

ABSTRACT

 Muscle fatigue affecting glenohumeral and/or scapular muscles is suggested as one of the contributing factors to the development of subacromial impingement syndrome (SAIS). Nonetheless, the fatigability of shoulder girdle muscles in association with the pathomechanics of SAIS has not been reported. This study aimed to measure and compare fatigue progression within the shoulder girdle musculature of patients and healthy controls. 75 participants including 39 patients (20 females; 19 males) and 36 healthy controls (15 females; 21 males) participated in the study. Study evaluated the progression of muscle fatigue in 15 shoulder girdle muscles by means of surface and fine-wire EMG during submaximal contraction of four distinct movements (abduction, flexion, internal and external rotation). Shoulder strength, subjective pain experience (McGill Pain Questionnaire), and psychological status (Hospital Anxiety and Depression Scale) were also assessed. The results were compared between patient and control groups according to the gender. Despite marked fatigue observed in the majority of muscles particularly during flexion and abduction at 90°, overall results indicated a lower 38 tendency of fatigue progression in the impingement group across the tests $(0.05 \le p \le 0.05)$. Shoulder Strength, pain experience, and psychological status were significantly different between the two groups (P<0.05). Lower tendency to fatigue progression in the impingement group can be attributed to the presence of fear avoidance and pain-related muscle inhibition, which in turn lead to adaptations in motor programme to reduce muscle recruitment and activation. The significantly higher levels of pain experience and anxiety/depression in the impingement group further support this proposition.

 Key Words: Subacromial Impingement Syndrome; EMG; Muscle Fatigue; Fear-Avoidance, Muscle Inhibition; Psychological Status; Pain Experience

1. INTRODUCTION

 Subacromial Impingement Syndrome (SAIS) is a common cause of shoulder pain and dysfunction in general population and athletes particularly during arm elevation within the painful arc (70°-120° of abduction and overhead movements [\(Seitz et al., 2011\)](#page-22-0). The condition is a result of soft tissue compression (supraspinatus tendon in particular) within the subacromial space between the superior humerus and inferior acromion [\(Michener et al., 2003\)](#page-21-0). The condition often leads to incapacitating pain, functional disability, poor quality of life, and dependency. Shoulder pain is generally more prevalent in females compared to men (22.8%- 30.9% vs 13.3%-21.4%) of 25–64 years old [\(Pribicevic, 2012 \)](#page-22-1) and a strong association has been reported between SAIS and female gender [\(Camargo et al., 2007;](#page-18-0) [Tangtrakulwanich and](#page-23-0) [Kapkird, 2012\)](#page-23-0).

 In addition to intrinsic and extrinsic factors such as gender, anatomical misalignments, postural alterations, muscle strength/activation imbalances, and repetitive movements which have been linked to the development of SAIS [\(Koester et al., 2005;](#page-20-0) [Seitz et al., 2011\)](#page-22-0); shoulder girdle muscle fatigue has also been suggested as an intermediate biomechanical mechanism [\(Chopp](#page-19-0) [and Dickerson, 2012;](#page-19-0) [Chopp-Hurley et al., 2016;](#page-19-1) [Michener et al., 2003\)](#page-21-0). This proposition has been supported by observations of changes in the positioning of the humeral head and scapula following fatiguing protocols as the key shoulder girdle muscles attempt to stabilise the glenohumeral joint [\(Chopp-Hurley and Dickerson, 2015;](#page-19-2) [Chopp-Hurley et al., 2016\)](#page-19-1). While the rotator cuff muscles act to maintain a stable glenohumeral position and counteract destabilising sheer force of the deltoid [\(Terrier et al., 2007;](#page-23-1) [Yanagawa et al., 2008\)](#page-24-0), peri- scapular stabilising muscles contract to maintain the position of the scapula [\(Ludewig et al.,](#page-21-1) [2009;](#page-21-1) [Michener et al., 2003;](#page-21-0) [Phadke et al., 2009\)](#page-22-2). Furthermore, considering the imperative role of the shoulder musculature in producing such coordinated and finely balanced shoulder motion, impairments and dysfunction of key muscles could potentially alter the motion of the scapula, clavicle, and/or humerus [\(Ludewig and Cook, 2000;](#page-21-2) [Phadke et al., 2009;](#page-22-2) [Reddy et al.,](#page-22-3) [2000;](#page-22-3) [Struyf et al., 2014\)](#page-23-2). Hence, increased fatigability of glenohumeral and scapulothoracic muscles may alter normal shoulder kinematics (i.e. increased superior glenohumeral migration and altered scapular positioning) and lead to the narrowing of subacromial space.

 Rotator cuff fatigue and subsequent failure to counterbalance the upward pull of the deltoid on humerus has been strongly linked to the detrimental superior humeral translation [\(Chopp et al.,](#page-19-3) [2010\)](#page-19-3). This fatigue-induced abnormal kinematics and related impact on superior humeral head migration during arm elevation has been demonstrated by imaging studies using standard radiographs, magnetic resonance imaging, ultrasound, and computed tomography [\(Collins et](#page-19-4) [al., 1987;](#page-19-4) [Yamaguchi et al., 2000\)](#page-24-1). A similar fatigue-induced phenomenon is expected to affect the normal function of key scapular stabilizing muscles (primarily serratus anterior and trapezius). In healthy shoulder, the scapula rotates upwards, tilts posteriorly, and retracts as the arm is abducted in order to increase subacromial space for the tissues between acromion and superior humerus [\(Michener et al., 2003\)](#page-21-0). It has been shown that progression of fatigue causes downward rotation, anterior tilting and protraction of the scapula which subsequently leads to the rotation of the acromion into the subacromial space (scapular dyskinesis) [\(Chopp et al.,](#page-19-5) [2011;](#page-19-5) [Ludewig and Cook, 2000\)](#page-21-2).

 Localised muscular fatigue during muscular contraction is a time-dependent phenomenon expressed by tremor, pain, and incapability to maintain desired force output [\(De Luca, 1984\)](#page-19-6). EMG is broadly used to quantify muscular fatigue by means of lower-frequency shift during sustained submaximal contraction and use of median frequency (MDF) slope as a fatigue index [\(Hawkes et al., 2015\)](#page-20-1). The major body of related research has however focused on identifying the fatigue-induced changes in the kinematics of healthy shoulder in relation to the positioning of the head of humerus and orientation of scapula leaving a knowledge gap on the possible role

 of muscle fatigue in the pathomechanics of SAIS. Hence, the present study used a combination of surface and fine-wire EMG to compare the fatigability of 15 shoulder girdle muscles/muscle segments of female and male patients with healthy controls during four characteristic shoulder movements to provide a better understanding of the role of muscle fatigue in association with the SAIS. Furthermore, considering general propositions that painful musculoskeletal conditions are associated with either increased or decreased fatigue of selected muscles due to fear avoidance and pain-related muscles inhibition phenomena; patients' pain experience and psychological status (anxiety and depression) were also evaluated [\(Alizadehkhaiyat et al.,](#page-18-1) [2007;](#page-18-1) [Leeuw et al., 2007;](#page-20-2) [Sundstrup et](#page-23-3) al., 2016; [Verbunt et al., 2005\)](#page-24-2).

2. METHODS

2.1. Participants

 A total of 75 controls and patients with SAIS participated in the study: 1) Control Group included 36 healthy volunteers with normal upper limb clinical assessment and no history of upper extremity painful conditions or surgery (15 females-42.9+9.3 years old; 21 males- 47.6 ± 10.3 years old); 2) Patient group comprised of 39 participants (20 females-55.5 \pm 5.3 years old; 19 males-54.2+8.1 years old) diagnosed by the same clinician from a single Upper Limb Unit. All patients presented with persistent shoulder pain for at least 12 weeks and a range of positive specific clinical tests (Painful arc, Neer's, Hawkin's, Lift Off, Empty Can) for the SAIS [\(Diercks et al., 2014\)](#page-20-3). Patients with a coexisting musculoskeletal disorder affecting the upper limb, treatment other than for pain relief during the last three months, positive imaging (rotator cuff tear, instability, osteoarthritis), and systemic diseases affecting the function of neck, back and upper extremity were excluded. The study received Local Research Ethics Committee approval and participants gave written informed consent.

2.2. Shoulder Strength Measurement

 The Mecmesin Shoulder Myometer and Emperor Lite software (Mecmesin Ltd. Slinfold, UK) were used to measure isometric MVC of different shoulder muscle groups with a real time feedback. The myometer was fixed to an adjustable extension arm attached to a chair designed for the strength measurements [\(Alizadehkhaiyat et al., 2014\)](#page-18-2). Participants were seated in upright position with both hips and knees flexed to 90° and feet apart and flat on the ground. Strength was measured during four standard movements: (1) forward elevation with the shoulder at 90° flexion, elbow in extension and the forearm in pronation; (2) scapular plane elevation with the shoulder at 90° of abduction, elbow in extension and the hand in 'full can' position; (3) and (4) external- and internal rotation with the shoulder in neutral position, the elbow in 90° flexion tucked to the side of the body and the forearm in neutral position. A goniometer ensured the correct arm positions. The strap of Mecmesin myometer was placed at the wrist level. After familiarisation, three MVC measurements were performed during 3-s trials with 1-minute rest in between the measurements. Participants received verbal encouragement during the experiment in order to apply maximal muscle contraction. The average the three measurements was considered 100% MVC.

2.3. EMG - Fatigue Protocol

 EMG was recorded from 15 shoulder muscles/muscle segments during four distinctive shoulder movements through a fatiguing protocol. After skin preparation, disposable, self- adhesive pre-gelled Ag/AgCl bipolar EMG electrodes with conducting area of 10mm diameter and inter-electrode distance of 20mm (Noraxon Inc., Arizon, USA) were placed on anterior, middle, and posterior deltoid (AD, MD, PD), pectoralis major (PM), upper trapezius (UT), lower trapezius (UT), serratus anterior (SA), latissimus dorsi (LD), teres major (TM), biceps brachii (BB), levator scapulae (LS) according to guidelines [\(Delagi et al., 1994\)](#page-19-7). Bipolar disposable hooked fine-wire electrodes (Nicolet Biomedical, Division of VIASYS, Madison, USA) were used to record signals from the supraspinatus (SSP), infraspinatus (ISP), subscapularis (SUBS), and Rhomboid (RM) [\(Delagi et al., 1994\)](#page-19-7).

 EMG signals were recoded using a TeleMyo 2400 G2 Telemetry System (Noraxon Inc., Arizona, USA). The EMG signals were recorded during a fatigue protocol by means of a sustained submaximal force exertion at 25% MVC of absolute strength in the testing positions described above (Section 2.2). After familiarization with the test, participants were instructed to exert a constant steady force at 25% MVC for 60-s or until exhaustion point guided by a real time visual feedback provided on a PC screen (i.e. sustained (>5s) drop of >5% in force). Recorded signals were differentially amplified (common mode rejection ratio >100 dB; input impedance >100 Mohm; gain 500 dB), digitised at a sampling rate of 3000 Hz and band-pass filtered ([10–500]Hz for surface electrodes and [10–1500]Hz for fine wire electrodes), and analysed off-line using MyoResearch XP software (Noraxon Inc., Arizona, USA). Muscle fatigue was quantified by means of changes in the median frequency (MDF) of the EMG signal over time: MDF was calculated at 1-s intervals, normalized to initial MDF, and the mean rate of the change (Slope) of MDF during contraction (assessed by least square linear regression) was used as the fatigue index (Slope%/min). A regression t-test was performed to determine whether the slope differed significantly from zero, with a significant p-value indicating EMG evidence of fatigue.

2.4. Pain and Psychological Status

 Subjective pain experience and psychological status were assessed using McGill Pain Questionnaire (MPQ)[\(Melzack, 1975\)](#page-21-3) and Hospital Anxiety and Depression Scale (HADS), respectively [\(Bjelland et al., 2002\)](#page-18-3). MPQ provides a multidimensional evaluation of pain quality in terms of location, temporal pattern, description; and present intensity and has been suggested as an important tool for clinical evaluation of painful conditions [\(Camargo et al.,](#page-18-4) [2009\)](#page-18-4). The HADS emphasizes the role of anxiety and depression in relation to chronic conditions and their impact on intervention outcomes. HADS has been reported to be efficient in assessing patients with chronic musculoskeletal pain including the common upper extremity conditions such as lateral epicondylitis, rotator cuff tears, and SAIS [\(Alizadehkhaiyat et al.,](#page-18-1) [2007;](#page-18-1) [Cho et al., 2015\)](#page-18-5).

2.5. Data Management and Statistical Analysis

 Descriptive statistics for shoulder muscle strength, pain (MPQ), and psychological status (HADS) were determined according to the originally established scoring formula for calculating the subscale and total scores of each questionnaire/functional score. With regard to EMG, Fast Fourier Transformation (FFT) and power spectrum analysis were applied to determine the MDF values in 1-s epochs which were then normalised relative to the start value. The mean rate of change of MDF over the duration of fatiguing tasks (Slope) was determined by linear regression and expressed as the fatigue index (MDF Slope%/min). A regression t-test was applied to determine whether the measured slope differed significantly from zero: a significant p-value indicating EMG evidence of fatigue. The fatigue index is used to report and compare the fatigability of individual muscles during the experiments (25% MVC of forward flexion, abduction, external and internal rotation) in female and male groups of SAIS patients and controls.

 Results are reported separately for female and male groups of patient and controls and expressed as mean ± standard deviation (SD) or standard error of the mean (SEM) as appropriate. The Shapiro-Wilk test was used to analyse normal distribution assumption of the quantitative outcomes. The variables were compared between the patient and control groups: for the data not normally distributed the non-parametric Mann-Whitney U test and for the data with normal distribution the independent-sample t-test were used to determine significant between-group differences. The level of significance was set at p<0.05. The SPSS statistical package (Version 20.0; IBM, Armonk, NY, USA) was used for analysis and modeling of the data.

3. RESULTS

3.1 Muscle Strength, Pain, and Psychological Status

 Results for strength, pain, and psychological assessments are presented in Table 1. The strength measurements revealed markedly lower strength in all muscle groups (p<0.001) in female patients as compared to healthy controls with the highest deficit (~50%) observed in relation to flexors, abductors and internal rotators. Male Patients also had significantly reduced muscle 201 strength for all muscle groups $(p<0.001)$ compared to controls with the highest deficit $(\sim 30\%)$ observed for internal rotators. The same as muscles strength, all measured pain and psychological variables indicated a significant difference between and SIAS patients and controls in both female and male groups (p<0.001) (i.e. higher amount of pain experience, anxiety and depression in patients).

3.2 Muscle Fatigue

 The fatigue results (fatigue index) are presented as mean ± standard deviation (SD) for female and male groups of patient and controls in Figures 1 and 2, respectively

Muscle Fatigue in Female Participants

 There was a general trend for less fatigue development in female patients compared to controls. During forward flexion, patients showed lower fatigability trend in all muscles compared to health controls particularly in relation to the AD, TM, and ISP where a significantly lower level 213 of fatigue ($p<0.05$) was found compared to controls. The highest amount of fatigue progression in patients was observed in the deltoids, AD in particular, followed by the BB and three major rotator cuff muscles; and in controls in the deltoids, rotator cuff (ISP in particular), and SA. During abduction, fatigue developed in all muscles except RM and TM in patients and RM, TM, ISP, and SUBS in controls. While ISP showed the highest fatigue development in patients, a marked fatigue in key scapular muscles (LT and SA) and deltoids occurred in both patients and controls. Despite differing in the fatigability patterns of some muscles, no significant difference was found between patients and controls during abduction.

 The external rotation task demonstrated a similar fatigability pattern between patients and controls with the highest fatigue developing in the ISP. While scapular muscles demonstrated a minimal effect of fatigue in controls, the same muscle group showed considerable involvement of the LT and RM in patients. During the internal rotation task, the UT was the only scapular muscle affected by fatigue in patients while a marked fatigue development in UT, LT and RM was observed in controls. Rotator cuff muscles all showed a higher fatigue trend in controls, SSP and SUBS in particular. The deltoid fatigue reflected similar patterns in both patients and controls.

Muscle Fatigue in Male Participants

 Similar to females, there was a general trend for less fatigue development in male patients compared to controls. During the forward flexion task, the highest level of fatigue in patients occurred in ISP followed by the deltoids and two scapular muscles: LT and SA. In controls, several muscles were fatigued with the highest in SUBS followed by AD, RM, TM, SA, and ISP. Abduction task generated marked fatigue in the majority of muscles in both groups except LS in patients and LS and PM in controls. A higher amount of fatigue progression occurred in the deltoids, rotator cuff, BB and SA of patients and deltoids, rotator cuff, and major scapular 237 muscles (LT, and SA) of controls.

 During external rotation task, both patients and controls demonstrated the highest level of fatigue in ISP followed by TM. A trend towards higher fatigue in patients was observed during this task compared to other three fatiguing tasks, similar to the pattern in female patients. Internal rotation task generated a modest level of fatigue in patients only in SSP while it was associated with marked fatigue development in several muscles of controls including SSP, deltoids (MD and PD), and UT. A significant difference in the fatigue level was noted between 244 controls and patients for MD $(p<0.01)$.

4. DISCUSSION

 Literature suggests that maintaining the subacromial space is essential to rotator cuff health. Among studied movements, rotator cuff muscles presented with marked fatigue progression more prominently during abduction at 90°, which incorporate the 'painful arc' as one of the key clinical characteristics of SAIS, in both female and male patients,. This is in agreement with the proposed mechanistic fatigue-related SAIS theory which suggests rotator cuff fatigue leads to superior humeral translation during arm elevation due to failure in maintaining the humeral head compression in the glenoid cavity [\(Chopp and Dickerson, 2012;](#page-19-0) [Chopp-Hurley](#page-19-2) [and Dickerson, 2015\)](#page-19-2). In a study of shoulder muscle fatigue during an isometric flexion task at 90° of humeral elevation, deltoids, ISP and SSP were the first muscles to show signs of fatigue [\(Nieminen et al., 1995\)](#page-22-4).

 It has also been shown that SSP functional losses are compensated by ISP in combination with the SUBS in order to counterbalance increased detrimental deltoid muscle forces during arm abduction and elevation. This is usually accompanied by pathological co-activation of large muscles with an adducting component (PM and LD) to support joint stability during arm abduction by offsetting destabilising high deltoid forces and resultant posterior-superior shift of the reaction force vector piercing point [\(Steenbrink et al., 2006;](#page-22-5) [Steenbrink et al., 2009;](#page-22-6) [Steenbrink et al., 2010\)](#page-23-4). These compensatory mechanisms may explain the higher trend observed for the fatigue progression in ISP, SUBS, PM, and LD in SAIS patients during abduction. Furthermore, the overall higher fatigability of key scapular muscles during abduction is consistent with the second fatigue-related SAIS theory suggesting that fatigued and dysfunctional scapular muscles may lead to inappropriate positioning of the scapula (scapular dyskinesis) and subsequent reduction of the subacromial space [\(Phadke et al., 2009\)](#page-22-2). Different parts of trapezius are generally more active during abduction compared to other movements, which together with SA are aligned with a substantial mechanical advantage for scapular upward rotation. Increased activity of UT as a common compensatory strategy used by SAIS patients to assist clavicular and arm elevation and subsequent effort from LT and SA to counterbalance increased UT activity could explain marked fatigue progression observed in these muscles during abduction in SAIS patients [\(Lukasiewicz et al., 1999;](#page-21-4) [McClure et al.,](#page-21-5) [2006\)](#page-21-5).

 The overall results indicated a lower tendency of fatigue progression in patients compared to controls across the tests. While this finding could partially be attributed to a lower MVC intensity in patients due to pain, the presence of individual variations commonly associated with painful musculoskeletal conditions (including shoulder pain) might have substantially contributed to the lower progression of shoulder muscle fatigue in SAIS [\(Hodges and Tucker,](#page-20-4) [2011\)](#page-20-4). This is further supported by observations that some individuals apply similar activation patterns during arm elevation tasks when pain is induced in their shoulder compared to a non- painful condition or perform specific tasks in a more stereotyped style compared to others [\(Moseley and Hodges, 2006;](#page-21-6) [Muceli et al., 2014\)](#page-21-7). It has also been shown that patients with shoulder pain present with a range of muscle recruitment strategies and heterogeneous adaptation in motor control in response to pain due to this variability factor [\(Hodges and](#page-20-4) [Tucker, 2011;](#page-20-4) [Struyf et al., 2015\)](#page-23-5). Previous reports have interrelated the individual response to pain to an increase of motor control variability as CNS examines different biomechanical pathways to sufficiently accomplish the motor task while the "damaged" tissue is preserved [\(Muceli et al., 2014\)](#page-21-7). Furthermore, other studies have shown subject-specific and non- stereotyped adaptations in the activity of individual muscles (reorganization of motor control) in response to painful stimuli in order to cope with the pain and accomplish the requested functional task [\(Gizzi et al., 2015\)](#page-20-5).

 Two other well-recognised phenomena might also contribute to a lower progression of fatigue in SAIS patients: fear avoidance pathway (fear of pain) and/or pain-related inhibition mechanism (pain-adaptation theory with less muscle contribution). Fear-avoidance pathway with its four components of catastrophizing, fear of pain, fear of movement, and fear-avoidance beliefs has been suggested to generate a vicious cycle of dysfunction over time leading to disability by means of influencing muscle activity and contribution towards the movements [\(Carleton et al., 2006;](#page-18-6) [Verbunt et al., 2005\)](#page-24-2). It is generally accepted that fear of pain (made up of psychophysiological, behavioural, and cognitive elements) and consequent pain-avoidance are fundamental components of the fear-avoidance pathway within which fear comprises an emotional reaction to an instantaneous threat while pain incorporates psychological, social, and pathological aspects [\(Carleton et al., 2006;](#page-18-6) [Lentz et al., 2009\)](#page-21-8). It is generally speculated that pain-related beliefs, as such forceful movements aggravate pain, initiate an inhibitory feedback through high force excitation of golgi organs leading to diminished neural drive with subsequent impact on muscle recruitment during isometric contractions [\(Graven-Nielsen et al.,](#page-20-6) [2002\)](#page-20-6). The fact that present study found a significantly higher levels of pain and anxiety in patient groups further supports the potential role of fear-avoidance pathway towards lower tendency to fatigue progression in patients. This finding is also in line with the propositions that pain-related fear has a positive association with shoulder-related disability and changes such as reduced shoulder function or full-avoidance of a movement are associated with a range of psychosocial features [\(Karels et al., 2007;](#page-20-7) [Lentz et al., 2009\)](#page-21-8).

 In terms of muscle inhibition mechanism; literature suggest that in patients with chronic musculoskeletal pain the ability for rapid force development and subsequent functional capacity is markedly impaired during movements by pain inhibition of motor outflow and inflicting a threat response [\(Carleton et al., 2006;](#page-18-6) [Steingrimsdottir et al., 2004\)](#page-23-6). In an EMG study of relationships between biopsychosocial factors and chronic pain, Sundstrup et al,[\(Sundstrup et al., 2016\)](#page-23-3) demonstrated a markedly reduced neuromuscular function of the shoulder and hand in individuals with chronic upper limb pain compared to healthy controls. This pathway encompasses stimulation of the mechanoreceptors within affected joint/muscle tissue and thus blocking the nociceptive signal and pain gate over time through frequent excitation of inhibitory interneurons [\(Zimny, 1988\)](#page-24-3). It has been proposed that decreased excitability of the motor cortex induced by pain-induced inhibition pathway is preferentially located in the muscles nearby the painful area and can last for many hours after the recovery from pain [\(Le Pera et al., 2001\)](#page-20-8).

 With regard to the shoulder, it has been shown that pain-dependent inhibition of the primary motor cortex is associated with employing a compensatory muscle activation strategy and different motor programme (from subtle changes in the contribution level of synergist muscles to a complete avoidance of movement) to maintain motor output during painful movement while protecting injured/painful tissues [\(Hodges and Tucker, 2011;](#page-20-4) [Struyf et al., 2015\)](#page-23-5). Electromyographic studies of the shoulder have reported a significantly decreased glenohumeral (primarily rotator cuff and deltoids) muscle activity during abduction and flexion in SAIS patients compared to healthy controls which in turn could contribute to the development of SAIS by means of increased superior translation of the humeral head [\(Myers](#page-22-7) [et al., 2009;](#page-22-7) [Reddy et al., 2000\)](#page-22-3). In terms of scapular muscles, several investigators have reported reduced activity of trapezius, middle and lower serratus anterior during arm elevation and rotational movements in patients with painful shoulder pathologies including SAIS as compared to healthy controls [\(Ludewig and Cook, 2000;](#page-21-2) [Scovazzo et al., 1991\)](#page-22-8). This marked reduction in rate of EMG rise in the presence of upper limb chronic pain has been suggested as a neural adaptation mechanism due to reduced motor neuron firing frequency and recruitment of high-threshold motor units [\(Sundstrup et al., 2016;](#page-23-3) [Van Cutsem et al., 1998\)](#page-23-7). Hence, these two protection mechanisms (fear-avoidance and pain-related muscle inhibition) could have attributed to the generally lower or similar level of fatigue progression between patients and controls as a result of alterations in muscle activation and contribution (decreased firing or de-recruitment of some motor units) in the muscles affected by pain experience/perception.

Study Limitations

 While shoulder muscle fatigue has been increasingly studied using EMG in healthy subjects particularly during isometric arm elevation tasks, experimental evaluation of muscle fatigue development in painful conditions such as SAIS remains a significant challenge due to inherent limitations in measurement and protocol capabilities that complicate comparisons with healthy controls [\(Chopp et al., 2011;](#page-19-5) [Chopp et al., 2010\)](#page-19-3). The main limitations include difficulty in designing a functional movement with sustainable contraction at a level that can categorically fatigue upper extremity muscles due to concomitant anticipation of pain or pain experience. Some authors have reported that subjects with pain exert submaximal force rather than "true" maximal force during MVC testing with subsequent influence on the rate of fatigue development [\(Candotti et al., 2009\)](#page-18-7). Nevertheless, patients in the present study developed marked localized muscle fatigue while performing the evaluation protocol as fatigue index (slope%/min) differed significantly from zero (See section 2-3 for details. Furthermore, it has been shown that upper extremity motor strategies and related muscle activation patterns are altered because of pain experience by means of fear avoidance (fear of pain) and pain-related muscle inhibition to protect affected tissues [\(Alizadehkhaiyat et al., 2007;](#page-18-1) [Diederichsen et al.,](#page-19-8) [2009\)](#page-19-8). These mechanisms can subsequently affect the recruitment strategy and contribution of muscles into movements and influence fatigue initiation and development [\(Leeuw et al., 2007;](#page-20-2) [Sundstrup et al., 2016;](#page-23-3) [Verbunt et al., 2005\)](#page-24-2). In order to moderate this limitation a pain-free submaximal voluntary contractions (25% MVC) together with synchronised EMG and visual feedback were used in the study during fatiguing protocols for evaluating muscle fatigue. The application of such-submaximal contractions would have facilitated a more realistic measure of muscles fatigue by producing sufficient fatiguing force (25% MVC) while limiting the pain experience and potential sources of confounding.

 The usage of fine-wire intramuscular EMG electrodes to record from deep muscles, such as the rotator cuff muscles, is associated with common technical difficulties such as poor electrode placement and electrode migration during movement. Large standard deviations, mainly due to relatively small sample size and individual variations in the muscle activity patterns might blur the results. It might be possible that the pain experienced during the MVC testing by some participants would have affected MVC assessments and subsequent fatigue protocol. The study attempted to minimise such effect by means of using a normalised fatigue index. Authors are aware of this limitation but also acknowledge that there is no supreme method for such measurements in painful conditions such as SAIS. The sample size was relatively small because of separate data reporting for female and male groups of patients and controls. This approach was chosen considering a significant association between SAIS and female gender[\(Tangtrakulwanich and Kapkird, 2012\)](#page-23-0) and higher prevalence of shoulder pain in females as compared to men (22.8%-30.9% vs 13.3%-21.4% in the 25–64 years) [\(Pribicevic,](#page-22-1) [2012 \)](#page-22-1). Although study attempted to minimise pain during EMG experiments by applying a pain-free submaximal contraction, it might not have possible to fully avoid pain experience by some participants.

CONCLUSION

 While fatigue-related mechanisms have been suggested to contribute to the development of SAIS, existing knowledge on the fatigability of shoulder girdle muscles in SAIS patients is sparse mainly due to technical and methodological challenges. The present study explored and compared fatigue progression in SAIS patients and healthy pain-free controls during four distinct shoulder movements along with subjective pain experience and psychological status. Despite notable development of fatigue in the majority of studied muscles in SAIS patients, it was not significantly different from that in healthy controls. This finding can be hypothetically explained through two major phenomena, 'fear-avoidance and pain-related muscle inhibition', and subsequent adaptations in motor programme and recruitment strategy. This is further supported by significantly higher pain experience and anxiety/depression levels observed in patients. The findings provide a base of knowledge for future clinical studies aiming to develop optimal and evidence-based prevention and rehabilitation interventions. Future studies investigating shoulder muscle fatigue during different pain-free motions representative of daily and work/sport-related functions are required.

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Table and Figure Legends

Table1. Comparisons of strength, pain, and psychological status - Mean (SD) - of the affected

shoulders of female and male SAIS patients with healthy controls

 MPQ: McGill pain questionnaire; **HADS:** Hospital Anxiety and Depression Scale (AC: Anxiety Component; DC: Depression Component); All measurements showed statistically significant differences between patients and controls in both female and male groups (p<0.001).

- **Figure 1.** Mean muscle fatigue of 15 shoulder girdle muscles presented as medium frequency
- slope (%/min) for **female** impingement patients and controls at 25% maximum voluntary
- contraction (MVC) during isometric flexion, abduction, external rotation and internal rotation.

- **Figure 2.** Mean muscle fatigue of 15 shoulder girdle muscles presented as medium frequency
- slope (%/min) for **male** impingement patients and controls at 25% maximum voluntary
- contraction (MVC) during isometric flexion, abduction, external rotation and internal rotation.
- **LS:** Levator Scapulae; **UT:** Upper Trapezius; **LT:** Lower Trapezius: **SA:** Serratus Anterior; **RHOM:** Rhomboid
- Major; **LD:** Latissimus Doris; **TM:** Teres Major; **PM:** Pectoralis Major; **BB**: Biceps Brachii; **SSP:** Supraspinatus; **ISP:** Infraspinatus; **SUBS:** Subscapularis; **AD:** Anterior Deltoid; **MD:** Middle Deltoid, **PD:** Posterior Deltoid. *: *p* values significant at <0.05

 LS: Levator Scapulae; **UT:** Upper Trapezius; **LT:** Lower Trapezius: **SA:** Serratus Anterior; **RHOM:** Rhomboid Major; **LD:** Latissimus Doris; **TM:** Teres Major; **PM:** Pectoralis Major; **BB**: Biceps Brachii; **SSP:** Supraspinatus; **ISP:** Infraspinatus; **SUBS:** Subscapularis; **AD:** Anterior Deltoid; **MD:** Middle Deltoid, **PD:** Posterior Deltoid. ***:** p values significant at <0.05