Università degli Studi di Padova

CORSO DI LAUREA MAGISTRALE IN
SCIENZE RIABILITATIVE DELLE PROFESSIONI SANITARIE
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TESI DI LAUREA

PROGNOSTIC FACTORS OF NON-SURGICAL INTERVENTION FOR FROZEN SHOULDER CONTRACTURE SYNDROME: A RETROSPECTIVE STUDY

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Anno Accademico 2021/2022

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Abstract

Background and aim. Frozen Shoulder Contracture Syndrome (FSCS), also known as Frozen Shoulder, is a musculoskeletal disease that typically involves substantial pain, movement restriction and considerable morbidity. FSCS management include education, non-surgical interventions, such as physiotherapy and intra-articular injections, and surgical treatment that should be performed in case of failure of conservative treatment, as recent evidence displays. As for prognostic factors associated with treatment, evidence suggests that the outcome of interventions for FSCS may be moderated by the stage of disease, female sex and diabetes. No study has yet attempted to investigate whether psychosocial factors affect the outcome of conservative treatment for FSCS. In fact, what we know to have predictive value for individuals with FSCS concerns only the biological sphere.

The aim of this study is to identify which patient's characteristics, resulting from usual physiotherapy biopsychosocial assessment, are associated with better objective and subjective outcomes after conservative treatment.

Methods. Medical records from 52 patients affected by FSCS were selected. All patients met the inclusion criteria and had completed a 3-month treatment program that included intra-articular injections (corticosteroid and anesthetic) and physical therapy.

Data of range of motion (ROM), Shoulder Pain and Disability Index (SPADI) and Short Form Health Survey 36 (SF-36) were extracted at baseline and after 3 months. Prognostic factors selected for investigation were age, gender, BMI, comorbidity, duration of symptoms, dominant limb affected, SF-36 Physical (PCS) and Mental (MCS) summaries.

Patient stratification and multivariable linear regression was used to analyze prognostic factors associated with outcome measures.

Results. All patients had significant improvement after treatment. Older age (>60 years group) was associated with worse outcome in shoulder flexion, SPADI and SF-36. Higher PCS scores seem to

predict greater ROM improvement and shorter duration of symptoms may be associated with lower pain ratings. Gender, BMI and dominant affected limb did not show any significant association.

Conclusion. Higher levels of physical health (SF-36 physical summary) seem to predict greater ROM improvement at 3 months in patients with frozen shoulder contracture syndrome. Shorter duration of symptoms may be associated with greater pain relief, while older patients' improvement appears to be less pronounced compared to younger subjects.

1. Introduction

Frozen Shoulder Contracture Syndrome (FSCS) is a poorly understood condition that typically involves significant pain, movement restriction and considerable morbidity(1). Although FSCS is a common diagnosis treated by orthopaedic surgeons and other physicians caring for musculoskeletal problems, diagnostic criteria and classification for FSCS are still debated (2).

1.1. Background

The first description of a disabling combination of pain and restricted movement affecting the shoulder was made by Duplay in 1896. He defined this condition “périarthrite scapula-humérale” and attributed signs and symptoms to the inflammation of the subacromial bursa(3).

The definition of such condition as “frozen shoulder” has been proposed by Codman in 1934. He depicted a disease characterized by grossly normal radiograph, self-resolving clinical course, and unknown etiology(4).

In 1945 Neviaser examined the pathophysiology of ten cases of FSCS and suggested the term “adhesive capsulitis”, highlighting the presence of fibrosis and adhesions between joint capsule and humeral head, as well as inflammation of the joint capsule (5). The term “adhesive capsulitis” has garnered consensus for several years, until few studies searching for arthroscopic findings of capsular adherence demonstrated absence of such tissue alteration (6)(7). For these reasons the term “adhesive capsulitis” cannot be considered correct even though it is still in use.

Other authors have proposed different terminologies to describe FSCS, showing through the years the attempt to understand this complex condition. The term FSCS was chosen in consideration of its widespread use in scientific literature.

1.2. Classification

Although FSCS was initially considered a primary disorder, then investigators demonstrated that FSCS development is linked to underlying causes. Lundberg introduced the term “secondary frozen

shoulder" to identify all cases of stiff shoulder with a definite etiology (soft tissue injury or fractures) (5).

In 2011 Zuckermann and Rokito proposed a modified classification of secondary FSCS, identifying three subgroups: intrinsic, extrinsic, and systemic subtypes(8). Their surveyed 190 members of the American Shoulder and Elbow Surgeons (ASES) and found 66% of those members either agreeing or strongly agreeing with this approach (8).

The International Society of Arthroscopy, Knee Surgery and Orthopaedic Sport Medicine (ISAKOS) and their Upper Extremity Committee disagree with this classification, suggesting that the term FSCS should be applied to shoulder stiffness in the absence of an identifiable cause, while any stiffness with a known cause should be termed "secondary shoulder stiffness" (9).

1.3. Epidemiology

The latest publication outlined that prevalence of FSCS ranges between 2 and 5% of the general population (1,10), but these data refer essentially to two fairly dated studies. The first is that of Bridgman of 1972 (11), which reports a prevalence of 2.3% among non-diabetic subjects, and the second is that of Bunker, which reports a prevalence of 5% of FSCS among patients who presented to his clinic for shoulder pain/disease (12).

Bunker himself states that, since shoulder disease only affects 15% of the population, then it would be reasonable to suggest that the real incidence of FSCS is about 0.75% of the population (13). These data are in line with those proposed by a study on prevalence of FS in diabetic and non-diabetic subjects, resulting in a prevalence of 0,5% in the non-diabetic population (14).

These data are in contrast with a study of Walker-Bone et al (15), which found a prevalence of FSCS of 8.2% in males and 10.1% in females, appears in contrast. This apparent overestimation of cases appears to be due to bias in the recruitment and in diagnostic criteria used in the study, which were based on a questionnaire and a test protocol done by a nurse.

On the contrary, authors agree that FSCS affects more frequently between 40 and 60 years of age (16), for both males and females (17), with the mean age at onset being 50.5 ± 8.4 years (10). The prevalence of FS in the population over 65 in fact drops to 0.35% (18).

1.4. Diagnosis

According to Lewis (1), there is not a gold standard test to diagnose FSCS, while diagnosis is based on: (i) clinical examination, (ii) exclusion of other concomitant pathologies and (iii) normal glenohumeral radiographs.

It is not clear what it constitutes a positive clinical examination; Fields et al (19) claim the diagnosis of FSCS coincides with the gradual onset of shoulder pain and limited range of motion (ROM) with respect to external rotation and forward flexion, other authors suggest an equal restriction of active and passive glenohumeral external rotation as diagnostic criterion (13). However, there is a general agreement that the limitation of mobility should be accompanied by normal radiographic findings.

Other studies have tried to investigate the radiological findings of FSCS on ultrasound (US) and magnetic resonance imaging (MRI) (20,21). MRI features for FSCS diagnosis that show sensitivity and specificity of > 80% include rotator interval and axillary joint capsule enhancement and inferior glenohumeral ligament (IGHL) hyperintensity; IGHL thickening showed a sensitivity of > 80% and a specificity of 79% (20). Another meta-analysis investigated the role of US in the diagnosis of FS (21). US features that showed highest level of sensitivity and specificity (all >80%) were axillary recess capsule thickening, rotator interval abnormality and ROM restriction.

1.5. Pathological findings

A recent systematic review has described some of the pathological processes involved in the development of FSCS (22), identifying a wide range of pathological alterations in patients affected by FSCS, including histological changes, molecular alterations and metabolic changes.

The histological finding has not shown evidence of an acute inflammatory infiltrate but displayed typical signs of nonspecific chronic inflammation: increased tissue edema, synovial membrane thickening, and fibroblasts, adipocytes and blood vessels proliferation, together with an increased deposition of extracellular matrix.

At a molecular level there is a local increase in pro-inflammatory mediators, mainly interleukin (IL-1α and IL-1β) and tumor necrosis factor (TNF-α), and a reduction in matrix metalloproteinases (MMPs) that regulate the turnover and degradation of extracellular matrix. Such increases have been demonstrated in the rotator interval, synovium and subacromial bursa, however the joint capsule was shown to contain the greatest number of pro-inflammatory mediators. Evidence of increased activity of factors promoting fibroblast activation and nerve growth can also be found, together with metabolic alteration leading to a consistent increase of lipids in the blood stream.

Metabolic alterations evaluated through blood sample examination included a consistent increase in lipids. Then, it was hypothesized that an initial event may trigger an inflammatory cascade that proceeds to chronic fibrosis and the development of FSCS. The overexpression of pro-inflammatory mediators can lead to an activation of fibroblasts, which, in association with the reduced activity of MMPs, could explain the increased fibrosis deposition. The elevated lipids may predispose to a pro-inflammatory environment, making some subjects more susceptible to the propagation of the inflammatory cascade. The sequence of alterations is showed in figure 1.

It remains uncertain which are the initial triggers may be and why the shoulder appears more susceptible to reduced mobility as compared to other joints.

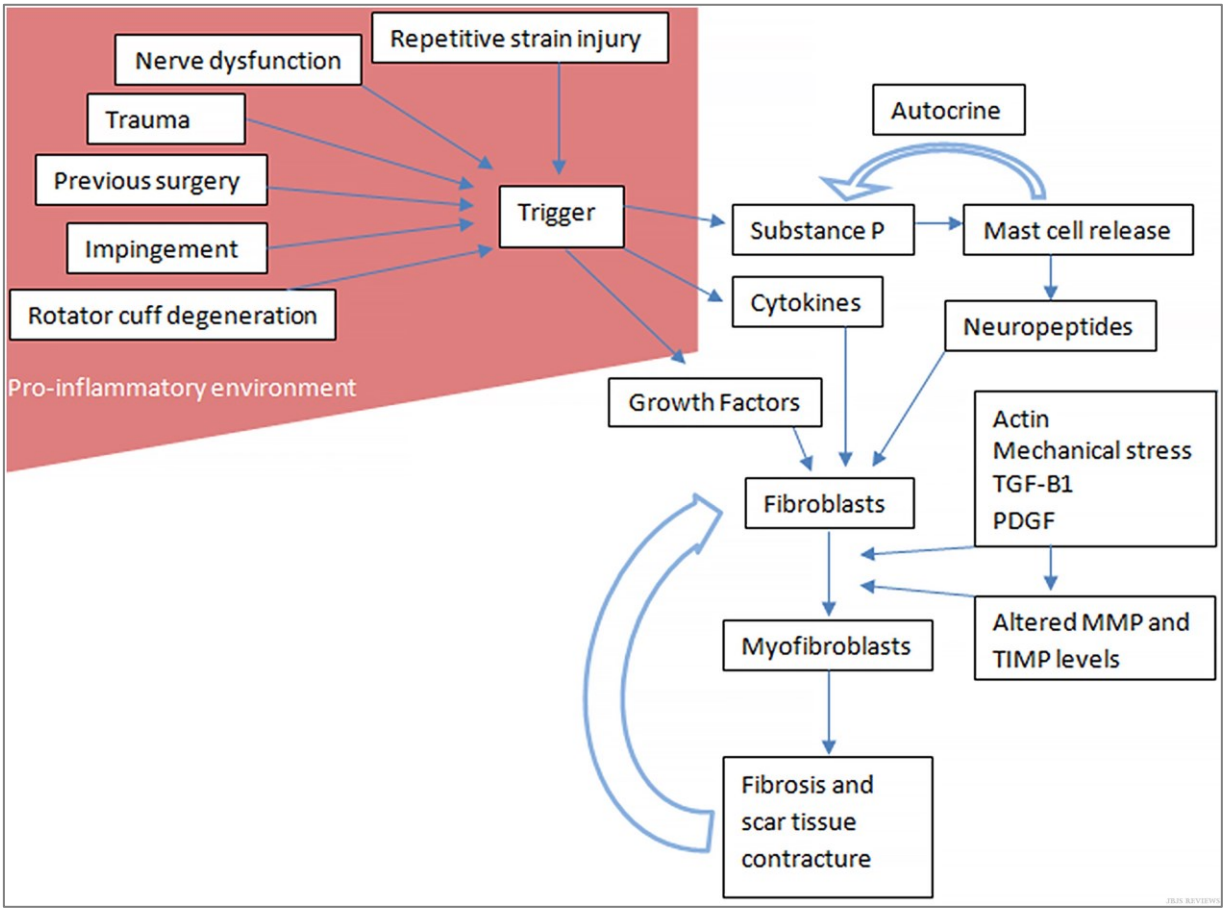

Figure 1. Proposed sequence of alterations in the development of FSCS. (Source: Jump et al, 2021)

1.6. Natural history of FSCS

As highlighted by Abrassart et al, despite the assessment of symptoms being fairly consistent, consensus quickly breaks down when it comes to natural history of the disorder (23).

The scarce consensus regards, above all, the phases that characterize the pathology and its resolution. FS was initially described by Reeves as a three progressive stages: (i) frozen or pain, (ii) freezing or stiffness and (iii) thawing or recovery phase; the average duration of FSCS being 30.1 months (range 12-42 months) (24).

Although most studies perpetuate the three phases model, various alternatives to it have been proposed, including two-phase, four-phase and phaseless descriptions (23). According to Hanchard et al, the terminology “pain-predominant” and “stiffness-predominant” should be used to classify the stage of the condition, with precedence for pain where there is doubt (25).

As for the resolution, Lewis states that the common conception of spontaneous recovery may not be correct, with 50% of people diagnosed with FSCS experiencing pain and/or stiffness at an average seven-year post-onset (1).

The issue of spontaneous resolution of FSCS was comprehensively addressed by a systematic review by Wong (26). As stated by the author, evidence on this issue is contradictory and there is a lack of studies supporting the presence of a recovery phase; therefore, the theory of complete resolution without treatment for FSCS patients appears unsupported.

According to Wong, it is surprising how low-quality evidence has led to such long-lasting theories despite the presence of conflicting data.

1.7. Management

Similarly to other musculoskeletal problems, the first step in the treatment of FSCS is patient education (27,28). As already mentioned above, the available evidence does not confirm a spontaneous resolution of the disease (26). Additionally, as stated by Lewis, when patients are informed about the duration of the natural history of the disease, some may want faster improvement of symptom and mobility (1).

The nature of the symptoms, the cause, the treatment modalities and the associated prognosis have to be explained to the subjects, and it is mandatory for the clinician to present this information in a comprehensive and personalized way (29).

After the education phase, treatment for FSCS can be either surgical or conservative. Surgical treatment may include manipulation under anesthesia (MUA) or arthroscopic capsular release (ACR) (30,31). Non-surgical intervention include physiotherapy, intra-articular corticosteroid injections, intra-articular hyaluronic acid injections, hydrodistension procedures and nerve block (32–34). Surgical procedures should be performed in case of failure of conservative treatments as they have no beneficial effect on late functional and clinical outcomes (30,32).

Regarding conservative treatment, the association between intra-articular corticosteroid injections, manual therapy, and exercise appears to be superior to physiotherapy and injections alone (35,36). Moreover, there are no difference between high- and low-dose corticosteroid treatments (37). Intra-articular corticosteroid injections are associated with better outcomes in patients with FSCS of less than 1-year (35) or 6 months duration (37).

Adding arthrographic hydrodistension procedures to corticosteroid injections seems to be associated with positive effects on pain; however, these benefits are not clinically significant (35).

A recent meta-analysis investigated the effectiveness of hyaluronic acid intra-articular injections compared to other non-surgical therapies (33); results display a beneficial effect only for external rotation recovery, whereas the effect in relieving pain and improving flexion and abduction may be equal to other conservative procedures.

Another conservative treatment modality recently investigated is suprascapular nerve block. This procedure is associated with significant improvement in pain and ROM compared with other treatments for FSCS, despite the presence of low-quality evidence (34).

Physiotherapy for the management of FSCS may include manual therapy and exercise (both supervised and home-based). Exercise alone and exercise combined with passive treatment improve ROM, function and pain; moreover, adding exercises seem to improve active ROM compared with a program without exercises (38). Passive joint mobilization may be associated to an improvement in symptoms, ROM and Constant score when associated to self-treatment; however, these data need to be considered with caution as they may not achieve clinically important difference (37).

1.8. Prognostic factors and biopsychosocial model

Despite the large existing body of evidence regarding the biological sphere in FSCS, few studies have tried to investigate psychosocial factors related to this disease, their influence in the onset of the pathology and their role in treatment outcomes.

Evidence displays that incidence of FSCS increases with age and it occurs more commonly in individuals between 40 and 65 years of age (39,40); women seem to be more predisposes to develop the disease than men and having FSCS on one side places an individual at risk for opposite side involvement (40).

Higher prevalence of FS in subjects with diabetes (both types 1 and 2) is well documented and Thomas et al reported a prevalence of 4.3% of FSCS in diabetic patients and 0.5% in general medical patients (14). According to Cohen, diabetic population has 2-4 times greater incidence of FSCS as compared to general population and individuals with thyropathy are 4 times more likely to develop FSCS (10). Cerebrovascular, coronary artery, autoimmune and Dupuytren's diseases are also related to an increased frequency of FSCS (41). Diabetes may play a role in the course of symptoms as well, with diabetic patients experiencing worse outcomes from FSCS than those without diabetes (42).

Psychological disorders seem to be correlated with FSCS, and patients suffering depression and anxiety had higher self-reported pain, decreased quality of life and functional restriction in daily activities but no significant difference in ROM compared to patients with no depression or anxiety (43).

Considering structural relationship between pain catastrophizing, self-efficacy and pain intensity in patients with FSCS, data suggest that pain intensity increases the risk of chronic pain; it also reduces self-efficacy and increases pain catastrophizing (44).

Psychological factors may play a role also for postoperative FSCS (secondary FSCS); a study by Niehaus et al found a higher incidence of FSCS in patients reporting unwillingness to take prescribed pain medications after arthroscopic shoulders procedures (45).

Other prognostic factors for post-operative FSCS have also been outlined by a study by Koorevar et al (46); authors propose a prediction model, not yet validated, combining four variables: diabetes mellitus, arthroscopic surgery, early shoulder physiotherapy and Disabilities of the Arm, Shoulder and Hand (DASH) score. According to the authors, the capsule may be at greater risk of being

traumatized during arthroscopic surgery compared to open surgery; moreover, they observed that clinical signs of FSCS disappeared when the capsule was allowed more rest.

Prognostic factors associated with treatment outcomes have been investigated for surgical procedures and conservative approach in FSCS, but evidence is still limited.

A recent meta-analysis investigated potential patient-specific moderating factors in non-surgical treatment for FSCS; outcomes seem to be modulated by the stage of disease, female sex and diabetes (47). When considering only nerve block procedures, older age and higher educational level were found to be the main factors associated with satisfactory quality of life and increased functional capacity (48).

Either diabetes mellitus, the presence of chronic symptoms or presence of bilateral FS appear to be relevant factors to identify patients that might profit from earlier surgery (49).

No study has yet investigated whether biopsychosocial assessment of health status of patients with FSCS can predict the outcome of a conservative treatment.

A recent study by Chester et al aimed to identify clinical and psychological characteristics associated with better outcomes in patients with shoulder pain undergoing physiotherapy (50). Among the four factors identified to have association with the treatment outcome (baseline disability, patient expectations, pain self-efficacy, pain severity at rest), only one was related to the symptoms; psychological factors, such as patient expectations, self-efficacy and baseline disability perception, were consistently associated with patient-rated outcome.

Similarly, Physical and Mental Component of the Short Form Health Survey 36 (SF-36) can differentiate pattern of response to physiotherapy in patients with soft tissue shoulder disorders (51).

2. Aim

Although FSCS is a widely studied disease, recovery remains controversial. In fact, whilst many patients achieve full recovery, some remain with long-term pain and joint limitation (23,52); identifying these patients is critical for healthcare professionals.

In recent years, evidence has shown that general health and psychosocial factors play a role in the prognosis and treatment of various musculoskeletal diseases (53,54). Clinical guidelines have increasingly been oriented towards a multidisciplinary and biopsychosocial approach (55,56), and, for this purpose, numerous instruments have become part of the evaluation strategies of physiotherapists.

It is still unclear whether some of these tools can help identify patients with a poorer prognosis among those undergoing conservative treatment for FSCS.

Thus, the aim of this study is to identify which patient's characteristics, among the usual physiotherapy assessment tools, are associated with better objective and subjective outcomes at 3 months after conservative treatment.

3. Materials and methods

3.1. Study design and ethical considerations

The research has been designed as a retrospective cohort study. Data were extracted from the archives of two outpatient clinics in the province of Treviso, Italy. All patients who agreed to the treatment signed a written informed consent form for participation. Notification has been sent to the Ethic Board of Treviso hospital.

3.2. Patients

Medical records of 52 consecutive patients diagnosed with primary FSCS, regardless the stage of the condition, were retrospectively selected in December 2021. All patients were required to have completed a 3-month course of treatment and be older than 18 years of age. Criteria for diagnosis of FSCS included clinical hisoty of shoulder pain of unknown cause (insidious onset), limitation of all glenohumeral movements (passive ROM evaluated with digital inclinometer) with firm or empty end-feel compared to contralateral shoulder, and radiographic imaging negative for osteoarthritis. As control cohort, 20 consecutive patients without FSCS were evaluated.

The exclusion criteria include neck pain (identified using the "repeated movements test" and Wainner's cluster (57)), previous shoulder trauma or surgical operations to the shoulders over the past 10 years, a positive ultrasound exam for full-thickness rotator cuff tear performed by the physical therapist, contraindication to corticosteroid injection or physical therapy treatment, score ≥37 points on Tampa Scale of Kinesiophobia (58).

Inclusion and exclusion criteria are summarized in table 1.

Table 1. Inclusion/Exclusion criteria

Inclusion criteria	Exclusion criteria
– Adult male or female patients presenting with shoulder pain of unknown cause – All glenohumeral movements are limited, with firm or empty end-feel compared to contralateral shoulder (evaluation performed with digital inclinometer) – Radiographic imaging negative for osteoarthritis – 3-month course of treatment completed	– Neck pain identified using the "repeated movements test" and Wainner's cluster (57) – Previous shoulder trauma or surgical operations to the shoulders over the past 10 years – Positive ultrasound exam for full-thickness rotator cuff tear performed by the physical therapist – Contraindication to corticosteroid injection or physical therapy treatment – Score ≥37 points on Tampa Scale of Kinesiophobia (58)

3.3. Treatment

Conservative treatment consisted of unguided corticosteroid/anesthetic injections performed by an experienced orthopaedist and 30-minutes session of physical therapy together with home-based stretching exercises. The first injection was administered to all patients at baseline and, if needed, one or two following injections were delivered during follow-up sessions. Physical therapy consisted of 6 painful end-range mobilization techniques at patient's tolerance, delivered twice a week during the first 2 weeks and once a week during the following 3 months. Home-based activity consisted of 4 stretching exercises to be performed for 30 minutes, twice a day throughout the three months.

3.4. Data collection

Outcome measurements. To evaluate treatment outcomes, items from objective and subjective examination have been selected at first consultation (T0) and after 3 months (T1).

For objective examination, data on passive range of motion (ROM) in shoulder external rotation (ER 0°), flexion (F), abduction (ABD) and external rotation in 90° abduction (ER 90°) were extracted. Difference between ROM values at baseline and after three months (Δ ROM) was considered. ROM measurement had been achieved using a Tracker Freedom wireless inclinometer (JTECH Medical, Midvale, UT) (59). To ensure reliability, each measurement had been performed 3 times and the average was recorded. This procedure is reported to be reliable when carried out by the same examiner (60) and has an interclass correlation coefficient (ICC) between 0.88 and 0.89, and a minimal detectable change (MDC) of 8° for F (61), an ICC between 0.76 and 0.96, and a MDC of 5.1° for ER, an ICC between 0.73 and 0.92, and an MDC of 6.6° for ABD (59,60). The examiner was a physical therapist with more than 10 years of experience using this technology.

For subjective examination, the italian version of the Shoulder Pain and Disability Index (SPADI) was selected (62). Both SPADI total score and SPADI Pain subscale have been investigated as variables to assess treatment outcome. The SPADI is a self-administered index consisting of 13 items divided into two subscales: pain and disability; pain subscale consist of 5 items and scores are expressed as a percentage, where zero represents no pain and 100% represents maximum pain (63). SPADI has demonstrated acceptable psychometric properties, therefore, it is recommended as an outcome tool for FSCS (40). Moreover, the relationship between changes in shoulder ROM and SPADI suggest that they measure overlapping underlying phenomena (64). The MDC at the 95% confidence level has been reported to be 18.0 and the minimal clinically important difference (MCID) has been reported to be between 8 and 13 (65).

In addition, data from the Italian version of the Short Form Health Survey 36 (SF-36) (66) have been extracted from medical records. The SF-36 is a multipurpose, short-form health survey with 36 questions.

SF-36 is widely used by physiotherapists as a tool for assessing general physical and mental health in clinical practice. It yields an eight-scale profile of scores as well as physical and mental health summary measures (fig.1). The Physical Component (PCS) and Mental Component (MCS) of SF-36 have been investigated as prognostic variables for the analysis.

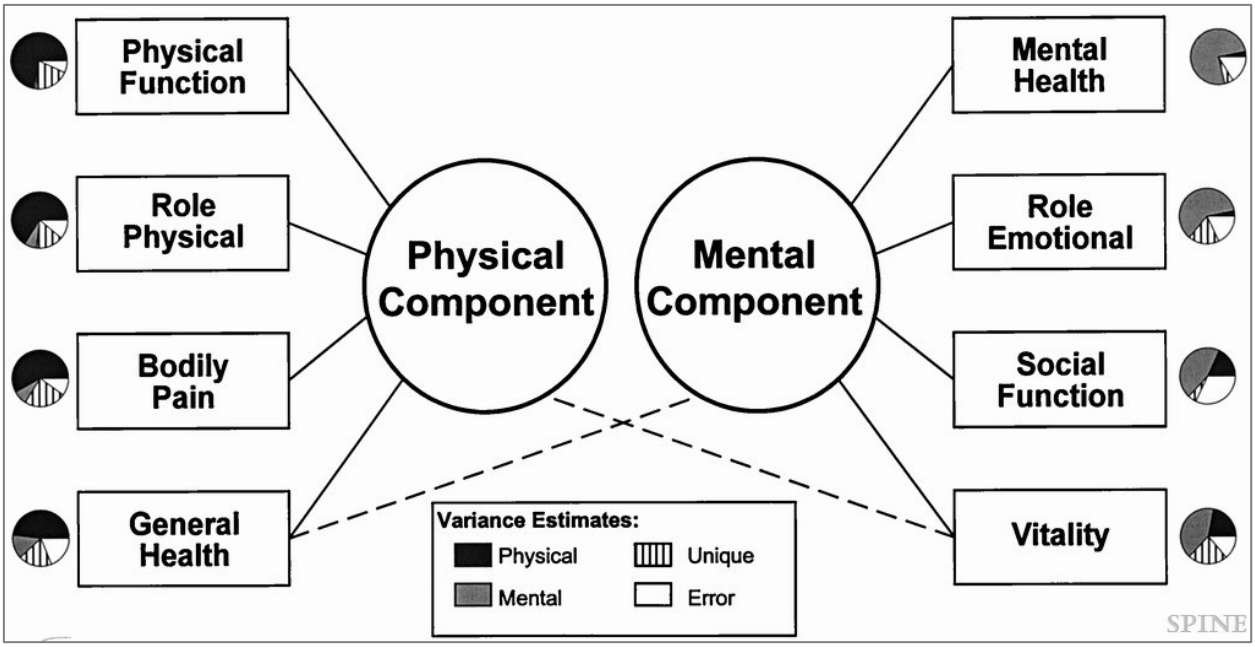

Figure 2. SF-36 scales measure physical and mental components of health. (Source: Ware, Kosinski and Keller. 68)

Reliability estimates for physical and mental summary scores exceed 0.90 and the median reliability coefficient for each of the eight scale is equal or greater than 0.80 except for Social functioning (median reliability of 0.76) (67).

Validation studies have shown that Physical Functioning, Role- Physical, and Bodily Pain scales and the PCS summary have been shown to be the most valid SF-36 scales for measuring physical health; the Mental Health, Role-Emotional, and Social Functioning scales and the MCS summary measure have been shown to be the most valid of the SF-36 scales as mental health measures (67).

Putative prognostic factors. Variables were identified among information and assessment tools that Italian physiotherapists usually employ in clinical practice. Two investigators (DV and LD) selected

variables, based on availability of supporting evidence in the musculoskeletal literature or clinical rationale. These variables were examined in association with treatment outcome for FSCS.

The variables were organized by domains: demographic, disorder-related and patients health perception.

Demographic information extracted from medical records were age, gender and body mass index (BMI). Information from 20 non-FSCS consecutive subjects were also collected for comparison of demographic characteristics. Patients ages were divided in two age groups, with one group including subjects between 40 and 60 years of age and the other including subjects between 60 and 80 years of age. This cutoff was selected in consideration of the fact that, in the general population, the most affected age group is the one ranging from 40 to 60 years (68), while in the case of comorbidities (especially diabetes mellitus) it is the over 60 age group (69). Gender has been selected as previous evidence displayed a moderating role of female sex in conservative treatment outcome of FSCS (47). Considering the accumulating evidence to suggest the role of obesity in predicting the development of pain, even at non-weight-bearing sites, BMI has been included as putative prognostic variable for the investigation (70).

Disorder-related information selected from medical record were symptoms duration and dominant upper limb involvement. A previous review identified stage of disease as a moderating factor for conservative treatment (47), however, as previously mentioned, the three phases model has been recently questioned; therefore, duration of symptoms has been chosen as variable to be investigated. Involvement of dominant limb has been selected as researchers felt it could affect the outcome of conservative intervention.

Patient health perception was considered in order to evaluate the possible prognostic role of psychological and social components. For this reason, the PCS and MCS of SF-36 (figure 2) have been investigated as prognostic variables for the analysis, as seen in other studies (51,71). The PCS and MCS scales were scored using norm-based methods involving three steps (72). First, the eight SF-36 scales are standardized using means and standard deviations from the general population; they

are then aggregated using factor score coefficient and finally the aggregate PCS and MCS scores are standardized using a linear T-score transformation to have a mean of 50 and a standard deviation of 10 in the general population.

3.5. Statistics

Baseline variables of demographic, disorder-related and patient health perception characteristics were explored. Initially, stratification of patients was performed considering age, sex and dominant limb involvement and statistical analysis was conducted using two-tailed *t* test with significance for $p<0,05$. To further evaluate the association between the prognostic variables (sex, age, duration, affected shoulder, dominant limb, BMI) and the outcome (SPADI Pain subscale and Δ ROM ER 0°), a multivariate linear regression analysis was used considering the significant coefficient for $p<0,05$. The same model was used to verify whether there was an association between assessment indices (PCS and MCS) and outcome (Δ ROM ER 0°) unadjusted and adjusted for variables (sex, age, duration, affected shoulder, dominant limb, BMI).

4. Results

4.1. Baseline characteristics of the cohort.

Baseline characteristics of the 52 subjects included in the study are displayed in table 2. Demographic data of the non-FSCS group are included for comparison. All non-FSCS patients addressed to the outpatient clinics for shoulder complains; non-FSCS disorders were non-specific shoulder pain (9 subjects), rotator-cuff tear/tendinopathy (7 subjects), osteoarthritis (3 subjects), humerus fracture (1 subject).

Table 2. *Baseline characteristics of the cohorts of FSCS (n=52) and non-FSCS (n=20) patients.*

		FSCS (n=52)	**Non-FSCS** (n=20)
Age (year)[1]		55,3±7 (min 42; max 71)	50,9±13,6 (min 27; max 76)
>60 years		13 (25%)	5 (25%)
Sex (M/F)		26/26	12/8
BMI[1]		23,4±3,2 (min 18; max 30)	20,6±3,8 (min 14,4; max 29,3)
Diseased shoulder (DX/SX)		24/28	NC[3]
Dominant shouder (Yes/No)		20/32	NC[3]
Symptoms duration (month) [1]		6,7±8,5 (min 1; max 60)	NC[3]
SF-36	**Physical summary**[2]	41 (±6)	NC[3]
	Mental summary[2]	48 (±12)	NC[3]

[1]: data are expressed as mean (minimum; maximum value)

[2]: data are expressed as mean (± SD)

[3]: not considered for the group analysis

Demographics from the two cohorts reveal consistency of the characteristics of FSCS and non-FSCS population and the parameters analyzed display non-significant differences between groups. This shows that FSCS population is representative of the normal adult population that refers to physiotherapy centers for shoulder complains.

4.2. Outcome measurements.

All FSCS participants had improved all readouts at 3-month follow-up and many had reached nearly full shoulder functioning. Objective (ROM, table 3) and patient-reported outcome (SPADI and SF-36, table 4 and table 5 respectively) variables display significant improvement.

Shoulder ROM (objective outcome). ROM was evaluated using six different parameters (flexion, extension, abduction, IR, ER at 90° of abduction, and ER at 0°). Notably, 3-month treatment of the patients resulted in a general and significant improvement in passive ROM. Data for each movement direction are displayed in table 3.

Changes in ROM for flexion, abduction, IR and ER were greater than the respective MDC (59,61).

Table 3. *Average Passive Range of Motion*

	Baseline[1]	3-mo Follow-up[1]	P value
Flexion	129±19,47 (124-135)	170±10,41 (167-173)	<0,001
Extension	37±10,35 (35-40)	54±5,01 (52-55)	<0,001
Abduction	59±17,71 (55-64)	95±13,51 (91-99)	<0,001
IR	36±11,29 (33-39)	65±10,43 (62-68)	<0,001
ER at 90° of abduction	41±18,95 (36-47)	85±13,58 (81-89)	<0,001
ER at 0° of abduction	28±14,21 (24-32)	57±10,41 (54-60)	<0,001

[1]: data are expressed as mean (± SD)

Abbreviations: ER, External rotation; IR, Internal rotation.

SPADI (patient-reported outcome). Similarly to ROM, also patient-rated pain and disability reveal significant improvement at 3-month follow-up. Data for pain and disability subscales of SPADI are displayed in table 4.

Changes in SPADI subscales scores were greater than reported MDC and MCID (65). These data are symptomatic of the fact that the 3-month conservative treatment is an adequate time frame to improve both pain sensation and disability in patients with FSCS.

Table 4. *Average SPADI score*

	Baseline[1]	3-mo Follow-up[1]	P value
Pain	59±21,4 (53-65)	5±6,1 (3-6)	<0,001
Disability	51±24,1 (44-58)	3±4,6 (1-4)	<0,001

[1]: data are expressed as mean (± SD)

SF-36 (patient-reported outcome). Finally, also patient health perception measures display significant improvement at 3-month follow-up. Data extracted from each item of the SF-36 are reported in table 5. The data show that the functional improvements in ROM, pain sensation and disability obtained with conservative treatment are reflected in a general improvement of subject's psychological and physical condition. This improvement in patient's health perception suggests a tendency to resume normal daily life, which was previously prevented by FSCS.

Table 5. *Average SF-36 scores.*

	Baseline[1]	3-mo Follow-up[1]	P value
SF-36_PF	78±17,7 (73-82)	96±8,9 (94-99)	<0,001
SF-36_RP	47±37,4 (36-57)	91±19,8 (85-96)	<0,001
SF-36_BP	41±18,2 (36-46)	86,4±15,4 (82-91)	<0,001
SF-36_GH	71±19,1 (66-76)	81±13,3 (78-85)	0,0016
SF-36_V	58±19,2 (53-63)	74±14,9 (70-78)	<0,001
SF-36_SF	69±23,7 (62-75)	91±14,3 (87-95)	<0,001
SF-36_RE	70±38,9 (60-81)	98±10,3 (95-100)	<0,001
SF-36_MH	71±20,4 (66-77)	82±12,4 (79-85)	0,0017

[1]: data are expressed as mean (± SD)

Abbreviations: SF-36, Short Form Health Survey 36; PF, Physical Function, RP, Role Physical; BP, Bodily Pain; GH, General Health; V, Vitality; SF, Social Function; RE, Role Emotional; MH, Mental Health.

4.3. Putative Prognostic factors

Given that all patients improved their health and mental conditions, we aimed at evaluating if there are factors able to predict the outcome of the patients. The analysis of selected prognostic variables reveals that some demographic and self-reported characteristics may be related to changes in the outcome of conservative treatment for FSCS. We therefore decided to initially assess whether there were any demographic descriptors able to indicate a statistically significant improvement of the ROM, SPADI and SF-36 indicators after three months of treatment. To this purpose, we stratified the patient population by gender (male vs female), age (under 60 vs over 60), diseased shoulder (dx vs sx) and dominant shoulder.

The most significant results were those obtained by stratifying patients by age (under 60 vs over 60). The analysis that gave the most significant results was the one that stratified patients by age. The results show that there was a significant improvement in all outcomes, both objective and patient-reported, in both under 60 and over 60 patients. More interestingly, most of the functional and psychological improvements were significantly ameliorated in under 60 patients as compared to older

ones. Notably, most of the parameters at baseline (T0) were not significantly different between under 60 and over 60, thus demonstrating that the differences at T1 (3 months follow-up) are probably related to age and not to a better baseline condition of the under 60 cohort. Data are represented as box and whiskers plots (figure 3). More specifically, ROM for flexion, abduction, ER at 90 ° of

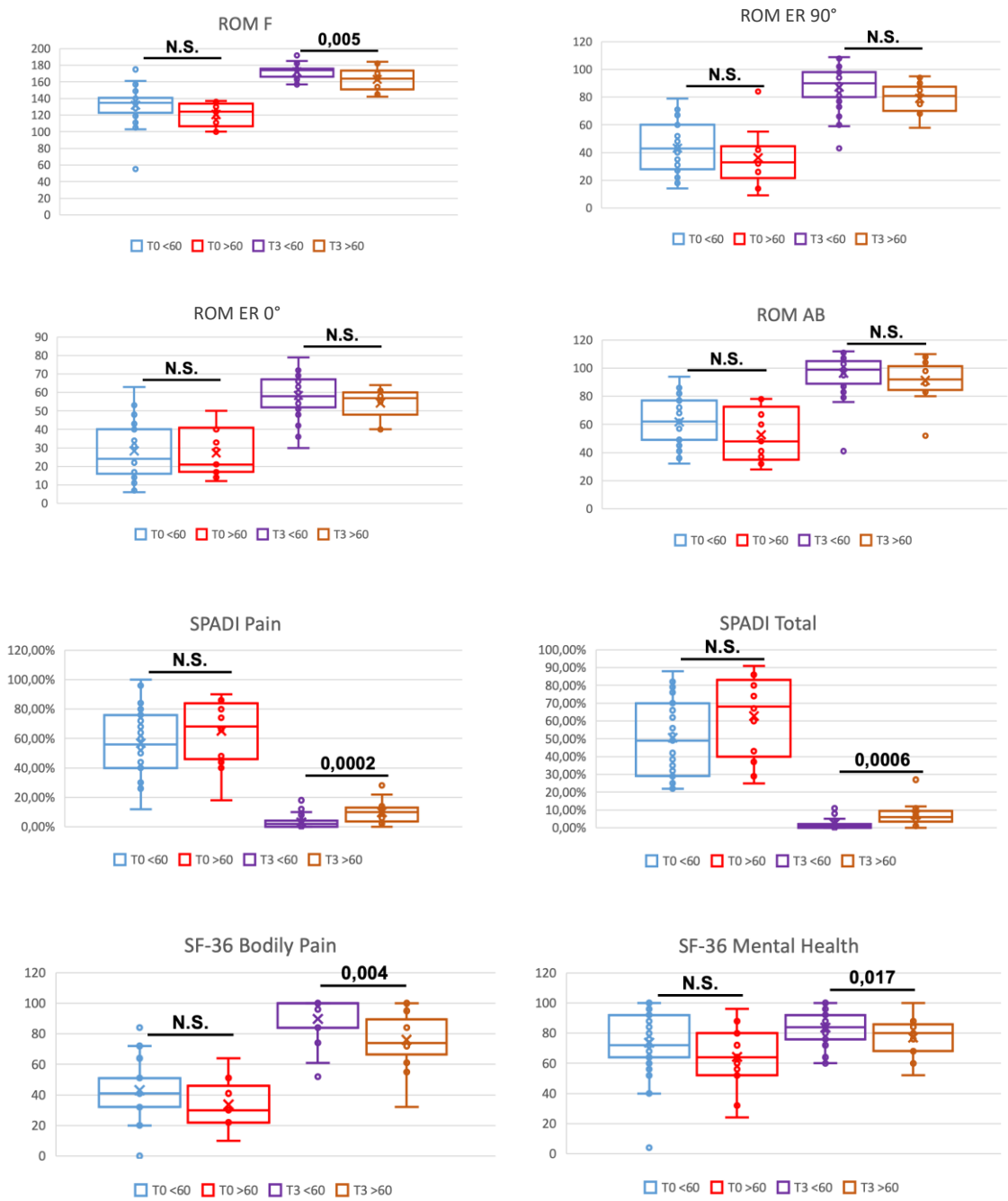

Figure 3. *Box and whiskers plots for selected variables: ROM flexion, ROM external rotation at 90° of abduction, ROM external rotation at 0°, ROM abduction, SPADI subscale Pain, SPADI total score, SF-36 Readouts.*

(continue on the next page)

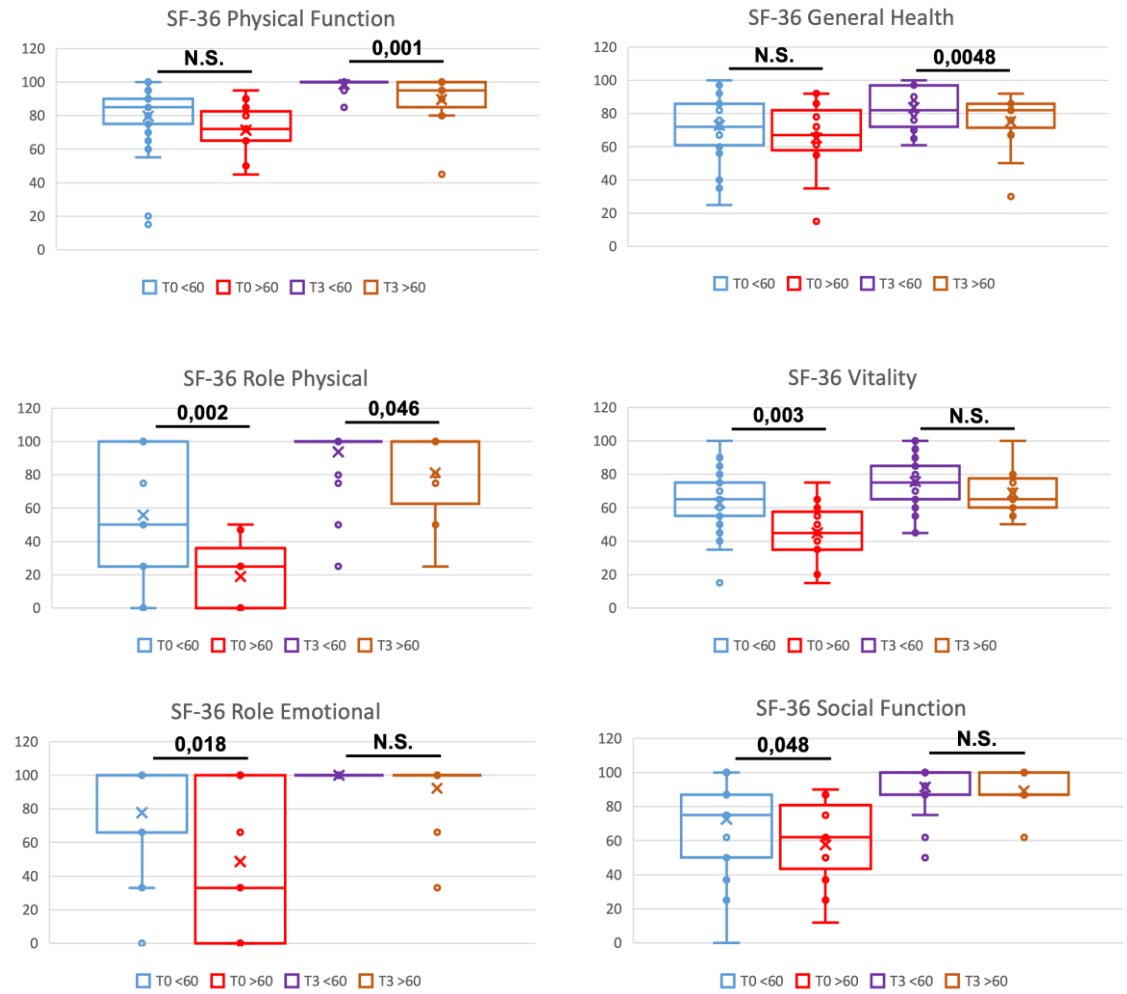

Figure 4. *Box and whiskers plots for selected variables: ROM flexion, ROM external rotation at 90° of abduction, ROM external rotation at 0°, ROM abduction, SPADI subscale Pain, SPADI total score, SF-36 Readouts.*

2-taled t test, significance<0,05; N.S.= not significant.

Each variable is represented for each age group at baseline and after 3 months. Baseline characteristics show significant difference for SF-36 items Role Physical (p=0,002), Vitality (p=0,003), Role Emotional (p=0,018), Social Function (p=0,048).

Improvement was significantly lower for older adults for flexion (p=0,005), SPADI Pain subscale (p=0,0002), SPADI total score (p=0,0006), SF-36 items Bodily Pain (p=0,004), Mental Health (p=0,017), Physical Function (p=0,001), General Health (p=0,0048).

Abbreviations: ROM, Range Of Movement; F, Flexion; ER 90°, External rotation at 90° of abduction; ER 0°, External rotation at 0° of abduction; AB, Abduction; SPADI, Shoulder Pain And Disability Index; SF-36, Short Form Health Survey 36.

abduction and ER at 0 ° improved in both age group, however, improvement of flexion was significantly lower for older subjects. Similarly, SPADI and SPADI-Pain subscale scores decreased in the two groups, however, scores for both variables were significantly lower in younger subjects, showing a more pronounced improvement in this age group. Finally, the readouts of SF36, namely Physical Function, Role Physical, Bodily Pain, General Health, Mental Health and Vitality, showed a significantly more pronounced improvement of physical and mental health in younger subjects.

In contrast to age, the other types of stratification evaluated (gender, diseased shoulder and dominant shoulder) did not show significant variations between the cohorts at end of treatment (T1).

In search for possible variables able to predict the outcome of patients with FSCS, the SF-36 variables were grouped in two cumulative readouts, Physical and Mental summaries, as described by Kennedy and colleagues (51). Multivariate linear regression was performed for difference in External rotation at 0° (Δ ROM ER 0°) and SPADI Pain subscale (SPADI-Pain) at baseline and after 3-month treatment.

Multivariate linear regression data for association between baseline SF-36 PCS and outcome Δ ROM ER 0° are displayed in table 6.

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Table 6. *Regression coefficient and significance for variable SF-36 Physical Summary*

	UNADJUSTED		ADJUSTED	
	Coefficient	**p**	**Coefficient**	**p**
SF-36 PHYSICAL SUMMARY	0.257	0.01*	0.118	0.041*

Multiple linear regression analysis (level of significance for p<0,05) was used to verify if there was an association between baseline characteristics (SF-36 PCS, Physical Summary) and outcome (Δ ROM ER 0°) not adjusted and adjusted for the variables (sex, age, duration, affected shoulder, dominant limb, BMI).

Regression coefficient reached significance before adjustment (p=0,01) and after adjustment (p=0,041).

Abbreviations: SF-36, Short Form Health Survey 36.

Notably, SF-36 PCS was significantly associated with a better outcome for Δ ROM ER 0° (p<0,005). In addition, SF-36 MCS reveals a trend of association for SPADI-Pain although not reaching significance (p=0,051). Duration of the disease also reached significant association for SPADI-Pain

variable (p=0,006) but did not show any association for ROM variable. Demographic characteristics such as sex, age and BMI were not associated with the outcome of treatment.

These data highlighted that patients with higher values of SF-36 PCS scores will show a greater improvement of Δ ROM ER 0°, relaying in a better response to conservative treatment.

5. Discussion

FSCS, also known as frozen shoulder or adhesive capsulitis, is a common pathologic condition of the shoulder joint. It is characterized by progressive shoulder pain and restriction of ROM (16). Despite FSCS affects a significant proportion of population (between 0.5 and 5% of the adult population) (10,13,14), its classification, diagnosis, natural course, treatment and prognosis remain controversial (8,13,26). Management of FSCS involves patient education (28,40) associated with conservative or surgical treatment (30,40). Non-surgical interventions include physiotherapy, intra-articular corticosteroid and hyaluronic acid injections, hydrodistension and nerve block procedures (33–35,40,73). Evidence suggests that surgical treatment have to be performed only in the case of failure of conservative treatment (30,32).

Evaluation of FSCS should include both objective and subjective assessment tools. Key impairments of body function in FSCS patients should be evaluated through passive shoulder ROM measurement (40); indeed, glenohumeral external rotation in adduction, external rotation in abduction, internal rotation in abduction, flexion and abduction should be assessed. Among subjective (or patient-reported) evaluation, the SPADI is a validated functional outcome measure for FSCS recommended in clinical practice (25,40). It is a 13-item patient self-report tool with 2 domains, the pain and the disability subscales (63). Each subscale is summed and transformed to a score out of 100, higher score indicating greater impairment or disability. A responsiveness study on FSCS patients suggests that SPADI and ROM evaluation measure overlapping underlying phenomena (64). A second subjective assessment tool is the SF-36, which has been used in previous studies as an outcome

measure for FSCS (74,75). It is a widely used, self-administered, 36-item general health measurement grouped in eight subscales (67). A score of 0 to 100 is obtained from each subscale, with higher scores indicating better health condition of the patient.

The present study aims to determine the prognostic value of a set of factors that are normally collected during assessment of patients with FSCS, to evaluate their influence on conservative treatment outcomes at 3 months. Furthermore, the investigation aims to identify moderating factors associated with a better or worse outcome of FSCS patients following conservative treatment.

Among several factors that are part of the evaluation of FSCS patients, variables included for investigation were selected based on available musculoskeletal prognostic literature or clinical expert opinion. Previous studies have yet tried to identify disorder specific features or patient's characteristics that may predict the outcome of treatment for FSCS. Although the evidences are scant, some studies hypothesized that female sex, diabetes, stage of disease, bilateral shoulder involvement and presence of chronic symptoms may predict a worse outcome of conservative treatment for FSCS (47,49). In this thesis, in the attempt to confirm data from literature and find new predictors of outcome for FSCS patients both demographic characteristics and disorder-related features have been selected for investigation. In addition, MCS and PCS of SF-36 have been extracted to investigate their prognostic value in FSCS patients. People affected by FSCS display lower score of MCS and PCS compared to normal population (71) and both variables were seen to be predictors of outcome for soft tissue shoulder disorders (including FSCS) (51). A single study attempted to determine whether psychological characteristics would predict treatment outcome for FSCS suggesting an influence of psychometric parameters (76). Nevertheless, the evaluation of these parameters is performed with questionnaires specific to the psychiatric field, thus rarely employed by physiotherapists dealing with musculoskeletal disorders.

In the present study participants were evenly distributed between male and female sex and age ranged from 42 to 71 years of age. Comparison with a group of non-FSCS patients showed that the FSCS

cohort is representative of the adult population referring to physiotherapy centers for shoulder complaints (table 2).

Following a 3-month conservative treatment (T3), all FSCS patients experienced a significant improvement in both objective and subjective outcome measures (tables 3 and 4) as respect to the start of therapeutic interventions (T0). This trend is in line with recent evidence considering the association of physiotherapy and corticosteroid infiltrations as the elective treatment for subjects with FSCS (30,32). Changes in ROM for flexion, abduction, IR and ER were greater than the respective MDC (59,61). Changes in SPADI subscales scores were also greater than reported MDC and MCID (65). Amelioration of mobility and symptoms after conservative treatment is associated with a general improvement of subjective physical, social and mental health (table 5).

Demographic characteristic were the evaluated in search of a possible predictor of outcome for FSCS patients. A first demographic feature analyzed was age. Cohort was divided in two subcohort, under 60 and over 60 patients. This cutoff was chosen on the basis of literature data showing that, in the general population, patients ranging from 40 to 60 years are the most affected by FSCS (68), while in patients affected by diabetes mellitus, the disease mainly affects those over 60 years of age (69). As for shoulder ROM variables, the values for all movement directions are consistently improved in both younger and older adults at T3 as respect to the baseline (T0), whereas only shoulder flexion improvement is significantly different between age groups, with higher values for under 60 patients at T3. Age appears to be a significant predictor of better outcome also for symptoms and self-rated health state, with older patients declaring higher level of pain and lower levels of physical and mental health after 3-month conservative treatment (T3) compared to under 60. Overall, it seems that older patients with FSCS improve after treatment, but they experience a less pronounced improvement. On the contrary, despite the older group showed a greater emotional distress linked to the interference of the pathology in the social and psychological sphere, this difference disappears after 3 months of treatment.

In this study, female sex does not seem to be a moderating factor for conservative treatment in FSCS. This data is in contrast with the meta-analysis by Zhang and colleagues (47) who reported higher efficacy of conservative treatment in study groups with lower proportion of women. In this meta-analysis the sample size was wider than ours, implying differences in power or in statistical significance. We then plan to expand our study cohort to increase the statistical significance of the study.

Finally, other demographic characteristics (dominant shoulder, right or left shoulder), as well as gender differences, did not yield significant results.

To further refine our search for one or more outcome predictors, we grouped the SF-36 values into Mental (MCS) and Physical (PCS) summary as suggested by Kennedy and colleagues (51). The physical health measure includes four scales of physical functioning, role-physical, bodily pain and general health. The mental health measure is composed of vitality, social functioning, role-emotional and mental health (67).

Demographic data do not show association with these indexes at linear regression analysis. Notably, the physical value resulted associated with an increased rotation angle (Δ ROM ER 0 °) between T0 and T3, a sign of the patient's increased ability to perform shoulder movements. Better physical health (SF-36 PCS) at baseline (T0) was a significant prognostic factor for shoulder ROM improvement: higher PCS scores are associated with greater improvement of shoulder ER. This data represents a useful finding for health professionals involved in the FSCS management as it allows to identify those patients who could benefit from different interventions or longer treatment.

Also symptoms duration also turned out to be a significant prognostic factor for pain relief after conservative treatment. This might be due to the prolonged exposure to noxious stimuli that triggers peripheral and central sensitization. Comparable results were obtained by Kennedy and colleagues (51). They found that patients suffering from soft tissue shoulder disorders had sharper course of improvement when they were characterized by better physical and mental health and a shorter duration of symptoms at baseline. In the present study better mental health (SF-36 MCS) did not

show any significant association with pain improvement, however, a trend of association was observed, perhaps suggesting that a larger sample could lead to significance.

This study has several strengths. It is the first to investigate if mental and physical health can be predictors of treatment outcomes in FSCS. Moreover, the main outcome measures (ROM and SPADI) are clinically relevant and have been shown to have strong measurement properties. It includes a cohort of consecutive clients with FSCS that were identified by strict diagnostic criteria and treated according to a rigorous protocol by specialized shoulder professionals. Although, results can not be generalized to other shoulder disorders, they are highly valuable for FSCS population.

This study has also some limitations. First, calculation of the sample size has not been considered for this investigation as all eligible subjects retrieved from the archives have been included. Second, even if the study is multicentric, data were obtained from two outpatient clinics only. Third, only one rating scale has been used for the purpose of assessing psycho-social health of the participants. Future research should be directed at investigating different psychological characteristics that could affect functional recovery in FSCS patients.

6. Conclusion

Higher levels of physical health (SF-36 physical summary) seem to predict greater ROM improvement at 3 months in patients with frozen shoulder contracture syndrome. Shorter duration of symptoms may be associated with greater pain relief, while older patients' improvement appears to be less pronounced compared to younger subjects.

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