found some potential explicit causes for SAPS and thus potential targets for conservative treatment. The is shown in the highlights of this thesis below:

- Co-contraction of the teres major and latissimus dorsi during abduction is a physiological finding. It occurs in the asymptomatic ageing shoulder, and likely represents a compensation mechanism for reduced active stabilisation by the rotator cuff during abduction due to degeneration[7].
- During abduction, patients with SAPS co-contract with the pectoralis major instead of the teres major like asymptomatic individuals do, resulting in reduced depression of the humerus with respect to the scapula[15]. This may compromise subacromial tissues.
- Increasing co-contraction of the teres major and latissimus dorsi in patients with SAPS is associated with long-term reduction/dissolvement of complaints[19].
- Someone's "handiness", expressed by motor complexity may play a role in whether individuals are able to adopt effective motor strategies[24,34]. Assessing motor complexity in the shoulder proved reliable although dependent on the length of data[34].
- Patients with SAPS show decreased motor complexity during an abduction and adduction task[35]. This may imply decreased ability to recover from complaints since adaptation by movement strategies is insufficient.
- Patients with SAPS frequently present with chronic symptoms complicated by impaired psychosocial functioning, and therefore a "regular" orthopaedic treatment program does not suffice; psychosocial factors may need to be addressed in a multimodal approach for better clinical outcome[48,52].

The knowledge obtained in this thesis has shed new light on pathophysiological thinking in SAPS and have formed the base for a future clinical trial (Co-Con trial, trial register number: NL8797). The latter supports the use of the Laboratory for Kinematics & Neuromechanics (LK&N) as a diagnostic lab in which the treatment modalities proposed in this thesis will be assessed. In earlier projects at the LK&N, performed in collaboration with colleagues from the Technical University of Delft, the theories and measurement tools used in this thesis have been developed and validated[66,69,72]. Now, in the Co-Con trial, we will collaborate with physiotherapists and aim to determine in a blinded randomised controlled trial whether co-contraction of the teres major and latissimus dorsi can be trained in patients with SAPS, and whether this results in early relief of symptoms.

Based on these results we anticipate to develop a first guideline for SAPS based on evidence from our LK&N lab, using specific humerus depressing exercises during abduction. Factors like motor complexity and psychosocial functioning, will be accounted for. This evidence-based approach is the only way to unravel complex entities like SAPS, and to optimise diagnostics and treatment for better patient outcome, thus adhering to the IDEAL (Idea, Development, Evaluation, Assessment, Long-term follow-up) principles: no innovation without evaluation[73].

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NEDERLANDSE SAMENVATTING

TOT NU TOE BEKEND

Tussen het schouderdak (acromion) en het opperarmbeen (humerus), bevindt zich de subacromiale ruimte (**Figuur 1**). In deze ruimte bevinden zich verschillende weefsels, zoals de supraspinatus pees, subacromiale slijmbeurs en bicepspees. Irritatie van deze weefsels en pijnklachten is de op één na meest voorkomende klacht van het bewegingsapparaat in de Nederlandse samenleving.

Het eerste onderzoek naar subacromiale pijn werd verricht in 1934. Sindsdien zijn er duizenden publicaties over de oorzaak verschenen. Er zijn diverse benamingen voor de klacht in gebruik geweest, tot het moment dat er in 2014 werd besloten dat bij gebrek aan kennis over de oorzaak, de klacht het best beschreven kan worden als het “Subacromiale Pijn Syndroom (SAPS)”.

Tal van oorzaken zijn er in verband gebracht met SAPS, maar eigenlijk zijn er maar een paar dingen zeker:

1. **De subacromiale ruimte is relatief te klein voor de weefsels die zich erin bevinden.** Deze weefsels, zoals de supraspinatus pees en slijmbeurs raken geïrriteerd en gezwollen, terwijl er geen ruimte is voor deze zwelling. Tijdens het opzij bewegen van de arm (abductie) treedt er een verdere vernauwing op van de subacromiale ruimte, doordat de humerus omhoog beweegt richting het acromion.
2. **In het ontstaan van SAPS, spelen factoren die te maken hebben met veroudering een rol.** Terwijl SAPS niet voorkomt bij kinderen en jongvolwassenen, vindt er een forse stijging in de incidentie van het ziektebeeld plaats bij mensen van 35 jaar en ouder. Dit toont aan dat er naar alle waarschijnlijkheid veranderingen in de schouder plaatsvinden tijdens het ouder worden, welke verband houden met het ontstaan van SAPS.
3. **Of iemand symptomen ontwikkelt of niet, hangt samen met hoe de persoon ermee omgaat, zowel lichamelijk als geestelijk.** Vanaf 30-jarige leeftijd, zijn de genoemde veranderingen passend bij het verouderingsproces zichtbaar in de schouder. Echter, het merendeel van deze mensen ontwikkelt geen klachten. Dit suggereert dat het aanpassingsvermogen een rol speelt in de ontwikkeling van klachten.

In tegenstelling tot wat lang werd gedacht, is er geen associatie tussen de vorm van het acromion en het ontstaan van SAPS. Hierdoor is de zogenaamde operatieve acromionplastiek wereldwijd fors in aantal afgenomen en is er meer ruimte gekomen voor een niet-operatieve (bv. fysiotherapeutische) behandeling van SAPS.

Fysiotherapie staat nu centraal in de behandeling van SAPS, echter, werkt dit bij ongeveer 40% van de patiënten onvoldoende. Dit komt met name door gebrek aan wetenschappelijke aanknopingspunten voor de fysiotherapeutische behandeling.

Dit proefschrift

Kenmerkend voor SAPS is dat mensen tijdens de abductiebeweging een forse toename van pijn ervaren. Hoogstwaarschijnlijk zorgt een verdere vernauwing van de subacromiale ruimte tijdens deze beweging voor een toename van de irritatie van de subacromiale weefsels en daarmee pijn. Onze hypothese is dat deze irritatie en pijn kan worden tegengegaan door tijdens abductie de humerus naar beneden te laten bewegen, weg van het acromion.

Er zijn een aantal spieren die het omhoog bewegen van de humerus, en dus subacromiale vernauwing, kunnen tegengaan. Over het algemeen wordt er zowel in de fysiotherapeutische behandeling van SAPS, alsook wetenschappelijk onderzoek, een focus gelegd op de spieren van het rotatoren manchet. In de jonge, gezonde schouder, zijn het inderdaad deze spieren die zorgen voor de stabiliteit van het schoudergewricht, als de deltaspier (deltoideus) wordt aangespannen en er een abductiebeweging in gang wordt gezet (**Figuur 1**). Er is ook aangetoond dat juist deze spieren tijdens het ouder worden bij mensen zonder klachten, maar ook bij mensen met SAPS een forse veroudering laten zien. Hierdoor kan het gebeuren dat de stabiliteit van het schoudergewricht afneemt en dat de humerus tijdens abductie te veel omhoog beweegt, met irritatie van subacromiale weefsels tot gevolg (**Figuur 2**). Dit zou zowel bij het ontstaan als het aanhouden van SAPS een bijdrage kunnen leveren.

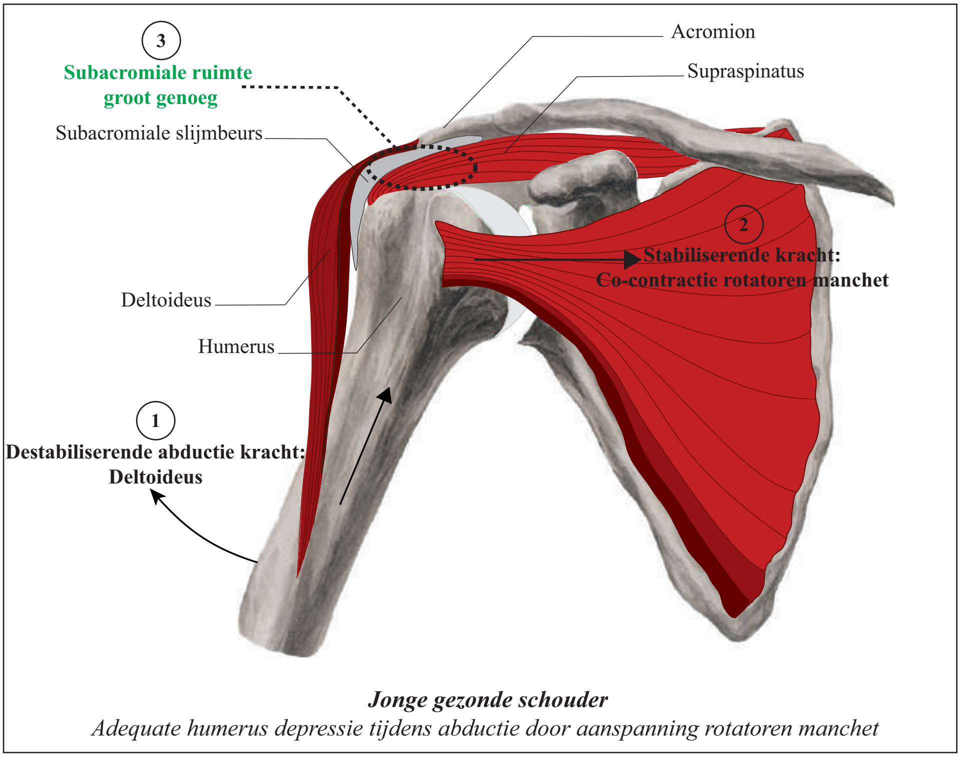
Uit recent onderzoek is gebleken dat vanuit biomechanisch oogpunt, niet de spieren van het rotatoren manchet, maar met name de adductor spieren de humerus naar beneden kunnen trekken tijdens abductie. De adductoren, zoals de teres major, latissimus dorsi of pectoralis major, zorgen er normaal gesproken voor dat de arm met kracht tegen het lichaam aan kan worden bewogen. Echter, activatie van adductoren tijdens abductie, genoemd co-contractie, zorgt ervoor dat de humerus naar beneden wordt getrokken tijdens abductie, weg van het acromion. Wij verwachten dat het aanleren van deze co-contractie van de arm adductoren (met name teres major) bij patiënten met SAPS kan helpen om subacromiale weefsels te ontzien en symptomen te verlichten (**Figuur 3**).

BEVINDINGEN IN DIT PROEFSCHRIFT

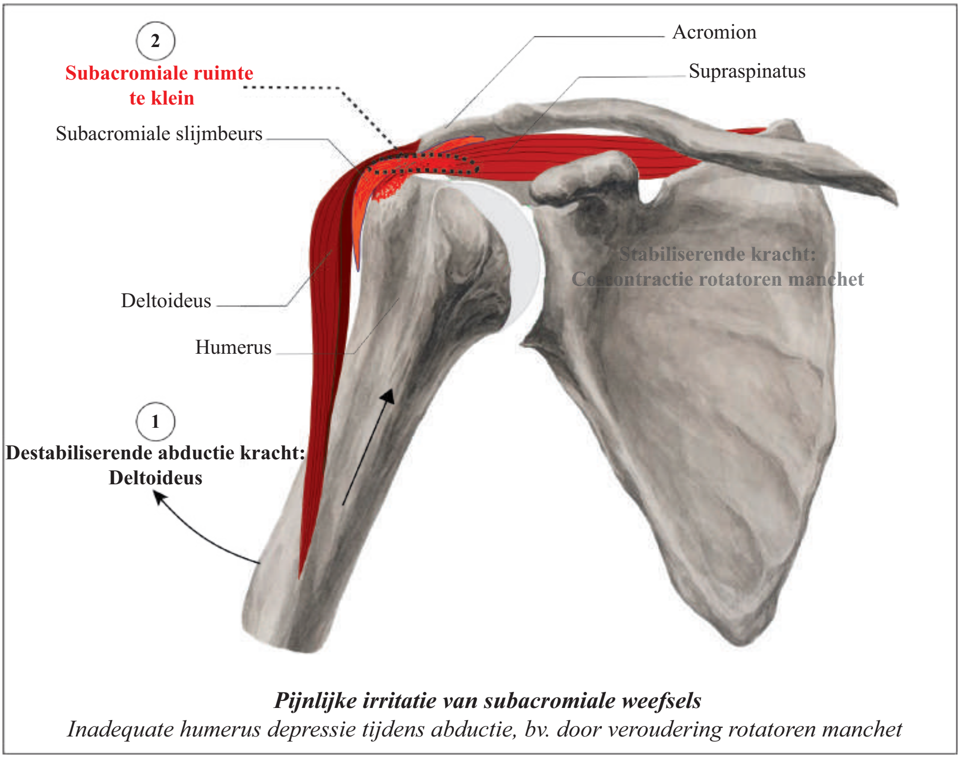
In DEEL 1 van dit proefschrift is voor het eerst onderzocht wat de rol van adductor co-contractie is in oudere personen zonder schouderklachten en bij patiënten met

SAPS. Vervolgens hebben wij in DEEL 2 gekeken naar factoren die een rol spelen bij het al dan niet kunnen aanpassen aan veroudering in de schouder (bv. door middel van adductor co-contractie) en zo mogelijk bijdragen aan het ontstaan van SAPS.

Met de acht onderzoeken van dit proefschrift wordt een wetenschappelijke basis gelegd voor de ontwikkeling van een specifieke fysiotherapeutische behandeling van SAPS.



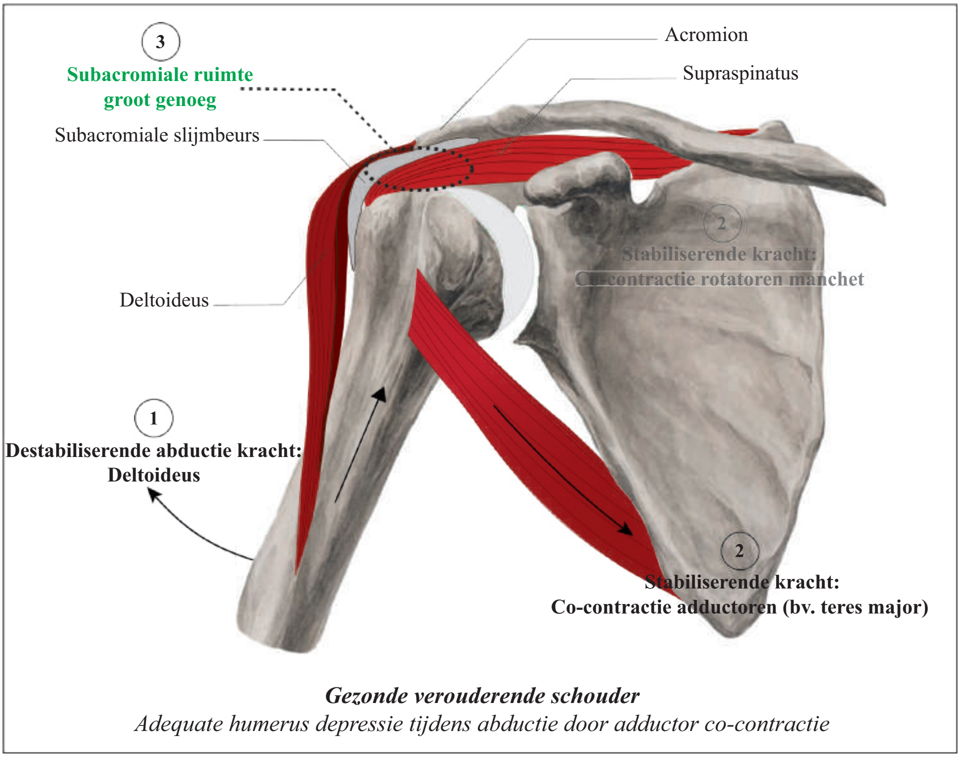
Figuur 1 | Destabiliserende kracht gegenereerd door deltoideus tijdens abductie, tegengegaan door co-contractie van het rotatoren manchet.



Figuur 2 | Destabiliserende kracht gegenereerd door deltoideus tijdens abductie, inadequaat gecompenseerd met co-contractie van het rotatoren manchet, resulterend in, mogelijk pijnlijke, irritatie van subacromiale weefsels.

DEEL I – Observaties ten aanzien van adductor co-contractie in de (a) symptomatisch verouderende schouder

In DEEL 1 worden vier onderzoeken gepresenteerd welke ieder vanuit een andere hoek belichten wat de rol van adductor co-contractie in SAPS is. Centraal in dit onderzoek staat het meten van spieractivatiepatronen door middel van elektromyografie. Om een spier aan te spannen, stuurt het brein een elektrisch signaal naar de betreffende spier, welke de spier aanzet tot contractie. Door middel van een elektrode op de huid ter plaatse van de spier, kan dit elektrische signaal worden opgevangen, waardoor er nauwkeurig gemeten kan worden of een spier aanspant of niet. Op deze manier hebben wij in ons onderzoek de activatie van de deltoideus en drie arm adductoren (pectoralis major, teres major en latissimus dorsi) gemeten tijdens een arm abductie en arm adductie taak.



Gezonde verouderende schouder
Adequate humerus depressie tijdens abductie door adductor co-contractie

Figuur 3 | Destabiliserende kracht gegenereerd door deltoideus tijdens abductie, inadequaat gecompenseerd met co-contractie van het rotatoren manchet, daarentegen gecompenseerd met co-contractie van adductoren (bv. teres major, latissimus dorsi).

In *hoofdstuk 1*, hebben wij door middel van elektromyografie onderzocht of, en hoe, de activatiepatronen van de deltoideus en drie arm adductoren veranderen met het ouder worden. In 60 asymptomatische (zonder schouderklachten) proefpersonen tussen de 21 en 60 jaar oud, zagen wij dat in tegenstelling tot bij jonge mensen, oudere personen een forse toename in co-contractie van de teres major en latissimus dorsi hebben. Tot op het moment van dit onderzoek, werd co-contractie van arm adductoren voornamelijk geassocieerd met pijn en de aanwezigheid van pathologie. Op basis van onze resultaten en eerdere studies over de biomechanische rol van de arm adductoren, kunnen wij concluderen dat het gevonden activatiepatroon waarschijnlijk een gezonde compensatie vertegenwoordigt voor veranderingen in de schouder die plaatsvinden tijdens het ouder worden (bv. verminderde kwaliteit van het rotatoren manchet).

Met deze kennis, hebben wij in *hoofdstuk 2* onderzocht of de mate van adductor co-contractie die aanwezig was bij asymptomatische proefpersonen (*hoofdstuk 1*), ook aanwezig is bij patiënten met SAPS. Met behulp van elektromyografie, hebben wij de activatiepatronen van de deltoideus en de drie arm adductoren vergeleken tussen 40 patiënten met SAPS en 30 asymptomatische proefpersonen van gelijke leeftijd en geslacht. Er is gebleken dat patiënten met SAPS ook co-contraheren met adductoren. Echter, waarbij asymptomatische proefpersonen dit met name doen met de teres major, doen mensen met SAPS dit met de pectoralis major. Vanuit biomechanisch oogpunt een belangrijk verschil. Vanuit zijn anatomische ligging heeft de teres major een sterk naar beneden gerichte kracht op de humerus, terwijl de kracht van de pectoralis veel meer horizontaal naar binnen gericht is. Voor het ontlasten van subacromiale weefsels tijdens een abductie beweging zou het efficiënter zijn om met de teres major, in plaats van pectoralis major te co-contraheren.

De kennis opgedaan in *hoofdstuk 1* & *2* komt overeen met onze hypothese dat een verminderde co-contractie van adductoren een rol kan spelen bij het ontstaan en/of onderhouden van SAPS. Als voorbereiding op een meer klinische toepassingsfase, is de vraag of een toename van adductor co-contractie ook geassocieerd is met een afname van klachten bij patiënten met SAPS onderzocht in *hoofdstuk* 3. Bij een groep van ongeveer 30 patiënten hebben wij activatiepatronen gemeten bij aanvang van het onderzoek en na circa 4 jaar. De resultaten lieten zien dat een toename van teres major co-contractie is geassocieerd met het overgaan van klachten, terwijl patiënten met aanhoudende klachten, een mindere mate van co-contractie van de teres major hadden. Deze resultaten zijn veelbelovend, maar laten nog wel ruimte voor discussie omtrent oorzaak en gevolg.

Gegeven dat symptomen al lang aanwezig waren voor aanvang van de studie en patiënten destijds minder co-contractie hadden dan na 4 jaar (met vrijwel afwezige symptomen), suggereert dat pijn niet de oorzaak is van adductor co-contractie. Om deze theorie te testen, werd in *hoofdstuk 4* onderzocht of het toedienen van een pijnstillende injectie in de subacromiale ruimte, leidt tot een toename van adductor co-contractie bij 34 patiënten met SAPS. Behoudens een minimale verandering van co-contractie van de latissimus dorsi, vonden er geen veranderingen in co-contractie patronen van de teres major en pectoralis major plaats. Dit suggereert dat de verminderde co-contractie van met name de teres major bij patiënten met SAPS geen gevolg van pijn lijkt te zijn. Dit onderscheid is cruciaal voor de focus van behandeling: op pijn of adductor co-contractie.

DEEL II – Factoren van invloed op het aanleren van adductor co-contractie en de perceptie van pijn bij patiënten bij SAPS.

Het vermogen tot aanpassing van spieractivatiepatronen is afhankelijk van zowel psychosociale factoren, als factoren gerelateerd aan aansturing van de schouder. Een factor van aansturing, de motor complexiteit, is een grove maat voor iemands "handigheid", en geeft informatie over de diversiteit waarmee iemand een bepaalde taak actief kan uitvoeren. Deze diversiteit zorgt er onder andere voor dat de belasting over verschillende spieren evenredig wordt verdeeld en dat iemand nieuwe bewegingspatronen kan aanleren. De motor complexiteit van de schouder werd bij 120 asymptomatische proefpersonen tussen de 18 en 70 jaar onderzocht (*hoofdstuk* 5). Er werd gevonden dat veroudering gepaard gaat met een afname van motor complexiteit van de schouder gedurende een abductie beweging. Dit betekent dat deze beweging op enig moment op een relatief stereotype manier wordt uitgevoerd. Mogelijk lukt het bepaalde personen dan ook niet meer om de juiste bewegingspatronen te hanteren, wat mogelijk kan leiden tot overbelasting van spieren of andere weefsels en klachten.

In *hoofdstuk 6* werd de motor complexiteit gemeten bij patiënten met SAPS en bij asymptomatische proefpersonen. Hieruit bleek dat zowel tijdens abductie alsook tijdens adductie mensen met SAPS een verminderde motor complexiteit hebben. Patiënten met SAPS lijken minder "handigheid" te hebben en kunnen zich dus mogelijk minder goed kunnen aanpassen aan veranderingen in de schouder, bijvoorbeeld als gevolg van veroudering. Het onderzoek naar motor complexiteit van de schouder staat nog in de kinderschoenen. Toekomstig onderzoek zal moeten uitwijzen of verminderde motor complexiteit bij patiënten met SAPS wijst op functionele achteruitgang en bijdraagt aan een verminderde capaciteit om effectieve bewegingspatronen aan te leren.

Om het schoudergewricht tijdens abductie te stabiliseren, is een intact gevoel over de positie van de humeruskop ten opzichte van de schouderkom nodig (proprioceptie). SAPS wordt vaak in verband gebracht met een verlies aan proprioceptie, daarom richt een deel van de fysiotherapeutische behandeling zich hier ook op. Echter, hiervoor bestaat (nog) geen wetenschappelijk bewijs. Daarom werden in een literatuuronderzoek alle relevante studies over proprioceptie bij mensen met SAPS besproken (*hoofdstuk* 7).

Uit de twaalf geïncludeerde studies met matige kwaliteit bleek dat er geen duidelijk bewijs is voor een verlies van proprioceptie in SAPS. Frequent toegepaste passieve interventies, zoals met kinesiologie tape, waren ineffectief. Daarentegen, zorgden actieve interventies met kracht- en stabilisatieoefeningen wel voor een verbetering van proprioceptie. Of proprioceptie met het ouder worden veranderd en of het bijdraagt aan extra stabiliserende kracht tijdens abductie door middel van adductor co-contractie wordt onderzocht in een studie waarin 120 asymptomatische proefpersonen tussen de 18 en 70 jaar oud metingen hebben ondergaan (manuscript in aanmaak, niet beschreven in dit proefschrift).

Tenslotte werd een derde factor die vaak bij chronische pijnsyndromen wordt gezien, geëvalueerd, de psychosociale gezondheid (*hoofdstuk 8*). Een verminderde mentale gezondheid, vitaliteit en algemene gezondheid bleek samen te hangen met het persisteren van klachten 4 jaar nadat patiënten voor SAPS waren behandeld. Wat oorzaak en gevolg is, blijft de vraag, maar dat deze factoren aandacht verdienen in de behandeling van patiënten met SAPS lijkt evident.

IMPLICATIES TOEKOMST

Een operatieve ingreep is lang de hoeksteen van de behandeling van SAPS geweest, echter met een groot faal percentage. Onderzoek heeft laten zien dat een conservatieve benadering, zoals met fysiotherapie, vergelijkbare of zelfs betere resultaten laat zien. De verschillende fysiotherapeutische behandelingen moeten wel beter wetenschappelijk onderbouwd worden. Het gebruik van een laboratorium zoals in het LUMC is daarbij essentieel om de juiste aangrijppunten te identificeren, maar zeker ook om eerst de correcte diagnose te stellen.

KERNPUNTEN VAN DIT PROEFSCHRIFT:

- Co-contractie van de teres major en latissimus dorsi is niet pathologisch. Het vindt plaats in de asymptomatische verouderende schouder, en vertegenwoordigt waarschijnlijk een compensatie voor verminderde actieve stabilisatie van het schoudergewricht tijdens abductie, ten gevolge van het verouderingsproces (bv. afname kracht spieren).
- Tijdens abductie, co-contraheren patiënten met SAPS met de pectoralis major, terwijl asymptomatische proefpersonen dit doen met de teres major. Dankzij het verschil in biomechanische eigenschappen tussen deze spieren, zou dit kunnen bijdragen aan een verminderde neerwaartse beweging van de humerus tijdens abductie. Dit kan leiden tot toegenomen vernauwing van de subacromiale ruimte en irritatie van weefsels gelegen in deze ruimte.
- Een toename van co-contractie van de teres major en latissimus dorsi in patiënten met SAPS is geassocieerd met het overgaan van klachten.
- Iemands “handigheid”, uitgedrukt in motor complexiteit, speelt mogelijk een rol in de capaciteit om effectieve bewegingspatronen aan te leren.
- Patiënten met SAPS presenteren zich veelal met chronische symptomen, gecompliceerd door verminderd psychosociaal functioneren. Om deze reden is een puur medische benadering niet afdoende en dienen psychosociale factoren mee te worden genomen in een multimodale benadering.

De kennis opgedaan in dit proefschrift leidt tot een verdere toename van de kennis rond de complexe entiteit van SAPS, zoals de rol van het trainen van adductor co-contractie in SAPS (Co-Con trial). Voor de diagnostiek is een laboratorium, zoals het Laboratorium voor Kinematica & Neuromechanica (LK&N) van het LUMC, essentieel. Innovatie kan alleen plaats vinden door klinische evaluatie met gedegen onderzoek wat ten gunste komt aan de patiënt.

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CURRICULUM VITAE

Celeste L. Overbeek was born on June 27th 1991, in Nieuwegein, The Netherlands. She graduated from high school (Voortgezet Wetenschappelijk Onderwijs) in 2009 and started her medical education at the Leiden University Medical Centre (LUMC) in the same year. Her interest in Orthopaedic Surgery started during an extra-curricular research internship at the Laboratory for Kinematics and Aeromechanics (LK&N) at the LUMC, in 2011. Under the supervision of Dr. P.B. de Witte and Prof.Dr. R.G.H.H. Nelissen, she studied which radiological findings are characteristic for patients with Subacromial Pain Syndrome (SAPS). Her interest got further fuelled during her research internship at the Hand and Upper Extremity Service at the Massachusetts General Hospital, Boston, USA, in 2013. After her senior clinical internship at the Orthopaedic Department of the LUMC, she was sure about her choice for Orthopaedic Surgery.

In 2016, she started her PhD at the LK&N under the supervision of drs. J. Nagels, Dr.ir. J.H. de Groot and Prof.Dr. R.G.H.H. Nelissen. During her PhD she used data gathered by previous PhD-students at the LK&N as a base for several manuscript and new studies into SAPS. In a collaboration with TU-Delft she developed a protocol for measurement of shoulder proprioception and motor entropy and validated this method in 120 asymptomatic individuals. She presented her work at multiple national and international scientific meetings.

In 2019, she started working as an orthopaedic resident not in training at the Alrijne Zorggroep. She greatly enjoyed this time and took the first clinical steps in Orthopaedic Surgery. She got accepted for the orthopaedic residency program in 2020 and started at the general surgery department at the Alrijne Ziekenhuis Leiderdorp under the supervision of Dr. A. Zeillemaker in July, 2020. Currently, she is working at the Department of Orthopaedic Surgery at the LUMC.