Differences in biomechanical and metabolic factors between patients with frozen shoulder and asymptomatic individuals. A cross-sectional study

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Highlights

- First study comparing biomechanics in patients with frozen shoulder and asymptomatics
- Large decreases in muscle strength in patients with frozen shoulder versus asymptomatics
- Plurimeter, not observation, detects different scapular kinematics in frozen shoulder
- No evidence of different levels of proprioception and glucose in patients with frozen shoulder

Abstract

Background: the pathogenesis of frozen shoulder (FS) is thought to be one of inflammation and fibrosis possibly influenced by hyperglycemia. Biomechanical changes of the shoulder joint in terms of muscle strength, scapular kinematics and proprioception might occur in FS.

Objectives: to compare muscle strength, scapular kinematics, proprioception, and blood glucose levels within patients with FS and to asymptomatic individuals.

Design: cross-sectional study.

Method: Thirty-five patients with FS and 35 asymptomatic age and gender-matched individuals underwent physical assessment to determine muscle strength (abduction, external and internal rotation), scapular kinematics (both visually and with a plurimeter), proprioception (joint position sense), and blood glucose level.

Results: Patients with FS showed a decrease in muscle strength in their affected shoulder compared to both the unaffected shoulder and asymptomatic individuals. Significant differences were found between the affected and unaffected shoulder in the FS group and between groups (FS versus controls) in scapular upward rotation (plurimeter) at 30° and 60° abduction. No difference in scapular kinematics (visual observation), proprioception, and blood glucose levels was found neither between shoulders in the FS group nor between groups.

Conclusion: A clinically relevant difference in muscle strength and increase in scapular upward rotation were found in the affected shoulder of patients with FS compared to their unaffected side and controls. However, no evidence of different levels of scapular kinematics (visual observation), proprioception, and blood glucose levels in the affected shoulder compared to the unaffected shoulder or controls is lacking.

Key words: frozen shoulder; blood glucose; muscle strength; scapular kinematics; proprioception; cross-sectional study

Introduction

Frozen shoulder (FS) is a condition most often characterized by severe shoulder pain and functional restriction of both active and passive shoulder motion (Abrassart et al., 2020). The prevalence of primary FS in the general population is 2-5% (Hsu et al., 2011). This increases up to 59% in subjects with type-2 Diabetes Mellitus (DM) (Prodromidis & Charalambous, 2016; Zreik et al., 2016; Juel et al., 2017), whereas the prevalence of DM in patients with FS ranges from 18% to 30% (Zreik et al., 2016). Furthermore, patients with DM have a fivefold higher risk of developing FS (Zreik et al., 2016). The pathogenesis of FS is characterized by (local) inflammation and subsequent fibrosis of the joint capsule and rotator interval mediated by among others inflammatory cytokines and matrix metalloproteinases (Cho et al., 2018).

Due to its association with chronic low-grade inflammation, DM leads to increased non-enzymatic cross-link formation and elevated levels of advanced glycation end products (AGEs) secondary to hyperglycemia (Juel et al., 2017). This results in a disruption of local collagen synthesis, reflected by accelerated cross-link formation in e.g., the capsule (Brownlee et al., 1988; Aronson, 2003; Hsu et al., 2011; Snedeker & Gautieri, 2014; Kraal et al., 2020). AGEs can create cross-links throughout the complete collagen molecule, where it usually only occurs at two locations (Brownlee et al., 1988). Additionally, some AGEs favor cross-link of collagen, consequently changing the biomechanical properties of collagen in e.g., the capsule (Juel et al., 2017). In patients with FS, evidence of elevated blood glucose levels (including glycosylated hemoglobin (HbA1c)) (Pietrzak, 2016; Holte et al., 2017) and AGEs (Hwang et al., 2016; Holte et al., 2017) is present, however, comparisons to asymptomatic individuals have not been investigated. Elevated levels of AGEs have been found in patients with FS without DM as well (Hwang et al., 2016) and the development of AGEs depends on the concentration of glucose and the exposure time. Therefore, even slight increases in HbA1c levels might be associated with FS. When considering HbA1c levels, the diagnosis of DM or prediabetes (6.5% and 5.7% respectively (American Diabetes Association, 2010)) may not be required, but the elevated level of HbA1c itself may be more important as a factor in patients with FS. Therefore, these patients may not reach the cut-off but have only slight increases in HbA1c. Due to the slight increases, the cascade of capsular contract might be initiated. Therefore, a comparison of HbA1c levels between patients with FS and asymptomatic individuals is necessary. HbA1c is the most commonly used marker of chronic glycemia, reflecting average blood glucose levels over a 2- to 3-month period (Nathan et al., 2007). This marker is more convenient compared to fasting plasma glucose and has less day-to-day perturbations (American Diabetes Association, 2010).

In addition to such a hyperglycemic hypothesis, biomechanical changes of the shoulder joint (e.g., loss of strength or proprioception) might occur without adequate or appropriate (pain) management. These changes might occur secondary to muscle guarding as a protective mechanism (often present in patients with FS (Hollmann et al., 2018)) and altered limb use, possibly resulting in osteopenia or muscle atrophy (Brun, 2019). Conflicting evidence has been reported for changes in shoulder internal and external rotation strength between patients with FS and asymptomatic individuals (Jurgel et al., 2005; Lin et al., 2009). Presence of pain may also result in decreased maximal voluntary muscle strength (Graven-Nielsen et al., 1997).
Restricted range of motion (ROM) and pain may impair shoulder function with earlier or more scapular rotation. Current research using sophisticated equipment (e.g., Optotrak) has shown that, in people with FS, the scapula of the affected shoulder moves earlier and faster in upward rotation during flexion and abduction compared to the unaffected shoulder (Vermeulen et al., 2002; Fayad et al., 2008). Whether these altered kinematics can be detected clinically with more easy applicable tools such as visual observation or a plurimeter is unknown.

Pain and swelling could interfere with proprioception at various neurophysiological levels of processing in the complex neurological pathway, although the exact mechanism remains unclear (Roijezon et al., 2015; Ager et al., 2020). Joint position sense, one sub-modality of proprioception, is frequently examined (Fabis et al., 2016) and refers to the ability of an individual to determine body segment positions and movements in space based on sensory signals provided by muscle, joint and skin to the brain (Goble, 2010). People with shoulder pain can present proprioception disturbances (Sahin et al., 2017; Lubiatowski et al., 2019; Ager et al., 2020). However, proprioception has not been investigated in patients with FS previously. Therefore, recognition of altered proprioception in subjects with FS may guide our interventions.

Therefore, the primary aim of the current study was to compare muscle strength, scapular kinematics, and proprioception between affected and unaffected shoulders in patients with FS. Secondarily, comparisons in the above-mentioned biomechanical factors and blood glucose levels between patients with FS and asymptomatic individuals were investigated. It was hypothesized that significant differences in the listed outcome measures would be found within patients with FS for the affected and unaffected side and between patients with FS and controls. This explorative knowledge might offer a foundation for additional longitudinal research to explore the role of HbA1c-levels, muscle strength, scapula kinematics, and proprioception in patients with FS as potential risk factors or treatment targets.

Methods

Study design

This cross-sectional study was performed at the department of Rehabilitation Sciences and Physiotherapy of authors' affiliation. The study was approved by the Human/clinical Research Ethics Committee of the authors' affiliation. Data was collected between May 2018 and September 2020 by the first author. Written informed consent was obtained from all participants prior to commencement of the study.

Participants

Patients with FS were recruited from the orthopedic and endocrinology departments of a local hospital and general practitioner practices in authors' city. A sample of convenience of asymptomatic individuals was recruited from relatives of study participants. Asymptomatic individuals were matched for age, gender, body mass index, and hand dominance to the patients with FS. The diagnosis of FS was established from a clinical guideline (Kelley et al., 2013) and set independently by two healthcare practitioners (physical therapist, orthopedic surgeon, or endocrinologist). Table 1 shows the eligibility criteria for both patients with FS and asymptomatic individuals.

Table 1. eligibility criteria.

	Inclusion	Exclusion
Overall	• Understand the Dutch language	• Pregnant or breastfeeding
Frozen shoulder	• FS in Stage 1 or 2 as defined by Hannafin & Chiaia (2000): duration of symptoms <9 months, pain with active and passive shoulder ROM & significant limitation of flexion, abduction, internal rotation, external rotation • At least a 25% passive ROM deficit in two or more motion planes and 50% decreased in external rotation at 0° of abduction compared to the unaffected shoulder (Kelley et al., 2013) • Pain and movement restriction for at least 1 month which reached a plateau or were deteriorating (Kelley et al., 2013)	• Symptoms improved in the last month • Shoulder surgery during the last year • Locked dislocation • Glenohumeral arthritis, fractures, or avascular necrosis

Asymptomatic individuals	• Matched for gender, age (±5 years), BMI (height and weight ±5 cm and ±5 kg, respectively), and hand dominance to the FS group	• More than seven days of pain or discomfort in the neck-shoulder region during the last year and pain intensity on a NRS >2/10 (Juul-Kristensen et al., 2006) • Pain or discomfort in more than three body regions for more than 30 days during the last year and pain intensity at the time of measurement on a NRS >2/10 (Juul-Kristensen et al., 2006) • History of upper arm or shoulder fracture, shoulder surgery, or another shoulder pathology • Neurologic disorders • Systemic diseases (e.g., DM, rheumatoid arthritis) • Cardiovascular diseases • Osteoarthritis • Depression or other psychiatric disorders • Medication intake: pain killers or drugs influencing pain <48 hours before the examination, opioids, anti-depressives, and anti-epileptics <2 weeks before the examination, and use of steroids or antihistamines

FS: frozen shoulder; ROM: range of motion; BMI: body mass index; NRS: numeric rating scale; DM: diabetes mellitus.

Procedure

First, participants had to complete three questionnaires: a socio-demographic questionnaire, the Shoulder Pain and Disability Index (SPADI) and the McGill Pain Questionnaire (MPQ). The specific questionnaires have been shown to be valid and reliable in people with FS (Roy et al., 2009; Katz & Melzack, 2011).

Second, an extensive physical examination of the shoulder was performed in a standardized order. Blood glucose levels (HbA1c), shoulder ROM, shoulder muscle strength, scapular kinematics (with visual observation and by using two plurimeters) during shoulder abduction, and shoulder proprioception (joint position sense) were measured.

Physical examination

An overview of the physical examination performed is presented in Table 2. Physical examination was performed by the first author, who was not blinded to participants' status (frozen shoulder or asymptomatic).

Table 2. Overview of physical examination performed.

Measurement outcome	Description
Blood glucose levels	The HbA1c was measured with the A1CNow$^+$-system (PTS diagnostics, Whitestown, USA). A drop of blood (5µL) was collected via a small pinprick after disinfecting the middle finger. This drop was used for analysis and thus calculation of the HbA1c.
Shoulder range of motion	Measured with an analogue plurimeter (Dr Jules Rippstein, La Conversion, Switzerland). Both active and passive ROM were measured at both shoulders, with active measurements always preceding passive ones. The side measured first was allocated based on an excel-generated random sequence. Shoulder range of motion measurements have been found to be reliable (Tveita et al., 2008).
External rotation (at 0°, 30°, 60° and 90° abduction)	Participants lay supine and the plurimeter was attached to the dorsal side of the distal forearm (Tveita et al., 2008). In each of the different abduction positions, shoulder external rotation was measured. The different shoulder abduction angles were previously determined with the help of a goniometer.
Internal rotation (at 30°, 60° and 90° abduction)	Participants lay supine and the plurimeter was attached to the volar side of the distal forearm (Tveita et al., 2008). In each of the different abduction positions, shoulder external and internal rotation was measured. The different shoulder abduction angles were previously determined with the help of a goniometer.

Flexion and abduction	Participants were in a sitting position, with the hips and knees flexed 90° and the feet flat on the floor. The plurimeter was attached to the upper arm, just below the insertion of the deltoid muscle (Tveita et al., 2008). Flexion and abduction movements were performed in the sagittal and frontal plane, respectively, with the thumb pointing upwards.
Shoulder muscle strength	Measured using a handheld dynamometer (Microfet 2.0, Hoggan Health Industries Inc., USA). All participants were asked to perform an isometric contraction, conform the make-test (Conable & Rosner, 2011). The side to be measured first was randomized in the same way as the shoulder ROM measurements. During all measurements, participants were sitting with their hips and knees flexed 90° and the feet flat on the floor. Handheld dynamometry is reliable and valid for measuring shoulder muscle strength (Cools et al., 2014).
Abduction	Participants were asked to position their arm in 90° abduction in the scapular plane with the thumb pointing upwards (full can position) (Klironomos et al., 2020). The dynamometer was placed at the radial side of the wrist and participants were asked to push against the dynamometer (i.e., make test (Conable & Rosner, 2011)). When the participant was unable to reach the 90° abduction position (e.g., due to pain), the test was performed 10° below the participant's maximal abduction position in the scapular plane.
External rotation	Participants were asked to position their arm at the side with the elbow flexed 90° and the forearm in neutral position (thumb pointing upwards) (Cools et al., 2014). The dynamometer was placed on the dorsal side of the wrist and participants were asked to push (make test) the hand outward (external rotation).

Internal rotation	Participants were asked to position their arm at the side with the elbow flexed 90° and the forearm in neutral position (thumb pointing upwards) (Cools et al., 2014). The dynamometer was placed on the volar side of the wrist and participants were asked to push (make test) the hand inward.
Lift-off	Measurement was done in the lift-off position (hand behind back) in those participants that were able to reach this position. Participants put their hand on the lower back, with the elbow flexed 90° and the forearm in a neutral position (thumb pointing upward) (Klironomos et al., 2020). The dynamometer was placed on the volar side of the wrist and participants were asked to push against it as trying to move the hand away from the back (make test).
Scapular kinematics	
Static visual observation	Three different shoulder positions were used: at rest, with both hands on the ipsilateral hips and at 90° shoulder abduction and observed from dorsal (Struyf et al., 2009). Abnormalities in the scapula position were rated as tilting, winging or both. This method for measuring static scapula posture has been shown to be reliable (Struyf et al., 2009).
Dynamic observation	Part of the Scapular Dyskinesis Test (McClure et al., 2009) was used for dynamic observation of the scapula. Participants were asked to elevate their arms in abduction for 5 times, while the examiner observed the behavior of the scapula from behind (at 150 cm). Scapular behavior was classified as normal, or subtle or obvious abnormality (McClure et al., 2009). The Scapular Dyskinesis Test has been shown to be reliable and valid for assessing the dynamic behavior of the scapula (McClure et al., 2009).
Scapular upward rotation (Fig. 1)	Measured by using two plurimeters (Dr Jules Rippstein, La Conversion, Switzerland) as previously described by Watson et al. (2005). Participants were asked to perform shoulder abduction in the frontal plane with the thumb pointing upward and full

	extension of the elbow, stopping at 30°, 60°, 90°, 120° and 150° degrees of abduction or their maximal achievable range. The SUR was measured at each angle of shoulder abduction. This method for measuring scapular upward rotation has been found to be reliable and valid (Watson et al., 2005; Camargo et al., 2018).
Proprioception	Measured by using a joint position sense test (Ager et al., 2017). During this test, participants were sitting with the hips and knees flexed 90° and the feet flat on the floor. They were first asked to move their arm, with the thumb pointing upwards, to a position half of the previously measured maximal shoulder flexion or abduction ROM with the eyes opened. A plurimeter attached to the upper arm just below the insertion of the deltoid muscle allowed the examiner to check this half position was correctly reached and provide feedback to participants. Participants then tried to actively relocate their arm in the half position of shoulder abduction and flexion but with eyes closed. The deviation in degrees between the achieved participants' position and the half positions of shoulder flexion and abduction ROM were taken as the joint position error and used for analysis. This method has been found to be reliable (Ager et al., 2017).

HbA1c: glycosylated hemoglobin

Figure 1. Measurement of scapular upward rotation by using two inclinometers.

Statistics

Based on the aim to detect effect sizes (ES) of at least 0.7 in muscle strength between both groups (based on medium to large ES), a power of 0.80 and an α-level of 0.05 at least 34 participants in each group were required. G*Power 3.1 was used to calculate the sample size. Normal distribution as well as success of matching was checked with the Shapiro-Wilk test and independent T-test (or Mann-Whitney-U), respectively. Mean, standard deviation (SD) and 95% confidence intervals (95%-CI) for each group are presented for continuous variables and for categorical variables number and percentage are presented. Mean differences (MD) and 95%-CI are presented for continuous variables regarding group differences. To determine the difference between affected and unaffected side in patients with FS linear mixed models were fitted using restricted maximum likelihood. To account for the dependence between measurements from the same individual, individual identifier was entered as random effect. Shoulder muscle strength, scapular upward rotation (SUR), and proprioception were entered as dependent variables and side (affected/unaffected) was the independent variable. Difference in scapular position between sides was determined with the Fisher's exact test.

For comparison between patients with FS and asymptomatic individuals for continuous variables, first the values of the dominant and non-dominant side in asymptomatic individuals were compared. If no difference was present, the mean of both sides was used for between-group comparison. If a difference between sides was present in asymptomatic individuals for continuous variables and for categorical variables, the affected dominant or affected non-dominant side of patients with FS was compared with their respective side in asymptomatic individuals. An additional distinction between affected and unaffected was made. Between-group differences were analyzed with an independent T-test (or Mann-Whitney-U) for continuous variables and Fisher's exact test for categorical variables. To assess the extent of differences between groups, ES was calculated using either Hedge's g or Glass Δ (in case of different SDs) (Lakens, 2013). Effect sizes were interpreted as follows: 0.2: small; 0.5: medium; ≥0.8: large (Sullivan & Feinn, 2012), where small is considered clinically irrelevant, medium possibly clinically relevant, and large clinically relevant. Since a multitude of hypothesis tests were performed, a multiple testing correction on the p-values was implemented. Therefore, the Bonferroni-correction was applied, and the significance level was set at α <.00042 (=.05/118). Statistical analysis was performed in R (version 3.6.2, Vienna Austria). Between and within group differences were analyzed using add-on packages compareGroups (Subirana et al., 2014), lme4 (Bates et al., 2015), and pbkrtest (Halekoh & Højsgaard, 2014).

Results

Participants

Figure 2 shows the participant flow. Finally, a total of 70 participants were included (35 with FS and 35 asymptomatic-matched individuals). Table 3 shows the characteristics of all included participants. The group characteristics show that matching and selection based on the inclusion criteria for FS were successful. There was a significant difference between groups in SPADI (both pain, disability, and total score), all domains of the MPQ. Additional information about the ROM in patients with FS can be found in Supplementary Table 1.

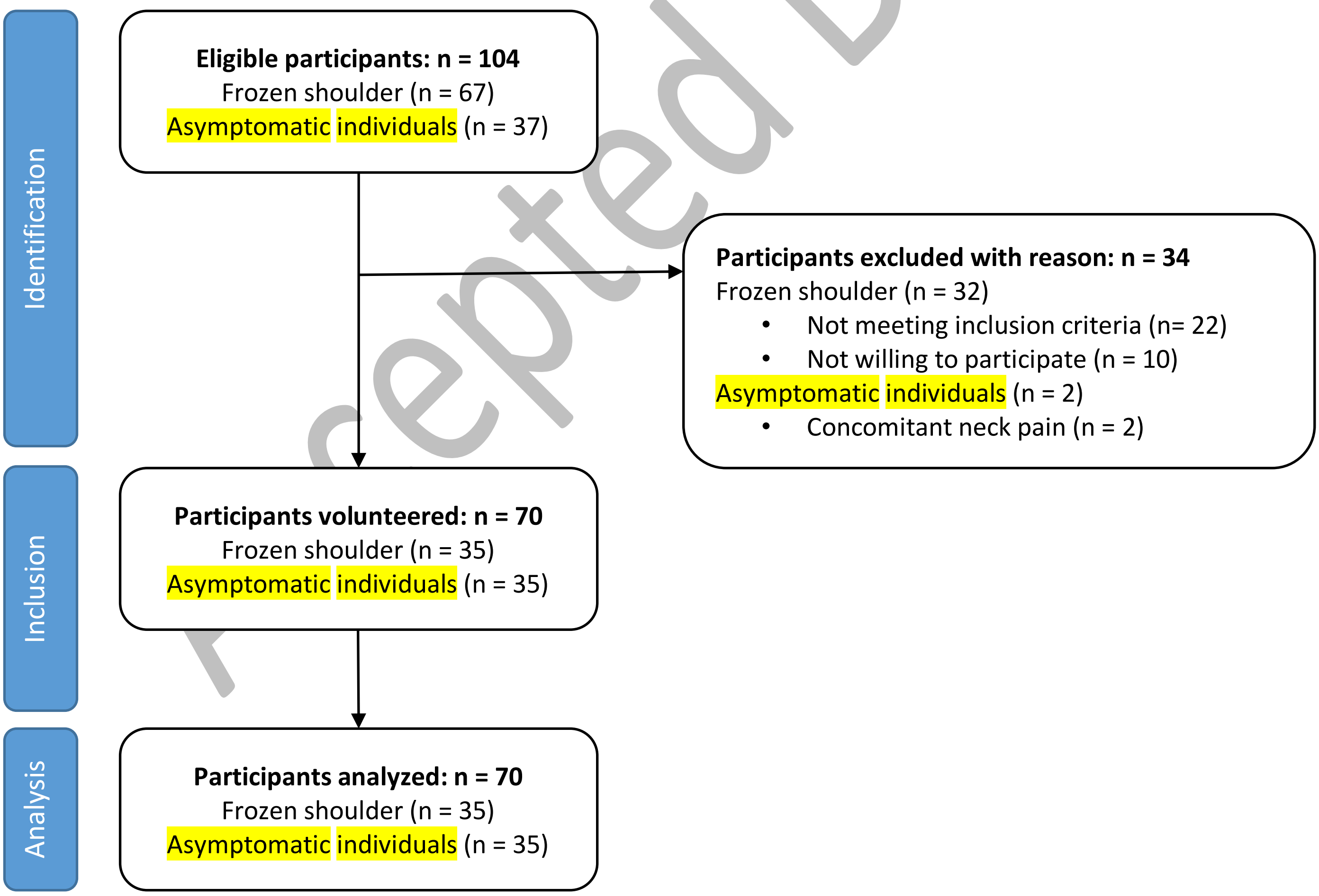

Figure 2. Participant flowchart.

Table 3. Participant anthropometric characteristics, mean, SD and [95%-CI] are presented for continuous variables; number and percentage are presented for nominal variables.

		Frozen shoulder (*n=35*)	**Asymptomatic (*n=35*)**	**Mean difference [95%-CI]**	**p-value**
Personal characteristics	Age (years)	53.40±8.95 [50.32;56.48]	52.60±6.93 [50.22;54.98]	0.80 [-3.02;4.62]	0.677
	Gender (Female)	23 (65.71%)	21 (60.00%)	NA	0.805
	Weight (kg)	75.25±15.21 [70.02;80.47]	72.26±13.34 [67.67;76.84]	2.99 [-3.83;9.82]	0.385
	Length (cm)	170.69±7.27 [168.19;173.18]	172.80±9.53 [169.53;176.07]	-2.11 [-6.16;1.93]	0.417
	BMI (kg/m^2)	25.71±4.24 [24.26;27.17]	24.07±3.10 [24.26;27.17]	1.65 [-0.13;3.42]	0.064
	Dominant side (right)	29 (82.86%)	29 (82.86%)	NA	1.000
	Affected side (right)	13 (39.39%)	NA	NA	NA
	Dominant side involved (yes)	14 (42.42%)	NA	NA	NA
	Cause frozen shoulder (primary)	15 (42.86%)	NA	NA	NA
	Diabetes Mellitus (yes)	2 (5.71%)	0 (0.00%)	NA	0.493
	How many days/week did you work?	4.50±1.00 [2.91;6.09]	4.06±0.81 [3.43;4.68]	0.44 [-1.03;1.92]	0.366
	How many hours/week did you work?	19.00±8.43 [8.54;29.46]	28.38±9.18 [20.70;36.05]	-9.38 [-20.58;1.83]	0.091
	How many days/week did you play sports?	3.30±1.70 [2.08;4.52]	3.35±1.77 3.35 [2.63;4.06]	-0.05 [-1.40;1.30]	0.899
	How many hours/week did you play sport?	3.06±2.34 [1.11;5.02]	4.67±3.26 [3.38;5.95]	-1.60 [-3.80;0.59]	0.159
Questionnaires	**SPADI (pain items, 0-100)**	**69.60±16.70 [63.86;75.34]**	**0.40±1.80 [-0.22;1.02]**	**69.20 [63.43;74.97]**	**<0.0001**
	SPADI (disability items, 0-100)	**65.14±19.54 [58.43;71.85]**	**0.18±0.87 [-0.12;0.48]**	**64.96 [58.25;71.68]**	**<0.0001**
	SPADI (total score, 0-100)	**66.86±17.15 [60.97;72.75]**	**0.26±0.95 [-0.06;0.59]**	**66.59 [60.70;72.49]**	**<0.0001**

	Frozen shoulder (*n=35)*	Asymptomatic (*n=35)*	Mean difference [95%-CI]	p-value
McGill (emotional, 0-15)	**3.06±3.39 [1.89;4.22]**	**0.06±0.24 [-0.02;0.14]**	**3.00 [1.83;4.17]**	**<0.0001**
McGill (sensory, 0-36)	**8.60±6.07 [6.51;10.69]**	**0.86±1.59 [0.31;1.40]**	**7.74 [5.60;9.89]**	**<0.0001**
McGill (evaluative, 0-12)	**5.09±2.96 [4.07;6.10]**	**1.03±1.90 [0.38;1.68]**	**4.06 [2.87;5.25]**	**<0.0001**
McGill (quality of life, 0-27)	**12.17±5.76 [10.19;14.15]**	**3.57±12.66 [-0.78;7.92]**	**8.60 [3.87;13.33]**	**<0.0001**
McGill (total score, 0-63)	**16.74±10.79 [13.04;20.45]**	**1.94±3.30 [0.81;3.08]**	**14.80 [10.95;18.65]**	**<0.0001**
McGill (current VAS, 0-100)	**34.51±26.04 [25.57;43.46]**	**2.18±4.55 [0.57;3.80]**	**32.33 [23.26;41.40]**	**<0.0001**

BMI: body mass index; NA: not applicable; ER: external rotation; IR: internal rotation; SPADI: shoulder pain and disability index.

Variables in bold indicate a significant difference between groups (p<0.0001).

Shoulder muscle strength, scapular kinematics, and shoulder proprioception

Within group comparisons

Table 4 shows the within-group comparison results for patients with FS (affected vs. unaffected shoulder) and asymptomatic individuals (dominant vs. non-dominant shoulder). In patients with FS *muscle strength* of the affected shoulder was decreased in all directions compared to the unaffected shoulder. *SUR* was increased in the affected shoulder at 30° and 60° abduction compared to the unaffected shoulder. No difference was found between the affected and unaffected shoulders for *scapular visual observation, SUR* at rest and at 90° abduction, and *shoulder joint position error* in the FS group.

In asymptomatic individuals, no difference between shoulders was found for shoulder *muscle strength* in all directions, *scapular visual observation, SUR,* and *shoulder joint position error*.

Between-group comparisons

Figure 3-5 and Table 5 show the between-group comparisons. In asymptomatic individuals, no difference between shoulders was found in any measurement. Therefore, all values of patients with FS were compared to the mean of the dominant and non-dominant shoulder in asymptomatic individuals.

Shoulder muscle strength in all directions (shoulder abduction and shoulder external and internal rotation, including the lift-off position) was lower in the affected shoulder in patients with FS compared to asymptomatic individuals. ES for shoulder muscle strength ranges from -2.37 to -1.49. In patients with FS *SUR* was increased at 30° and 60° abduction on the affected side, but not at rest and 90° abduction compared to asymptomatic individuals. ES for SUR vary from 0.78 to 3.67. Regarding *scapular visual observation* and shoulder *proprioception*, no differences between patients with FS and asymptomatic individuals were found.

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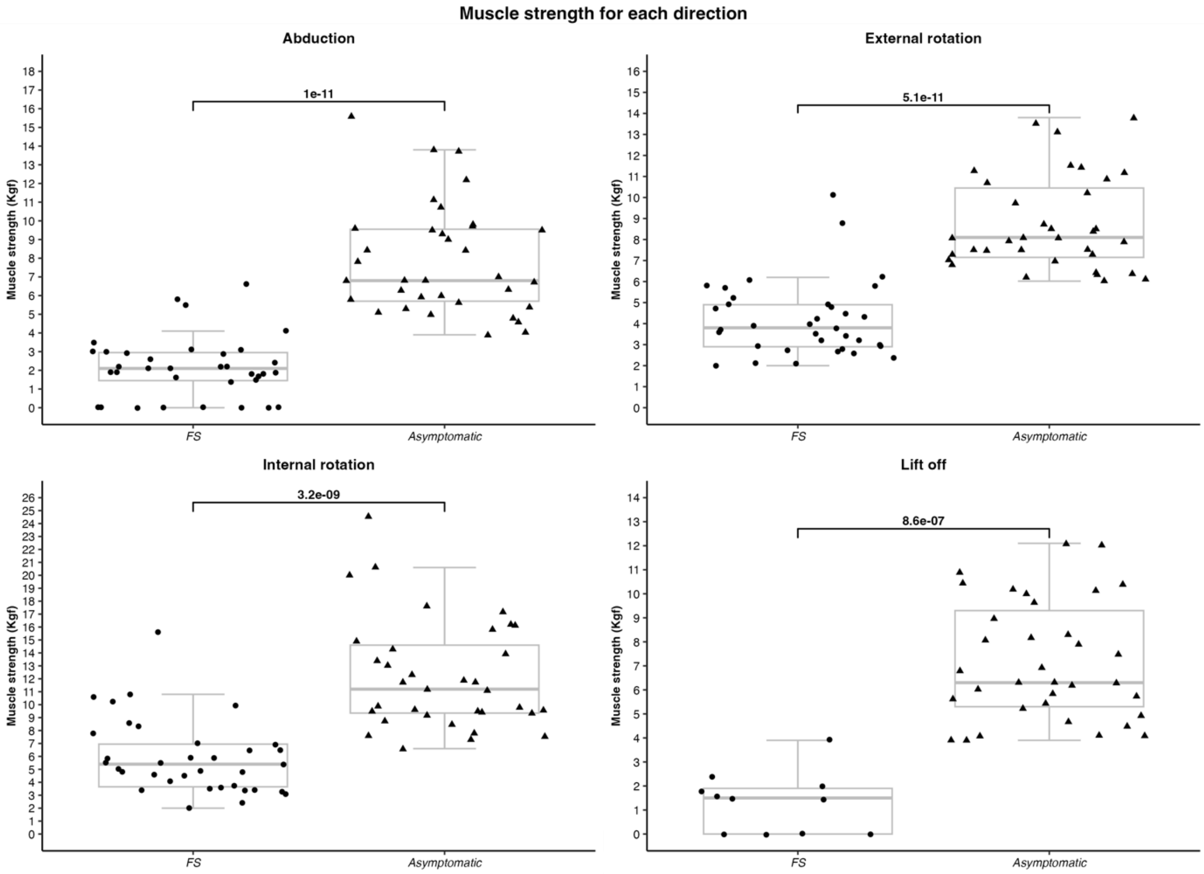

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286 *Figure 3. Group comparison for the 4 directions of muscle strength. FS: frozen shoulder.*

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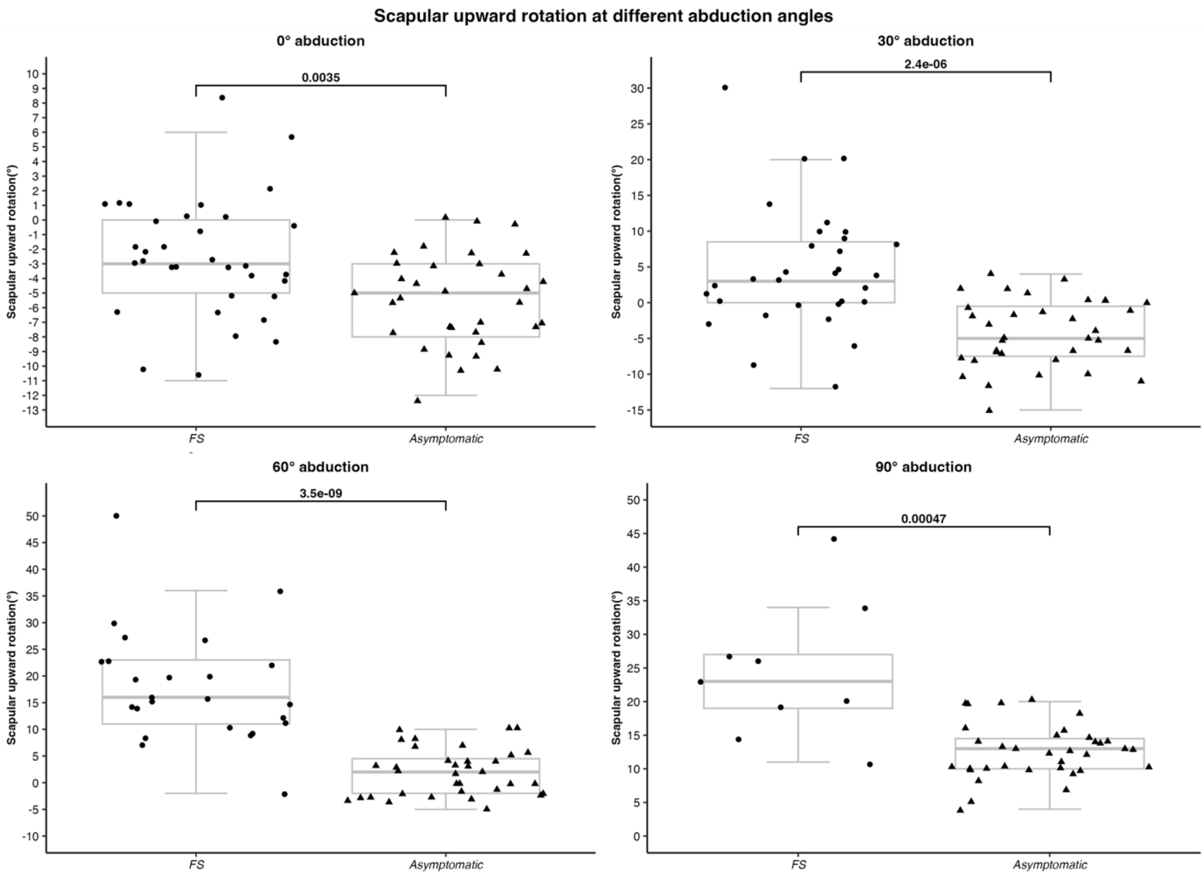

Figure 4. Group comparison for scapular upward rotation. FS: frozen shoulder.

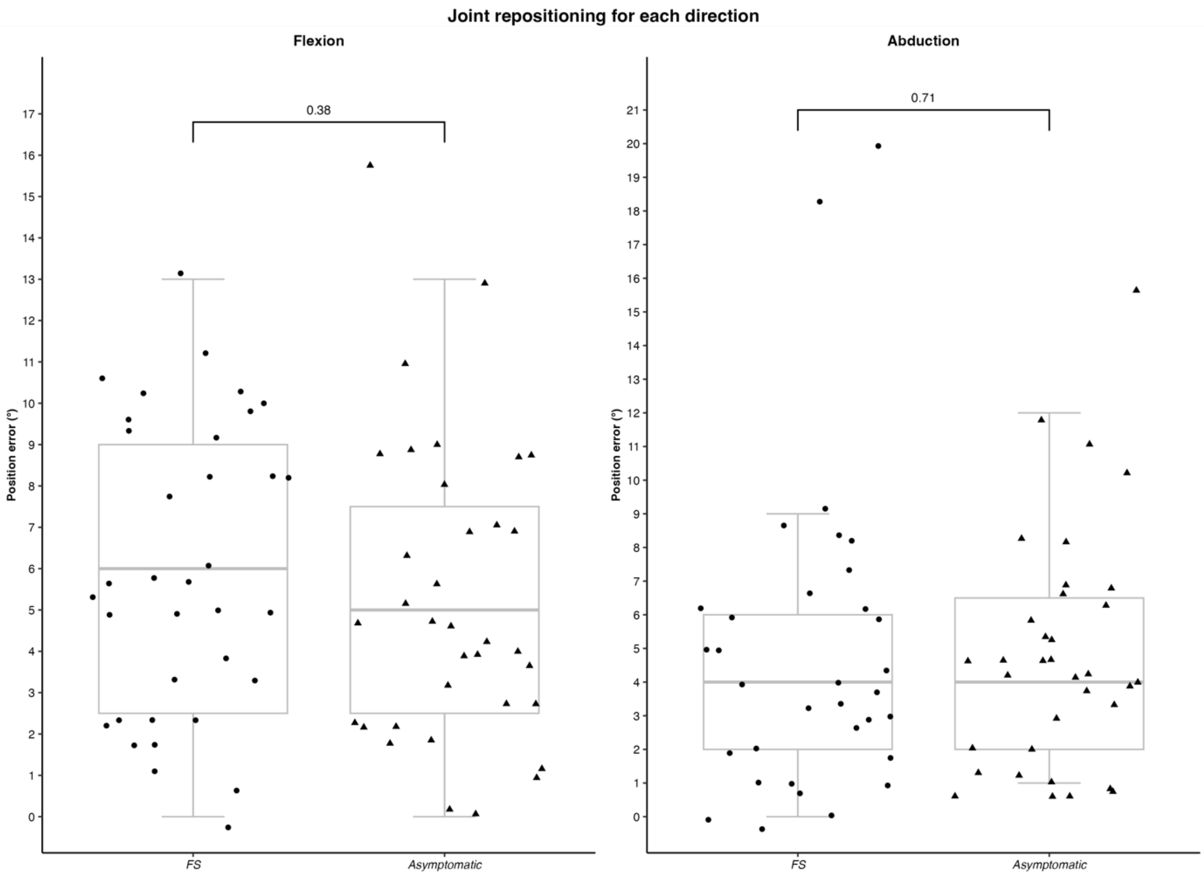

Figure 5. Group comparison for the 2 directions of joint repositioning. FS: frozen shoulder.

Table 4. Within-group results for shoulder muscle strength, scapular kinematics, and shoulder proprioception.

		Affected-unaffected comparison			Dominant-non-dominant comparison	
	Frozen shoulder (*n=35*)	**Mean difference [95%-CI]**	**p-value**	**Asymptomatic (*n=35*)**	**Mean difference [95%-CI]**	**p-value**
Muscle strength (kg)						
90° abduction affected side	2.14±1.66 [1.57;2.71]	**-3.55 [-4.23;-2.86]**	**<0.0001**	7.89±2.93 [6.89;8.90]	0.27 [-0.25;0.78]	0.3018
90° abduction unaffected side	5.69±2.77 [4.73;6.64]			7.63±2.80 [6.66;8.59]		
External rotation affected side	4.19±1.79 [3.57;4.80]	**-2.70 [-3.18;-2.22]**	**<0.0001**	8.69±2.21 [7.93;9.46]	0.35 [-0.16;0.87]	0.1757
External rotation unaffected side	6.89±2.17 [6.14;7.63]			8.34±2.12 [7.61;9.07]		
Internal rotation affected side	5.92±2.88 [4.93;6.91]	**-4.01 [-5.06;-2.83]**	**<0.0001**	12.21±4.23 [10.75;13.66]	0.47 [-0.15;1.09]	0.1349
Internal rotation unaffected side	9.93±4.27 [8.46;11.39]			11.74±3.84 [10.42;13.05]		
Lift-off affected side	1.33±1.25 [0.49;2.17]	**-3.94 [-5.05;-2.83]**	**<0.0001**	7.18±2.47 [6.33;8.03]	0.05 [-0.55;0.64]	0.8694
Lift-off unaffected side	5.22±1.79 [4.59;5.85]			7.13±2.49 [6.28;7.99]		
Static scapular observation (Nothing/tilting/winging/both)						
Rest position affected side	21 (60.00%)/4 (11.43%)/ 6 (17.14%)/4 (11.43%)	NA	0.2499	20 (57.14%)/5 (14.29%)/ 7 (20.00%)/3 (8.57%)	NA	0.4723
Rest position unaffected side	25 (71.43%)/1 (2.86%)/ 8 (22.86%)/1 (2.86%)			23 (65.71%)/1 (2.86%)/ 8 (22.86%)/3 (8.57%)		

Hands on hips affected side	9 (25.71%)/4 (11.43%)/ 14 (40.00%)/8 (22.86%)	NA	0.1521	8 (22.86%)/17 (48.57%)/ 4 (11.43%)/6 (17.14%)	NA	0.1911
Hands on hips unaffected side	13 (37.14%)/8 (22.86%)/ 6 (17.14%)/8 (22.86%)			9 (25.71%)/11 (31.43%)/ 2 (5.71%)/13 (37.14%)		
90° abduction affected side	17 (50.00%)/3 (8.82%)/ 12 (35.29%)/2 (5.88%)	NA	0.7000	18 (51.43%)/0 (0.00%)/ 8 (22.86%)/9 (25.71%)	NA	0.2215
90° abduction unaffected side	22 (62.86%)/2 (5.71%)/ 8 (22.86%)/3 (8.57%)			11 (31.43%)/0 (0.00%)/ 13 (37.14%)/11 (31.43%)		
Dynamic scapular observation (normal/subtle/obvious)						
affected side	4 (11.43%)/2 (5.71%)/29 (82.86%)	NA	0.0706	20 (57.14%)/6 (17.14%)/9 (25.71%)	NA	0.4657
unaffected side	8 (22.86%)/7 (20.00%)/20 (57.14%)			16 (45.71%)/5 (14.29%)/14 (40.00%)		
Scapular upward rotation (°)						
0° abduction affected side	-2.91±4.57 [-4.48;-1.34]	0.31 [-1.36; 1.99]	0.7048	-5.69±3.55 [-6.90;-4.47]	-2.23 [-3.58;-0.88]	0.0020
0° abduction unaffected side	-3.23±5.62 [-5.16;-1.30]			-3.46±3.43 [-4.64;-2.28]		
30° abduction affected side	4.55±8.59 [1.40;7.70]	**6.55 [3.16;9.95]**	**0.00041**	-4.31±4.70 [-5.93;-2.70]	-1.06 [-3.25;1.13]	0.0713
30° abduction unaffected side	-2.09±5.61 [-4.01;-0.16]			-2.40±3.87 [-3.73;-1.07]		
60° abduction affected side	18.04±10.64 [13.65;22.43]	**12.28 [8.05;16.51]**	**<0.0001**	1.94±4.39 [0.44;3.45]	-0.60 [-3.32;2.11]	0.0187
60° abduction unaffected side	5.66±5.78 [3.67;7.64]			4.31±5.00 [2.60;6.03]		

90° abduction affected side	24.22±10.15 [16.42;32.02]	7.26 [1.42;13.10]	0.0174	12.54±4.03 [11.16;13.93]	-2.23 [-4.05;-0.41]	0.0179
90° abduction unaffected side	17.26±6.73 [14.92;19.61]			14.77±5.41 [12.91;16.63]		
120° abduction affected side	NA	NA	NA	24.57±3.97 [23.21;25.93]	-1.06 [-3.25;1.13]	0.3332
120° abduction unaffected side	28.73±7.41 [26.10;31.36]			25.63±5.68 [23.68;27.58]		
150° abduction affected side	NA	NA	NA	36.23±5.91 [34.06;38.39]	-0.60 [-3.32;2.11]	0.6539
150° abduction unaffected side	39.64±7.03 [36.52;42.75]			36.88±6.59 [34.54;39.22]		
Joint position error (°)						
Flexion affected side	5.94±3.52 [4.73;7.15]	-0.63 [-2.43; 1.17]	0.4829	5.34±3.69 [4.07;6.61]	0.60 [-0.61;1.81]	0.3210
Flexion unaffected side	6.57±4.26 [5.11;8.03]			4.74±4.15 [3.32;6.17]		
Abduction affected side	4.88±4.49 [3.29;6.47]	-0.18 [-2.13; 1.78]	0.8540	4.86±3.52 [3.65;6.07]	-0.17 [-1.42;1.07]	0.7814
Abduction unaffected side	5.06±3.39 [3.89;6.22]			5.03±4.90 [3.34;6.71]		

NA: not applicable.

P-values in bold indicate a significant difference (p<0.00042)

Table 5. Between-group differences for shoulder muscle strength, scapular kinematics, and shoulder proprioception.

			Between-group comparison		
	Frozen shoulder (*n=35*)	**Asymptomatic (*n=35*)**	**Mean difference [95%-CI]**	**p-value**	**Effect size [95%-CI]**
		Muscle strength (kg)			
90° abduction affected side	**2.14±1.66 [1.57;2.71]**	**7.76±2.76 [6.81;8.71]**	**-5.62 [-6.71;-4.53]**	**<0.0001**	**-1.96 [-2.56;-1.36] (Glass Δ)**
External rotation affected side	**4.19±1.79 [3.57;4.80]**	**8.52±2.03 [7.82;9.22]**	**-4.33 [-5.25;-3.42]**	**<0.0001**	**-2.22 [-2.81;-1.62] (Hedge's g)**
Internal rotation affected side	**5.92±2.88 [4.93;6.91]**	**11.97±3.94 [10.62;13.32]**	**-6.05 [-7.70;-4.40]**	**<0.0001**	**-1.49 [-2.01;-0.95] (Glass Δ)**
Lift-off affected side	**1.33±1.25 [0.49;2.17]**	**7.16±2.32 [6.36;7.96]**	**-5.83 [-6.94;-4.72]**	**<0.0001**	**-2.37 [-3.08;-1.65] (Glass Δ)**
		Static scapular observation (Nothing/tilting/winging/both)			
Rest position dominant side affected	9 (64.29%)/1 (7.14%)/1 (7.14%)/3 (21.43%)	20 (57.14%)/5 (14.29%)/7 (20.00%)/3 (8.57%)	NA	0.4598	NA
Rest position non-dominant side affected	11 (57.89%)/3 (15.79%)/4 (21.05%)/1 (5.26%)	23 (65.71%)/1 (2.86%)/8 (22.86%)/3 (8.57%)	NA	0.4651	NA
Hands on hips dominant side affected	2 (14.29%)/3 (21.43%)/5 (35.71%)/4 (28.57%)	8 (22.86%)/17 (48.57%)/4 (11.43%)/6 (17.14%)	NA	0.1292	NA
non-dominant side affected	6 (31.58%)/1 (5.26%)/8 (42.11%)/4 (21.05%)	9 (25.71%)/11 (31.43%)/2 (5.71%)/13 (37.14%)	NA	0.0032	NA
90° abduction dominant side affected	5 (35.71%)/2 (14.29%)/6 (42.86%)/1 (7.14%)	18 (51.43%)/0 (0.00%)/8 (22.86%)/9 (25.71%)	NA	0.0424	NA
non-dominant side affected	12 (63.16%)/1 (5.26%)/5 (26.32%)/1 (5.25%)	11 (31.43%)/0 (0.00%)/13 (37.14%)/11 (31.43%)	NA	0.0180	NA

Dynamic scapular observation (normal/subtle/obvious)					
dominant side affected	2 (14.29%/0 (0.00%)/12 (85.71%)	20 (57.14%)/6 (17.14%)/9 (25.71%)	NA	0.0006	NA
non-dominant side affected	2 (10.53%)/1 (5.26%)/16 (84.21%)	16 (45.71%)/5 (14.29%)/14 (40.00%)	NA	0.0062	NA
Scapular upward rotation (°)					
0° abduction affected side	-2.91±4.57 [-4.48;-1.34]	-4.57±2.89 [-5.56;-3.58]	1.66 [-0.17;3.49]	0.0533	0.78 [0.21;1.35] (Glass Δ)
30° abduction affected side	**4.55±8.59 [1.40;7.70]**	**-3.36±2.97 [-4.38;-2.34]**	**7.91 [4.62;11.19]**	**<0.0001**	**1.89 [1.03;2.73] (Glass Δ)**
60° abduction affected side	**18.04±10.64 [13.65;22.43]**	**3.13±3.75 [1.84;4.42]**	**14.91 [10.36;19.46]**	**<0.0001**	**3.67 [2.32;4.99] (Glass Δ)**
90° abduction affected side	24.22±10.15 [16.42;32.02]	13.66±3.97 [12.29;15.02]	10.57 [2.72;18.41]	0.0141	2.90 [1.07;4.69] (Glass Δ)
120° abduction affected side	NA	25.10±3.72 [23.82;26.38]	NA	NA	NA
150° abduction affected side	NA	36.69±5.29 [34.87;38.50]	NA	NA	NA
Joint position error (°)					
Flexion affected side	5.94±3.52 [4.73;7.15]	5.04±3.51 [3.84;6.25]	0.90 [-0.78;2.58]	0.2634	0.16 [-0.30;0.63] (Hedge's g)
Abduction affected side	4.88±4.49 [3.29;6.47]	4.94±3.86 [3.62;6.27]	-0.06 [-2.10;1.97]	0.8391	<0.01 [-0.54;0.55] (Glass Δ)

NA: not applicable.

P-values in bold indicate a significant difference (p<0.00042)

Blood glucose levels

The mean ± SD [95%-CI] for HbA1c for patients with FS was 5.28±0.68% [5.03;5.53] and for asymptomatic individuals 4.86±0.36% [4.73;4.98]. There were no differences between groups for HbA1c-level (p=0.0056, ES (Hedge's g): 0.78 [0.27;1.28]).

Discussion

This is the first study that has compared shoulder muscle strength, scapular kinematics (with clinical applicable tools), shoulder proprioception, and blood glucose levels between patients with FS and asymptomatic individuals. Regarding shoulder muscle strength, patients with FS were weaker into shoulder abduction, external and internal rotation in their affected shoulder compared to both the unaffected shoulder and asymptomatic individuals. Patients with FS showed statistically elevated SUR as measured with a plurimeter at 30° and 60° abduction in their affected shoulder compared to the unaffected shoulder and controls. However, we could not visually detect significant differences in scapular kinematics between shoulders in patients with FS or when compared to controls. Moreover, no differences in shoulder proprioception were found between sides or groups. Finally, our results indicate that no difference was present between patients with FS and asymptomatic individuals regarding blood glucose levels (HbA1c).

Shoulder muscle strength

The differences in muscle strength between patients with FS and asymptomatic individuals were in the order of 4.33-6.05 Kg, with large ES. Therefore, these differences are considered clinically relevant and reflect true differences. Lin et al. (2009) found only a decreased internal rotation isometric muscle strength in patients with FS compared to asymptomatic individuals, but not in external rotation strength, whereas Jurgel et al. (2005) found a decreased muscle strength between patients with FS and controls in abduction and external rotation, but not in internal rotation. Our results are in line with these conflicting results, since they show a decrease in muscle strength between groups for shoulder abduction and internal and external rotation. These discrepancies between studies might be due to differences in sample size (8 and 10 vs. 35 in the present study) or the measurement method employed (isokinetic dynamometry vs. handheld dynamometry).

Scapular kinematics

Our results show moderate to large ES for a difference in SUR between patients with FS and controls (although not all are statistically significant), this indicate that the differences found in SUR below shoulder height can be considered clinically meaningful. The non-significant difference in SUR between patients with FS and asymptomatic individuals at 90° abduction might be explained by the low number of patients achieving 90° abduction (Figure 4). Consequently, this non-significant difference might be a result of a lack of statistical power. The use of a plurimeter is more useful than visual observation of scapular movement, since no differences between sides and groups were found with observation. With an increased SUR, patients try to compensate for the global ROM restriction and provide a more effective scapular position for arm elevation (Fayad et al., 2008). This compensation strategy was confirmed by Vermeulen et al. (2002), as they found normalized SUR after rehabilitation through intensive passive end-range mobilization techniques.

Our results show that patients with FS demonstrate earlier SUR in their affected shoulder compared to the unaffected shoulder during abduction, which is similar to prior studies (Vermeulen et al., 2002; Fayad et al., 2008). Fayad et al. (2008) analyzed the SUR further and found no difference in SUR between sides at rest, which is in accordance with our results. Moreover, they found more SUR in the affected shoulder compared to the unaffected shoulder at all elevation angles (Fayad et al., 2008), which is contrary to our results (only 30 and 60°abduction). The different methods employed for SUR measurement (3-dimensional equipment vs. 1-dimensional manual measurement) may explain this discrepancy.

Visual observation probably lacks sensitivity to detect changes in scapular kinematics in patients with FS compared to more objective techniques (i.e., using two plurimeters), since our results did not show a difference within participants and between groups.

Shoulder proprioception

Although it was expected that proprioception was altered in patients with FS compared to controls, this was not the case, and it might me due to two reasons. First, the pain experienced by the FS group was already decreased to a level that does not affect the proprioception anymore. Second, the method used for proprioception measurement (joint position sense test) may not be sufficiently sensible to detect differences in proprioception (Ager et al., 2020). Therefore, other modalities of shoulder proprioception testing such as kinesthesia, may be used in the future to detect differences, if any, in proprioception between patients with FS and asymptomatic individuals (Ager et al., 2020).

We are not aware of studies that have previously compared patients with FS to asymptomatic individuals in terms of proprioception. Indeed, most of the literature regarding proprioception testing has been done in people with shoulder instability where deficits in proprioception are more common (Ager et al., 2020).

Blood glucose levels

The study's results did not show statistically significant differences in HbA1c-levels between patients with FS and asymptomatic individuals. Although the ES was moderate, the absolute difference was only 0.42%. The moderate ES indicates that further exploration of HbA1c-levels is necessary. Although previous studies found elevated blood glucose levels in patients with FS (Pietrzak, 2016), others did not and found similar results to ours (Chan et al., 2017). Furthermore, equal HbA1c-levels between diabetic patients with and without FS have been shown (Balci et al., 1999; Yian et al., 2012). Our study's limitation, involving a single HbA1c measurement taken within a three-month window

(Goldstein et al., 2003), may explain this similarity with prior observations. It is plausible that this limited time interval may not capture the full impact of inflammatory and glycation on local tissue. Chan et al. (2017) used an alternative method by calculating accumulated HbA1c-levels, where an association of the complete inflammatory and glycation burden with FS could be demonstrated. Another option could involve examining fasting glucose levels, which have shown associations with FS (Park et al., 2020).

Clinical implications

The results of this study propose assessing shoulder muscle strength using a handheld dynamometer and evaluating scapular kinematics with a plurimeter. These measurements are important as they can be altered in patients with FS.

Impaired muscular performance may result in joint dysfunction (Lin et al., 2009) and evidence of impaired muscular strength was detected in patients with FS in the current study, it may be important to incorporate assessment of muscle performance in this population. If assessment reveals reduced muscle strength compared to the contralateral side, the next step could be to incorporate strength training in the rehabilitation program, preferably based on and guided by tissue irritability levels (Kelley et al., 2013).

Optimal scapular position and movement are required for achieving normal upper extremity function (Kibler & Sciascia, 2010). Our results provide evidence to support the assessment of SUR in patients with FS and we suggest using two plurimeters to assess the SUR instead of visual observation.

Strengths

A strength of the current study is the clinical assessment to assess various functional parameters in patients with FS, which is easy and convenient to use in clinical practice. This increases the clinical relevance. Despite the lack of a gold standard, which complicates diagnosis (Konarski et al., 2020), the diagnosis was established using strict eligibility criteria and was set independently by multiple healthcare practitioners. Therefore, we are confident that all patients were correctly diagnosed with FS and were in fact in the early phase of the disorder.

Limitations

Our results need to be interpreted with caution, in the light of some limitations. First, muscle strength was determined from only one repetition of handheld dynamometry, while the mean of multiple trials is recommended as it appears to be more reliable (Schrama et al., 2014). Additionally, the order of strength testing was only randomized by side and not by movement direction or muscle group tested. This could have resulted in muscle fatigue for the muscles tested later in the protocol (Chamorro et al., 2021). In future studies, it is recommended assessing muscle strength based on multiple trials and randomizing testing order of muscle groups. Finally, the assessor was not blinded for group selection, however, most measurements did not need an interpretation and the results were therefore reliable. Only the assessment of scapular kinematics with observation needs an interpretation of the assessor, but no difference in this outcome was found between the two groups. So, lack of blinding does not seem to affect these results.

Conclusion

In the early stage of FS, a decrease in muscle strength and altered scapular kinematics (determined with a plurimeter) where found compared to both the unaffected shoulder and asymptomatic individuals. Contrary, no evidence of altered static HbA1c-levels and proprioception were found in the early stage of FS compared to both the unaffected shoulder and asymptomatic individuals. It is therefore recommended to incorporate assessment of muscle strength and scapular kinematics in the assessment of patients with FS.

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Figure legends

Figure 1. Measurement of scapular upward rotation by using two inclinometers.

Figure 2. Participant flowchart.

Figure 3. Group comparison for the 4 directions of muscle strength. FS: frozen shoulder.

Figure 4. Group comparison for scapular upward rotation. FS: frozen shoulder.

Figure 5. Group comparison for the 2 directions of joint repositioning. FS: frozen shoulder.

Table legends

Table 1. Eligibility criteria.

Table 2. Overview of physical examination performed.

Table 3. Participant anthropometric characteristics, mean, SD and [95%-CI] are presented for continuous variables; number and percentage are presented for nominal variables.

Table 4. Within-group results for shoulder muscle strength, scapular kinematics, and shoulder proprioception.

Table 5. Between-group differences for shoulder muscle strength, scapular kinematics, and shoulder proprioception.

Supplementary Table 1: Results for shoulder range of motion in patients with frozen shoulder.

			Mean difference [95%-CI]	**p-value**
Active external rotation ROM (°)				
0° abduction	affected side	3.94±15.10 [-1.24;9.13]	-49.80 [-57.43;-42.17]	**<0.0001**
0° abduction	unaffected side	53.74±19.53 [47.04;60.45]		
30° abduction	affected side	10.43±17.51 [4.42;16.44]	-50.46 [-58.57;-42.35]	**<0.0001**
30° abduction	unaffected side	60.89±18.61 [54.49;67.28]		
60° abduction	affected side	12.28±16.07 [6.16;18.39]	-50.02 [-58.37;-41.67]	**<0.0001**
60° abduction	unaffected side	62.51±18.57 [56.13;68.89]		
90° abduction	affected side	25.82±20.48 [12.06;39.58]	-40.32 [-57.03;-23.62]	**<0.0001**
90° abduction	unaffected side	66.14±23.04 [58.23;74.06]		
Passive external rotation ROM (°)				
0° abduction	affected side	4.00±17.27 [-1.93;9.93]	-53.46 [-61.63;-45.63]	**<0.0001**
0° abduction	unaffected side	57.46±17.61 [51.41;63.51]		
30° abduction	affected side	11.68±18.72 [5.14;18.21]	-51.01 [-59.38;-42.64]	**<0.0001**
30° abduction	unaffected side	62.74±17.59 [56.70;68.78]		
60° abduction	affected side	14.83±17.05 [8.34;21.31]	-50.28 [-58.73;-41.82]	**<0.0001**
60° abduction	unaffected side	65.23±17.75 [59.13;71.33]		
90° abduction	affected side	32.45±20.33 [18.79;46.12]	-39.49 [-56.53;-22.45]	**<0.0001**
90° abduction	unaffected side	71.94±23.66 [63.81;80.07]		
Active internal rotation ROM (°)				
30° abduction	affected side	42.46±9.74 [39.11;45.80]	-9.06 [13.72;-4.40]	**0.00037**
30° abduction	unaffected side	51.51±9.44 [48.27;54.76]		
60° abduction	affected side	44.07±17.08 [37.57;50.57]	-17.73 [-25.93;-9.53]	**0.0001**
60° abduction	unaffected side	61.80±15.03 [56.64;66.96]		
90° abduction	affected side	43.55±20.02 [30.10;56.99]	-21.10 [-29.70;-12.49]	**0.0001**
90° abduction	unaffected side	65.00±15.86 [59.55;70.45]		
Passive internal rotation ROM (°)				
30° abduction	affected side	44.57±11.14 [40.74;48.40]	-11.11 [-15.51;-6.72]	**<0.0001**

30° abduction	unaffected side	55.69±6.29 [53.52;57.85]		
60° abduction	affected side	47.03±17.62 [40.33;53.74]	-20.34 [-27.46;-13.21]	**<0.0001**
60° abduction	unaffected side	67.37±9.83 [64.00;70.75]		
90° abduction	affected side	46.27±19.10 [33.44;59.10]	-21.83 [-31.19;-12.47]	**0.0002**
90° abduction	unaffected side	67.89±15.42 [62.59;73.18]		
Flexion & abduction ROM (°)				
Active flexion	affected side	95.83±28.50 [86.04;105.62]	-55.94 [-65.53;-46.36]	**<0.0001**
Active flexion	unaffected side	151.77±21.39 [144.42;159.12]		
Passive flexion	affected side	101.71±26.49 [92.61;110.81]	-54.86 [-64.09;-45.63]	**<0.0001**
Passive flexion	unaffected side	156.57±15.71 [151.18;161.97]		
Active abduction	affected side	71.94±29.86 [61.69;82.20]	-72.91 [-83.76;-62.07]	**<0.0001**
Active abduction	unaffected side	144.86±18.93 [138.36;151.36]		
Passive abduction	affected side	76.91±27.36 [67.52;86.31]	-74.77 [-84.36;-65.18]	**<0.0001**
Passive abduction	unaffected side	151.69±14.63 [146.66;156.71]		

ROM: range of motion;

P-values in bold indicate a significant difference (p<0.00042)