UNIVERSITÀ
CAMPUS BIO-MEDICO DI ROMA

Corso di Dottorato di Ricerca in

Scienze Biomediche Integrate e Bioetica

Curriculum *Osteo-Oncologica / Osteo-Oncological Diseases*

XXXV ciclo a.a. 2019-2020

CONSERVATIVE VERSUS SURGICAL TREATMENT FOR ROTATOR CUFF TEARS:

A PROSPECTIVE RANDOMIZED CONTROL TRIAL

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ABSTRACT

The appropriate treatment for rotator cuff tear (RCT) is debated. Both tendon repair and physical therapy have been shown to be successful in treating small to medium size rotator cuff tears. However, there are limited high-level studies that compare conservative treatment with physiotherapy. This randomized controlled trial aims to compare surgical and conservative treatment of RCT, in terms of functional outcomes, rotator cuff (RC) integrity, and muscle atrophy or fatty degeneration. From January 2020 to December 2022, 88 patients with atraumatic, symptomatic, isolated full-thickness supraspinatus tendon tears documented with MRI were recruited at Campus Bio Medio Hospital. Written informed consent was obtained from each patient. The study was registered on "ISRCTNregistry" (ISRCTN12733667). Patients were randomly assigned to surgical repair (Group 1) or conservative treatment (Group 2) and were evaluated by clinical scores and MRI at randomization and after 6 months from the treatment. The surgical treatment group (Group 1) included 45 patients (45 shoulders). There were 21 (47%) male and 24 (53%) female patients, with a mean age of 58,8 ± 7, 25 years (range 44-74 years). The right shoulder was involved in 39 (87%) patients and the left shoulder in 6 (13%) patients. Twenty-four patients were evaluated at 6 months (T1). The conservative treatment group (Group 2) included 44 patients (44 shoulders). There were 19 (43%) male and 25 (57%) female patients, with a mean age of 60,2 ± 6,9 years (range 46-74 years). The right shoulder was involved in 28 (64%) patients and the left shoulder in 16 (36%) patients. Seventeen patients were evaluated at 6 months (T1). Significant improvements in clinical outcomes (Constant score, ASES Shoulder Score, VAS and Oxford Shoulder Score) were found 6 months after surgery. Moreover, no significant implementation in clinical outcomes for patients treated with physiotherapy and no significant differences between T0 and T1 in terms of fatty degeneration and muscle atrophy in both groups were observed. Patients treated with surgery had no significant differences in clinical outcomes compared with patients treated with physiotherapy. Additional research and follow–up are needed to establish a recommendation for conservative or surgical treatment for individual patients.

1 Introduction

The increased demands of an aging population in health care have placed the Italian Healthcare System under a considerable financial burden [51]. The rising cost of healthcare threatens the financial stability of our current system. To address this concern, future healthcare practices must improve patient care while containing rising costs.

The frequency of degenerative rotator cuff tears (RCT) is increasing. With them, we have witnessed a significant increase in the number of rotator cuff repairs. However, this expensive process may incur additional healthcare expenses with little benefit over conservative treatment. Several studies have raised doubts over the benefits for rotator cuff repair compared with non-operative treatment in the management of non-traumatic RCT. Few published Level-I randomized controlled trials have compared the effectiveness of surgical and conservative treatment for RCT [30].

A randomized controlled trial has been designed to assess the effectiveness of surgical versus conservative treatment for rotator cuff tears, based on functional outcomes, preservation of RC integrity, and prevention of muscle atrophy and fatty degeneration.

1.1 Rotator cuff

1.1.1 Anatomy

The rotator cuff (RC) is a musculotendinous structure that plays a crucial role in stabilizing the shoulder joint kinematics. The rotator cuff (RC) serves as a crucial component in holding the humeral head securely in the glenoid, allowing for rotational movement. The RC comprises four muscles - supraspinatus, infraspinatus, teres minor, and subscapularis - and their tendons, which work together to keep the humeral head centered within the glenoid cavity and stabilize the glenohumeral joint [33].

The supraspinatus muscle is located in the supraspinatus fossa of the scapula and originates from the same named fossa. It connects to the greater tubercle of the humerus via its tendon. During the initial 90 degrees of arm forward flexion and abduction, it functions. The suprascapular nerve (from the superior trunk of the brachial plexus, C5 and C6) provides innervation to the supraspinatus muscle.

The infraspinatus muscle has its beginning at the infraspinatus fossa of the scapula and terminates at the greater tubercle of the humerus. It is responsible for rotating the arm outward. The muscle is innervated by the suprascapular nerve.

The teres minor muscle starts at the lateral border of the scapula and ends at the greater tubercle and surgical neck of the humerus. It is innervated by the axillary nerve.

The subscapularis muscle originates from the medial two-thirds of the subscapularis fossa and inserts on the lesser tubercle of the humerus. It passes across the anterior surface of the glenohumeral joint. It is the principal internal rotator of the arm but also acts in adduction. It is innervated by the upper and lower subscapular nerves.

1.2 Rotator cuff tear

1.2.1 Epidemiology

Rotator cuff (RC) disease is among the most common musculoskeletal disorders.
It is a disabling condition with a high prevalence rate, particularly in the working population, causing high direct and indirect costs [34]. Age is the most common risk factor for rotator cuff disease. The percentage of patients with RCT increases with age. In the American population of patients with RCT, 65% of those older than 70 years have a full-thickness tear [28].

1.2.2 Pathogenesis.

Rotator cuff tears could be traumatic or atraumatic [35].
Traumatic tears typically occur as a result of a sudden injury, such as a fall or a lifting accident. Traumatic rotator cuff tears are relatively uncommon, but they can occur in people of all ages. However, they are seen generally in young patients. Men are more likely to experience a traumatic rotator cuff tear than women.

Trauma is not the most common cause of rotator cuff tears.

Degenerative tears are more frequent. The majority of rotator cuff tears are due to degenerative changes, mostly in people over the age of 60.

Several risk factors have been found for the degenerative process that leads to RCT: age, smoking, family genetics, hypercholesterolemia, overload, microtrauma and impaction [32,47,58].

Rotator cuff tears are divided into full-thickness tears and partial tears [55]. Partial tears could progress in full. Risk factors for rotator cuff progression include: tear size, symptoms, location, and age. A small tear may remain dormant, while larger tears are more likely to progress. The position of the tear affects its progression. Tear located in the anterior region are more prone to cuff degeneration. Additionally, increasing age poses a risk factor, with individuals over 60 years of age more likely to experience tears that progress [52].

1.2.3 Symptoms

Symptoms of rotator cuff tears include pain in the shoulder, weakness in the affected arm and difficulty lifting or rotating the arm. The pain can be acute or it can be gradual and mild, but steadily increasing.

The diagnosis of a rotator cuff tear typically involves a physical examination and imaging tests [18]. The range of motion of the affected shoulder must be checked: RC tears could cause pain in the range of motion (painful arc) and scapular dyskinesis.

1.2.4 Clinical examination

The Jobe empty can test assesses the strength of the supraspinatus muscle. The arm being tested is lifted to a 90-degree forward bend, at a 30-degree angle away from the body, with the thumb pointing downwards as if pouring out a drink. The patient must resist a downward push while in this position. A positive Jobe test result indicates decreased strength in the affected shoulder compared to the unaffected one[27].

The full-can test (Figure 1) is another test used to evaluate the supraspinatus muscle. It is performed with the patient’s arms abducted at 90° of forward flexion in the plane of the scapula and approximately 45° of abduction, with the thumb pointing upward. A positive result of the Jobe test is indicated by the presence of pain or a decrease in strength during the examiners downward pressure[27]

Figure 1: full-can test

The drop-arm sign was described by Codman to evaluate the supraspinatus muscle. The examiner asks the patient to elevate the arm fully and then to slowly reverse the motion in the same arc. The test could be considered positive if f the arm suddenly fell or the patient experiences severe pain [27].

Infraspinatus and teres minor tendons could be evaluated with the External Rotation Strength Test or Patte Test, the External Rotation Lag Sign and the Drop Sign.

Patte’s test (Figure 2) evaluates the strength of lateral rotation in 90° of forward elevation. It is performed by passively taking the arm from a starting point of 90° abduction in the scapular plane and an elbow flexion of 90° without external rotation. The patient is asked externally rotate the shoulder from this position against resistance. The test is positive if the patient experiment pain or weakness.

Figure 2: Patte’s test

The External Rotation Lag Sign (ERLS) is performed by flexing the patient's elbow to 90 degrees and elevating their shoulder to 20 degrees while rotating the arm outward. The patient must hold this position while the examiner supports their elbow. A positive sign is indicated by a decrease or drop in the angle of arm [27].

Figure 3: External rotation lag sign

The drop sign is performed with the shoulder at 20 degrees of elevation (in the scapular plane) and near the maximal external rotation. The sign is positive if a lag or “drop” occurs when the examiner releases the arm of the patient[27].

The Subscapularis Tendon is evaluated with the lift-off, lag sign in internal rotation, bear-hug, belly-press, belly off, and Napoleon tests.

In the lift-off test (Figure 4) the hand of the affected arm is placed on the back (at the position of the mid-lumbar spine) and then is asked to the patient to internally rotate the arm to lift the hand posteriorly off of the back. The test is positive if the patient is unable to perform this movement.

Figure 4: lift-off test

In the Internal Rotation Lag Sign the affected arm is placed on the back. The elbow is flexed to 90°, and the shoulder is held at 20°elevation and 20° extension. The dorsum of the hand is passively lifted off the lumbar region. The sign is positive when a lag occurs.

The Belly test is performed with the arm at the side and the elbow flexed to 90°. In this position, the patient press the palm into the abdomen. The test is positive if the patient experiment pain or weakness or pushes the hand against the abdomen by means of elbow extension or shoulder extension.

To perform the bear-hug test, the patient has to put the palm of the involved side on top of his contralateral shoulder with his fingers extended and the elbow positioned anterior to the body. Then the patient tries to hold the starting position by means of resisted internal rotation as the examiner tries to pull the patient's hand from the shoulder with an external rotation force applied perpendicular to the forearm. This test is positive, if the patient is not able to keep his hand on his contralateral shoulder or if the patient reports recognizable shoulder pain.

The Napoleon test is a variation of the belly-press test, performed placing the hand on the belly and pushing the hand against the stomach.

1.2.5 Imaging

Imaging tests include radiography, ultrasound, and MRI/MR arthrography.

X-rays could be performed in standard AP, true AP (Grashey view), scapular Y (lateral), and axillary view.

Ultrasounds are less expensive than MRI. However, ultrasounds require skill to obtain appropriate images and can be not even reliable.

MRI has an important role in the assessment of the shoulder. In the field of rotator cuff tear the MRI is used to assess:

- Rotator cuff integrity
- Depth and extent of the tear
- The pattern of rotator cuff tear
- Grade of tendon retraction (Patte Stage)
- Fatty degeneration of cuff muscles
- Muscle atrophy

1.2.5.1 Depth and extent of the tear

Ellman et all[9] (Figure 5) classified partial thickness rotator cuff tears based on the size and location of the tear.

Grade:

- Grade 1: < 3 mm
- Grade 2: 3-6 mm
- Grade 3: > 3 mm

Location:

- A Articular surface (80 %)
- B Bursal Surface
- C Interstitial

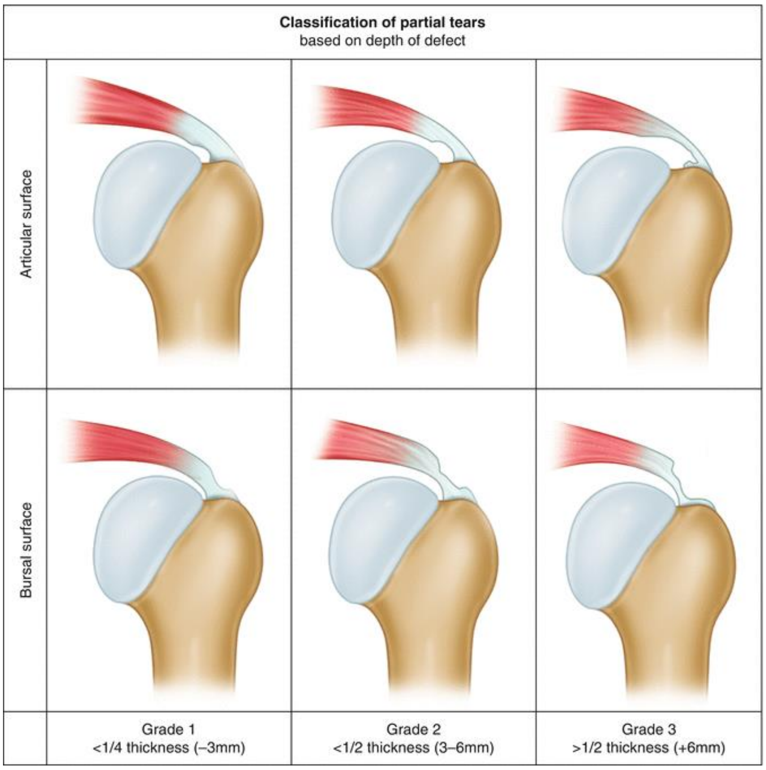


Figure 5: Ellman classification

The Snyder classification system is a method for categorizing rotator cuff tears based on the size and location of the tear[25].

Size

- 0: Normal
- 1: Minimal superficial bursal or synovial irritation or slight capsular fraying over a small area
- 2: Fraying and failure of some rotator cuff fibres in addition to synovial bursal or capsular injury.
- 3: More severe rotator cuff injury fraying and fragmentation of tendon fibres often involving the whole of a cuff tendon, usually <3cm
- 4: Very severe partial rotator cuff tear that contains a sizeable flap tear and more than one tendon

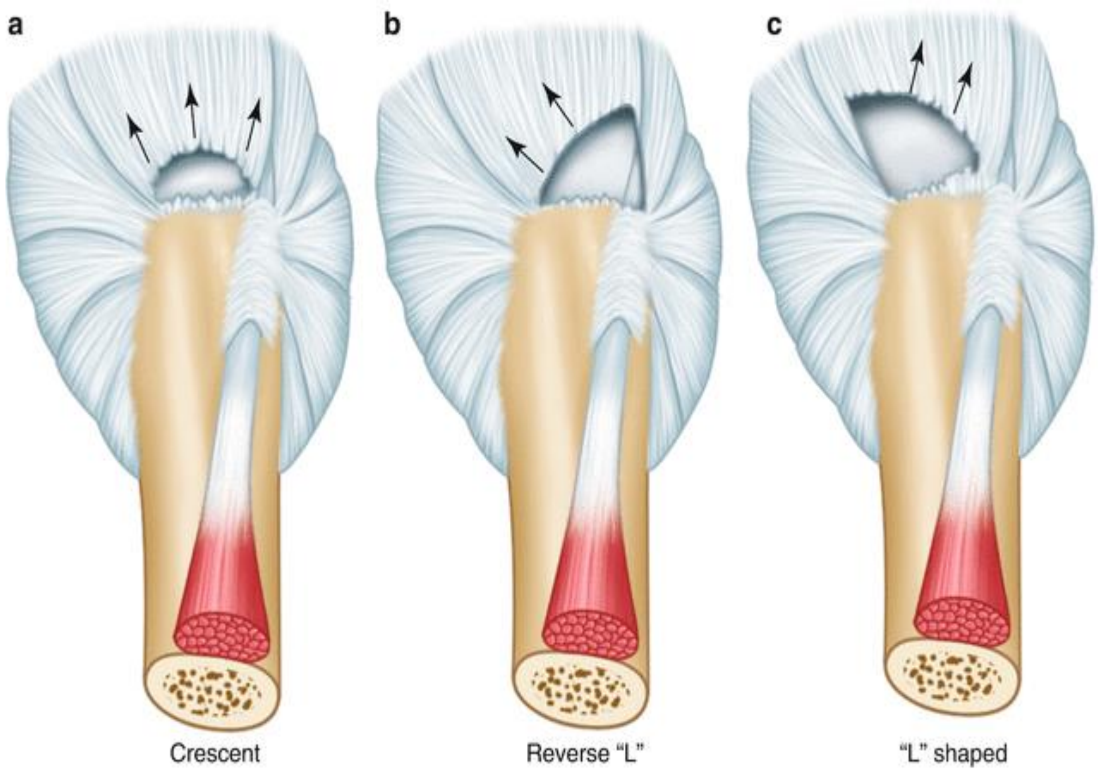
Location

- A: Articular surface
- B: Bursal surface
- C: Complete tear

PASTA stands for "partial articular-sided supraspinatus tendon avulsion," and it refers to a specific type of rotator cuff tear.

Ellman and Gartsman classified full-thickness rotator cuff tears in:

- Crescent (figure 6a)
- Reverse L (figure 6b)
- L-shaped (figure 6c)
- Trapezoidal (figure 6d).
- Massive full-thickness rotator cuff tear (figure 6e)



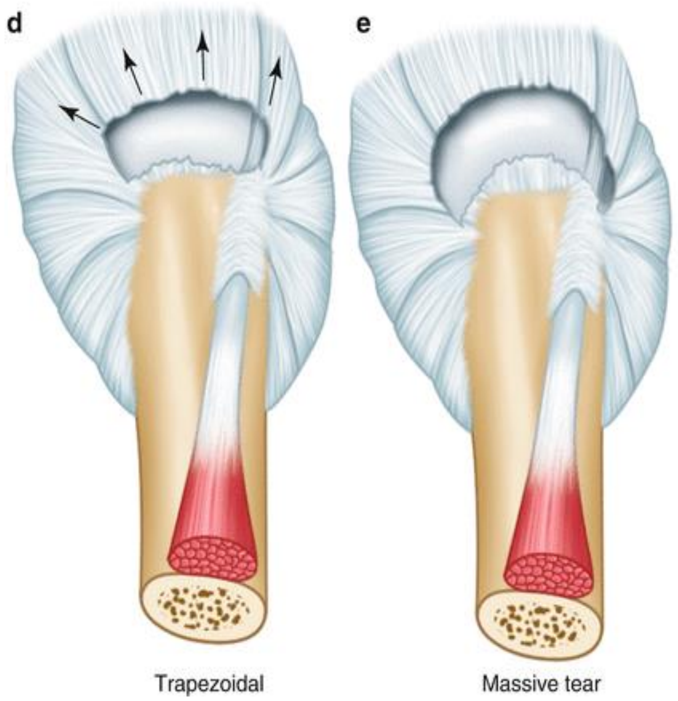


Figure 6: Ellman and Gartsman classification

De Orio-Colfield classified full-thickness rotator cuff tears in:

- Small: < 1cm
- Medium: 1-3 cm
- Large: 3-5 cm
- Massive: >5cm

Gerber et al [15] defined massive as a complete tear of at least 2 tendons

1.2.5.2 The pattern of rotator cuff tear

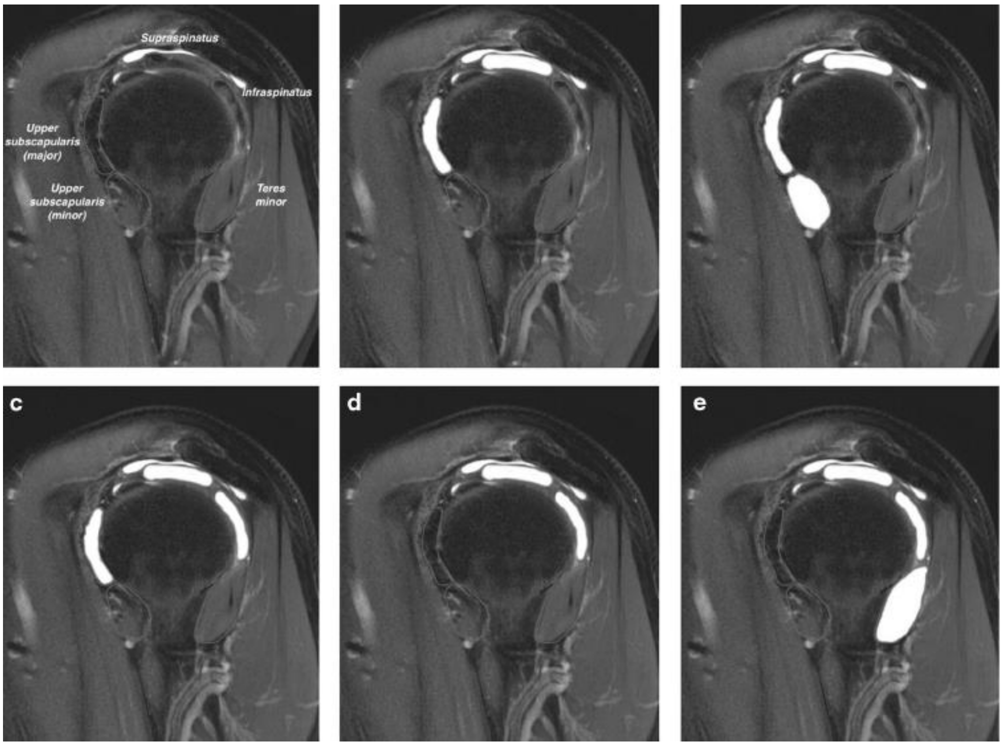
Collin et [7] (Figure 7) divided the rotator cuff into five components: supraspinatus; superior subscapularis; inferior subscapularis; infraspinatus; and teres minor. They classified rotator cuff tears based on the involved components:

- type A: supraspinatus and superior subscapularis tears;
- type B: supraspinatus and entire subscapularis tears;
- type C: supraspinatus, superior subscapularis, and infraspinatus tears;

- type D: supraspinatus and infraspinatus tears;
- type E: supraspinatus, infraspinatus, and teres minor tears

The Subscapularis muscle could be anatomically and functionally divided into superior and inferior portions. The superior two-thirds of the subscapularis insert with a tendon to the lesser tuberosity and it is innervated by the upper subscapular nerve; the inferior third of the subscapularis muscle remains muscular in its insertion and it is innervated by the lower subscapular nerve.

Collin et al found that shoulder ROM was significantly different between patients with type A and type B patterns. Patients with type A tears had active elevation above shoulder level; on the other side, most of the patients with type B tears had pseudoparalysis. This means that tears involving the supraspinatus and the entire subscapularis can not be compensated by other muscles (the anterior insertion of the rotator cable extends into the inferior subscapularis tendon). Moreover, the dysfunction of 3 rotator cuff muscles is a risk factor for pseudoparalysis [7].



Figuree 7: Collin classification

1.2.5.3 *Grade of tendon retraction*

Patte [46] (Figure 8) created a detailed classification system that combines tear size measurement using coronal and sagittal imaging, evaluation of tendon retraction, muscle weakness, and assessment of the long head of the biceps tendon's health. Frontal plane topography is divided into three levels.

:

- stage 1 is minimal retraction
- stage 2 is tendon retraction to the level of the humeral head
- stage 3 is tendon retraction at the level of the glenoid.

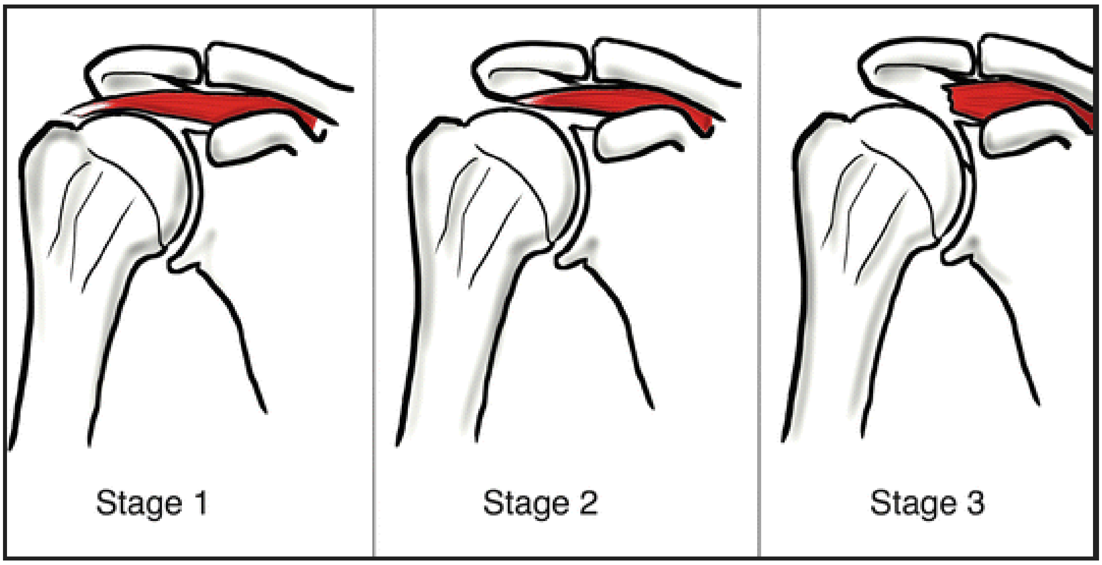


Figure 8: Patte classification

1.2.5.4 *Fatty degeneration of cuff muscles*

The classification of fatty infiltration of the rotator cuff musculature was described by Goutallier et al. for TC images and then modified by Fuchs et al for MR images (Figure 9) [16].

The original Goutallier classification was in 5 stages:

Grade 0: Normal muscle without fatty streaks

Grade 1: Muscle has some fatty streaking

Grade 2: Fatty infiltration present but less than muscle

Grade 3: Equal amount of fat and muscle tissue

Grade 4: More fat than muscle

Figure 9: Goutallier classification

Fuchs has simplified the original Goutallier classification into three categories Combining: grades 0 and 1 as normal and grades 3 and 4 as advanced degeneration.

1.2.5.5 Muscle atrophy

Muscle atrophy can be evaluated in a "qualitative" or "quantitative" way.

The "Tangent sign" [57] (Figure 10) could be used for the qualitative evaluation on sagittal T2-weighted MRI images. A line is drawn from the top edge of the scapular spine to the top edge of the coracoid process to determine the supraspinatus muscle's health. In a healthy supraspinatus, the muscle tissue should be above the tangent line, which is considered a negative tangent sign. If the muscle has atrophied, it will fall below the tangent line, resulting in a positive tangent sign.

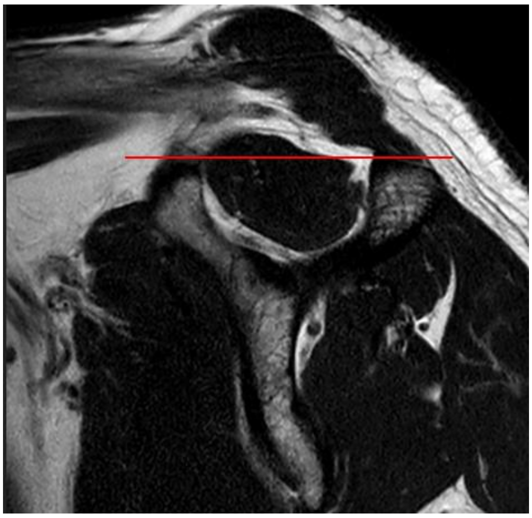


Figure 10: Tangent sign

The “quantitative" evaluation can be assessed using Thomazeau classification (Figure 11) [14]. It is based on the calculation of the “occupation ratio” (R) which is the ratio between the surface of the cross-section of the muscle belly and that of the fossa.

- Grade I: 1 >R > 0,6 ;
- Grade II: 0,6 > R > 0,4;
- Grade III: R < 0,4.

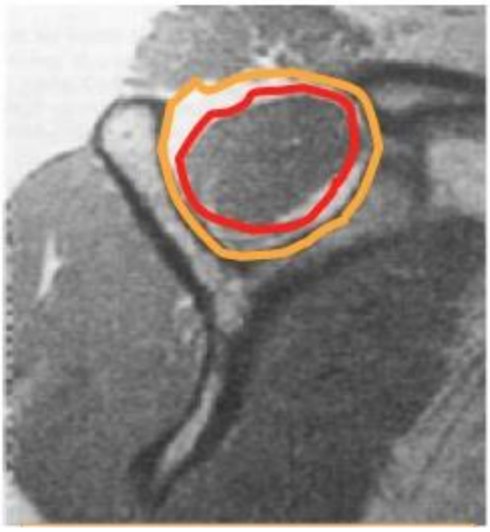


Figure 11: Thomazeau classification

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1.3 Rotator cuff tear treatment

The appropriate treatment for RCT is debated. The American Academy Orthopaedic Surgeons (AAOS) guidelines[54] state that RCR is an option for patients with chronic, symptomatic full-thickness RCT, but the quality of evidence is unconvincing. There is little compelling evidence also for conservative treatment [54]. Thus, the AAOS recommendations are inconclusive [54].

Clinical trials comparing surgery and conservative treatment for RCT are lacking. Surgical repair may result in post-operative stiffness, infection, and failure of the repaired tendon to heal. On the other hand, physiotherapy may predispose patients to continued irreversible tissue degeneration over time, with primarily repairable tears progressing to irreparable tears. In this case, RCT that could be addressed surgically can become irreparable.

Various surgical options are available for treating RCT, including partial repair, transferring the subscapularis tendon, teres major muscle transfer, reconstruction using a deltoid flap, transferring the latissimus dorsi or pectoralis major, superior capsule reconstruction, enhanced cuff repair, subacromial ballooning, and reverse total shoulder replacement [3,13,31,48].

On the other side, conservative treatment could consist of several protocols [2].

1.4 Evidence on rotator cuff tear treatment

1.4.1 Clinical outcome with non-operative management

Kuhn et al [22], in a multicenter prospective cohort study of 452 patients, evaluated the effectiveness of a specific physiotherapy program for atraumatic full-thickness RCT. Outcomes were assessed with a Short Form 12 score, American Shoulder and Elbow Surgeons score, Western Ontario Rotator Cuff score, Single Assessment Numeric Evaluation score, and Shoulder Activity Scale. They found significant improvements in patient-reported outcome scores at 6 and 12 weeks after treatment. However, 35 patients (9%) decided to have surgery in the first six weeks from the beginning of physiotherapy, and 24 patients between 6 and 12 weeks. The authors concluded that non-operative treatment was effective for treating atraumatic full-thickness rotator cuff tears in approximately 75% of patients followed up for 2 years.

Levy et al [26], in a prospective cohort study of 17 patients with nontraumatic, massive rotator cuff tears, evaluated an anterior deltoid rehabilitation program. They reported significant improvement in the ROM and function at a minimum follow-up of nine months after treatment.

Collin et al [8] evaluate the efficacy of a specifically designed rehabilitation program for 45 patients with irreparable massive RCT and shoulder pseudoparalysis. The treatment failed in patients with massive anterior rotator cuff tears or tears involving three or more tendons. However, 24 patients recovered more than 160° of anterior shoulder elevation.

1.4.2 Clinical outcome with operative management

Several studies have evaluated the outcome of patients after rotator cuff repairs.

Robinson et al [50], in a retrospective cohort study of prospectively collected data from 1600 consecutive rotator cuff repairs, reported a significant improvement in pain and ROM at the six-month follow-up after surgery. They found a retear rate of 13% with ultrasound imaging.

Millet et al [38] performed open-cuff repairs of 254 patients (263 shoulders) and found during the follow-up a survivorship rate of 94% at 5 years and 83% at 10 years. Increased survivorship was associated with single-tendon repairs. Moreover, they found a significant improvement in the outcome scores at a mean follow-up of 6.3 years.

Clinical results after rotator cuff repair were not correlated with age [11,43,45]

Rotator cuff repair improves sleep disturbances three to six months after surgery [29]

A good rate of patients treated with surgery returned to sports activity with a better or identical level compared to the preoperative level [1].

A meta-analysis found that the overall rate of return to sports after rotator cuff repair was 84.7%, with 65.9% of patients returning to play at a similar level after 4–17 months [21]

1.5 Aims

- The primary aim of this randomized controlled study was to compare functional outcomes of surgical and conservative treatment for patients with degenerative RCT.
- The secondary aim of this randomized controlled study was to investigate cuff integrity, muscle atrophy and fatty degeneration after surgical or conservative treatment for patients with degenerative RCT.

2 Material and method

A prospective randomized controlled trial was conducted to compare clinical outcomes of surgical and conservative treatment of degenerative RCT.

The ethics committee of “Campsus Bio-Medico University” approved the study. Written informed consent was obtained from each patient. The study was registered on “ISRCTNregistry” (ISRCTN12733667)

From January 2020 to December 2022 88 patients with atraumatic, symptomatic, isolated full-thickness supraspinatus tendon tears documented with MRI were recruited at Campus Bio Medio Hospital. The mean time of patients complaints before randomization was 12 ± 3 months.

The inclusion criteria were:

- age 45-75 years;
- atraumatic, symptomatic, isolated full-thickness supraspinatus tendon tear documented with MRI;
- full range of motion of the shoulder.

The exclusion criteria were:

- previous surgical treatment of the shoulder;
- frozen shoulder;
- radiological osteoarthritis of the glenohumeral joint;
- neurological disease or language barriers;
- tear involving the whole supraspinatus tendon combined with tear of two or three tendons;
- muscle fatty degeneration > of stage 2 according to Goutallier classification [14];

- muscle atrophy evaluated with Tangent sign [57];
- acute-on-chronic tears (after a traumatic event in a shoulder with preceding episodes of symptoms);
- impossibility to undergo MRI scan for any reason.

Patients were randomly assigned to one of two groups:

- surgical repair (Group 1, 46 patients)
- conservative treatment (Group 2, 42 patients).

Patients were randomly assigned to Group 1 or Group 2 using a computer-generated allocation

An experienced orthopedic surgeon performed surgical procedures in patients from Group 1.
A diagnostic arthroscopy was followed by subacromial decompression and biceps tenotomy in all patients.
The rotator cuff repair was performed by placing one row of double loaded suture anchors. The arm was then supported with an abduction sling pillow for 6 weeks.
A validated postoperative protocol was used (http://www.moonshoulder.com/impactstudy.html).

Conservative treatment consisted of a validated protocol for conservative RC rehabilitation under the supervision of an experienced shoulder physiotherapist. (http://www.moonshoulder.com/booklets/060109PatientRehabBooklet.pdf)
No supplementary treatment, such as cortisone injections or pain medication, was given.
Patients were evaluated by clinical scores and MRI at randomization and after 6 months.

Clinical scores were assessed in both study groups by two independent examiners.

The following scores were used:

- Constant score
  - The test is divided into four sections: pain (15 points), daily activities (20 points), strength (25 points), and mobility (40 points). The score reflects the level of functional ability, with higher scores indicating better function..
- ASES Shoulder Score
  - The pain score is determined by subtracting the VAS score from 10 and multiplying the result by 5. The 10 daily function questions are rated on a 4-point scale, ranging from 0 to 3, and can yield a maximum score of 30. This raw score is then multiplied by 5/3 to give a maximum functional score of 50 points. The pain and function scores are then combined to form the final ASES score, which ranges from 0 to 100. A higher score indicates better outcomes.
- VAS score for pain
  - The VAS consists of a 10 points scale, with two end points representing 0 ('no pain') and 10 ('pain as bad as it could possibly be')
- Patient Reported Outcome Measures (PROMS):
  - Disease-specific:
    - Oxford Shoulder Score (OSS)
    - Shoulder pain and disability index (SPADI)

To investigate the effectiveness of surgical and conservative treatment for RCT, all patients underwent magnetic resonance imaging (MRI) of the shoulder at randomization and at 6 months post-operatively.

MRI was used to assess:

- RC integrity
- extent of fatty degeneration according to Goutallier classification modified by Fuchs[14]
- amount of muscle atrophy by Tangent sign [57]

Two independent examiners assessed the MRIs.

2.1 Statistical analysis

Baseline and follow-up characteristics are presented as proportion, mean (standard deviation [SD]), or median (interquartile range) in case of a skewed distribution. Differences at baseline between the 2 treatment groups were tested using Mann-Whitney U tests for continuous variables and χ^2 tests for categoric variables.

To study the effect of the 2 different treatments, all follow-up analyses were performed as ‘‘per-protocol analyses”.

Blind statistics were performed.

3 Result

3.1 Demographics (Table 1)

The study group included 89 patients (89 shoulders). There were 40 (45%) male and 49 (55%) female patients, with a mean age of 59,4 ± 7,5 years (range 44-74 years). The right shoulder was involved in 66 (75%) patients and the left shoulder in 22 (25%) patients.

The surgical treatment group (Group 1) included 45 patients (45 shoulders). There were 21 (47%) male and 24 (53%) female patients, with a mean age of 58,8 ± 7, 25 years (range 44-74 years). The right shoulder was involved in 39 (87%) patients, and the left shoulder in 6 (13%) patients. 24 patients were evaluated at 6 months (T1).

The conservative treatment group (Group 2) included 44 patients (44 shoulders). There were 19 (43%) male and 25 (57%) (2/44) female patients, with a mean age of 60,2 ± 6,9 years (range 46-74 years). The right shoulder was involved in 28 (64%) patients, and the left shoulder in 16 (36%) patients. 17 patients were evaluated at 6 months (T1).

Table 1: Demographics

	Group 1 (surgical group)	Group 2 (conservative group)
N of patients	45	44
N of Male	21	19
N of Female	24	25
Age (mean ± SD)	58,8 ± 7, 25	60,2 ± 6,9
N of Right shoulder	39	28
N of Left shoulder	6	16
N of patients evaluated at 6 months	24	17

3.2 Complications

No patients experienced infections, neuro-vascular injuries or stifnees after surgery. 4 (8%) patients of the surgical group had a failure.

3.3 Clinical outcomes (Table 2)

The clinical evaluation was performed in all patients according to the study protocol.

3.3.1 Surgical repair group (Group 1)

3.3.1.1 T0

The average Constant score was 42,9 ± 7,39 points (range 32 – 77 points).

The average ASES Shoulder Score was 41,5 ± 12,3 points (range 11,67 – 78,31 points).

The average VAS was 6,6 ± 1.5 points (range 2 - 10 points).

The average Oxford Shoulder Score was 38,4 ± 6,3 points (range 22 - 50 points).

The average Shoulder pain and disability index was 64 ± 17 points (range 25,38 – 92,30 points).

3.3.1.2 T1

The average Constant score was 64 ± 8,4 points (range 48 - 84 points).

The average ASES Shoulder Score was 84,2 ± 16 points (range 49,9 - 100 points).

The average VAS was 2 ± 2,1 points (range 0 - 6 points).

The average Oxford Shoulder Score was 25,7 ± 11,7 points (range 13 - 55 points).

The average Shoulder pain and disability index was 13,6 ± 16.2 points (range 0 - 59 points).

3.3.1 Conservative group (Group 2)

3.3.1.1 T0

The average Constant score was 52,8 ± 13,9 points (range 20 - 84 points).

The average ASES Shoulder Score was 63,9 ± 14,1 points (range 43,3 – 93,32 points).

The average VAS was 4,87 ± 1,5 points (range 1 - 8 points).

The average Oxford Shoulder Score was 30,31 ± 16,9 points (range 0 – 75 points).

The average Shoulder pain and disability index was 40.04 ± 19 points (range 0- 73,8 points).

3.3.1.2 T1

The average Constant score was 62,5 ± 5,9 points (range 52 - 76 points).

The average ASES Shoulder Score was 82,4 ± 15,5 points (range 40 - 100 points).

The average VAS was 2,8 ± 2,2 points (range 0 - 8 points).

The average Oxford Shoulder Score was 28 ± 11,7 points (range 14- 50 points).

The average Shoulder pain and disability index was 14,8 ±16,1 points (range 0 – 58,4 points).

Table 2: Clinical outcomes

	Surgical repair group T0 (mean ± SD)	Conservative group T0 (mean ± SD)	Surgical repair group T1 (mean ± SD)	Conservative group T1 (mean ± SD)
Constant	42,9 ± 7,39	52,8 ± 13,9	64 ± 8,4	62,5 ± 5,9
ASES	41,5 ± 12,3	63,9 ± 14,1	84,2 ± 16	82,4 ± 15,5
VAS	6,6 ± 1.5	4,87 ± 1,5	2 ± 2,1	2,8 ± 2,2
OSS	38,4 ± 6,3	30,31 ± 16,9	25,7 ± 11,7	28 ± 11,7
SPADI	64 ± 17	40.04 ± 19	13,6 ± 16.2	14,8 ±16,

3.4 Imaging outcomes

The MRI was performed in all patients according to the study protocol.

3.4.1 Surgical repair group (Group 1)

3.4.1.1 T0

The average extent of fatty degeneration according to Goutallier classification modified by Fuchs was 1,1 + 0,6 points (range 0 - 3 points).

The average amount of muscle atrophy by Tangent sig was positive in 3 of 45 patients (6,6 %).

3.4.1.2 T1

The average extent of fatty degeneration according to Goutallier classification modified by Fuchs was 1,1 ± 0, 6 points (range 0 - 3 points).

The average amount of muscle atrophy by Tangent sig was positive in 3 of 45 patients (6,6 %).

3.4.2 Conservative group (Group 2)

3.4.2.1 T0

The average extent of fatty degeneration according to Goutallier classification modified by Fuchs was 0.75 ± 0.5 points (range 0 - 2 points).

No patients had a positive Tangent sig.

3.4.2.2 T1

The average extent of fatty degeneration according to Goutallier classification modified by Fuchs was 0,87 ± 0.6 points (range 0 -2 points).

No patients had a positive Tangent sig.

3.5 Differences in Clinical outcomes

3.5.1 Group 1 (Surgical)

There was a significant improvement in clinical outcomes between T0 and T1 for Constant score (p-value < 0.00001) (Figure 12, Table 3), ASES Shoulder Score (p-value = 0.0006) (Figure 13, Table 3), VAS (p-value < 0.00001) (Figure 14, Table 3), Oxford Shoulder Score (p-value < 0.00001) (Figure 15, Table 3).

The difference between T0 and T1 for Shoulder pain and disability index was not significant (p-value = 0.12356)

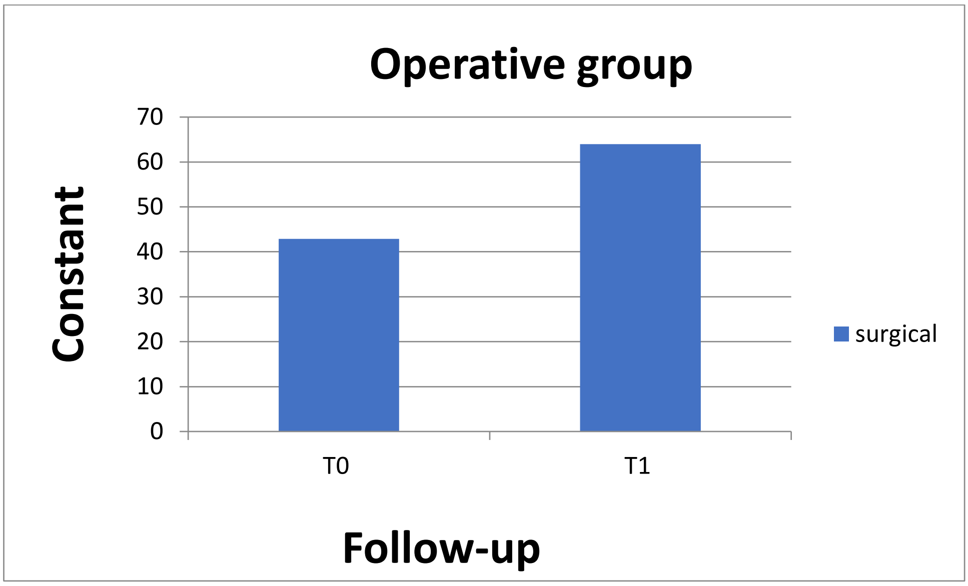

Figure 12: improvement in Costant score between T0 and T1in the operative group

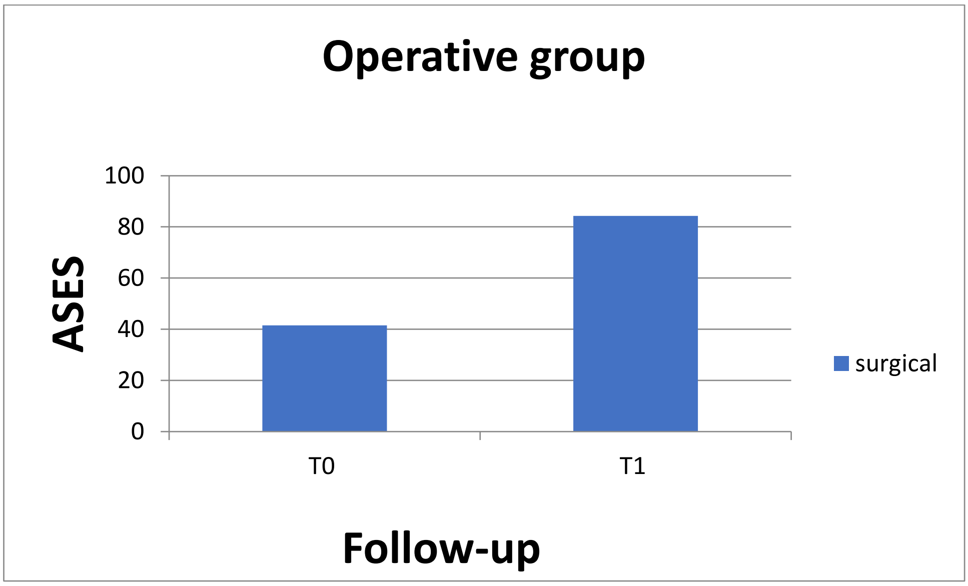

Figure 13: improvement in ASES score between T0 and T1 in the operative group

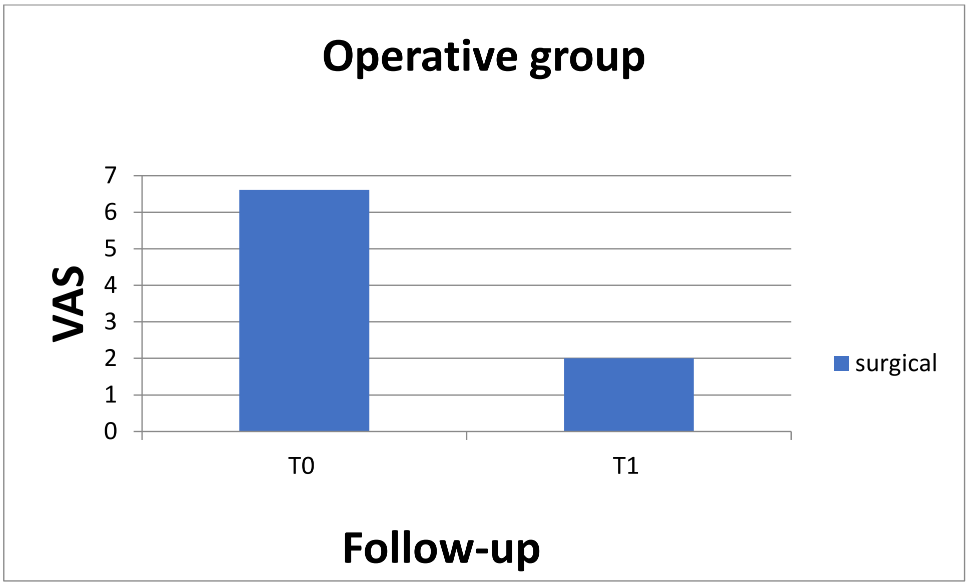

Figure 14 improvement in pain between T0 and T1 in the operative group

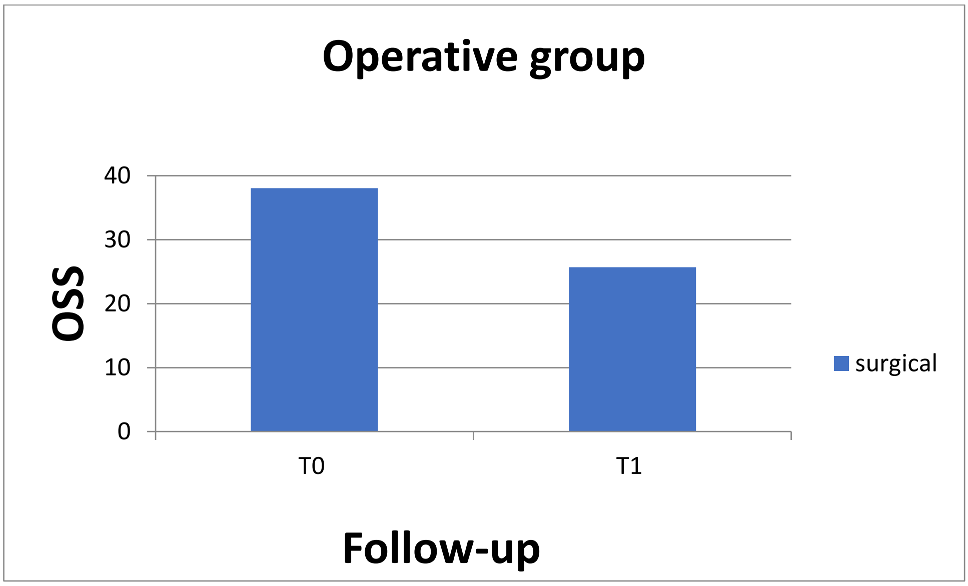

Figure 15 differences in OSS between T0 and T1 in the operative group

3.5.2 Group 2

There was a significant improvement in clinical outcomes between T0 and T1 for VAS scale (p = 0,00932) (Figure 16)

The difference between T0 and T1 was not significant for Constant score (p-value = 0.02382) (Figure 17, Table 3), ASES Shoulder Score (p-value = 0.11642) (Figure 18, Table 3), Oxford Shoulder Score (p-value = 0.3843)(Figure 19, Table 3), Shoulder pain and disability index (p-value is 0.3843) (Figure 20, Table 3)

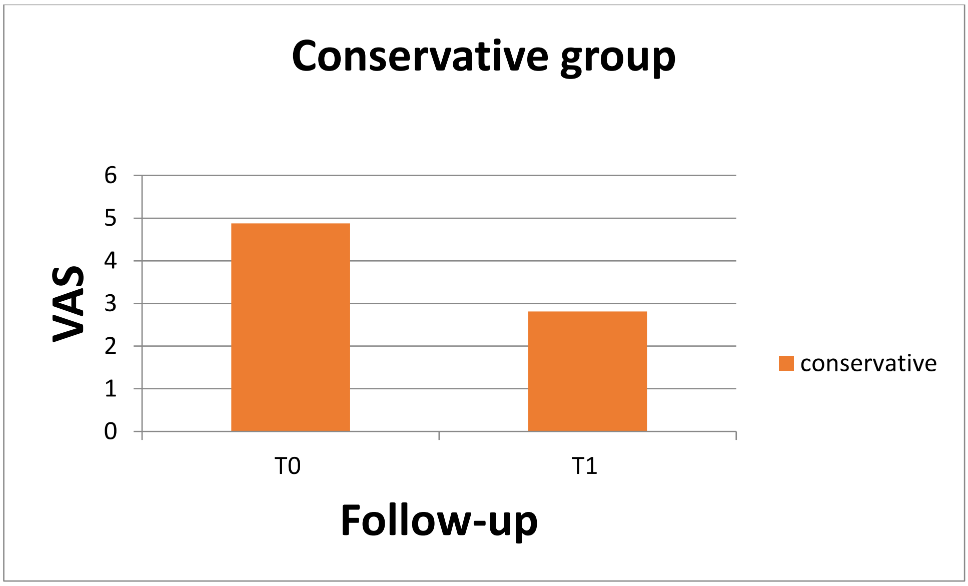

Figure 16: differences in VAS between T0 and T1 in the conservative group

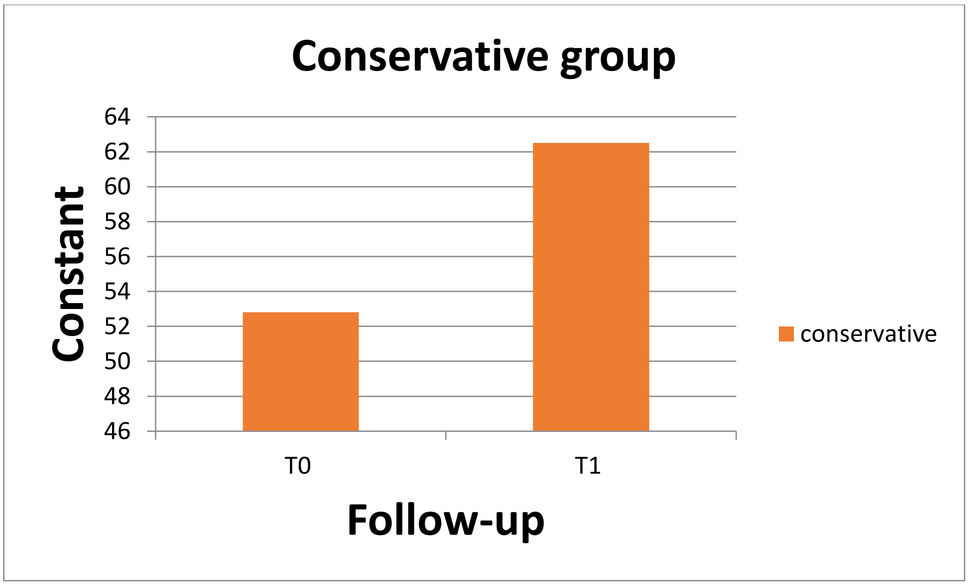

Figure 17: differences in CMS between T0 and T1 in the conservative group

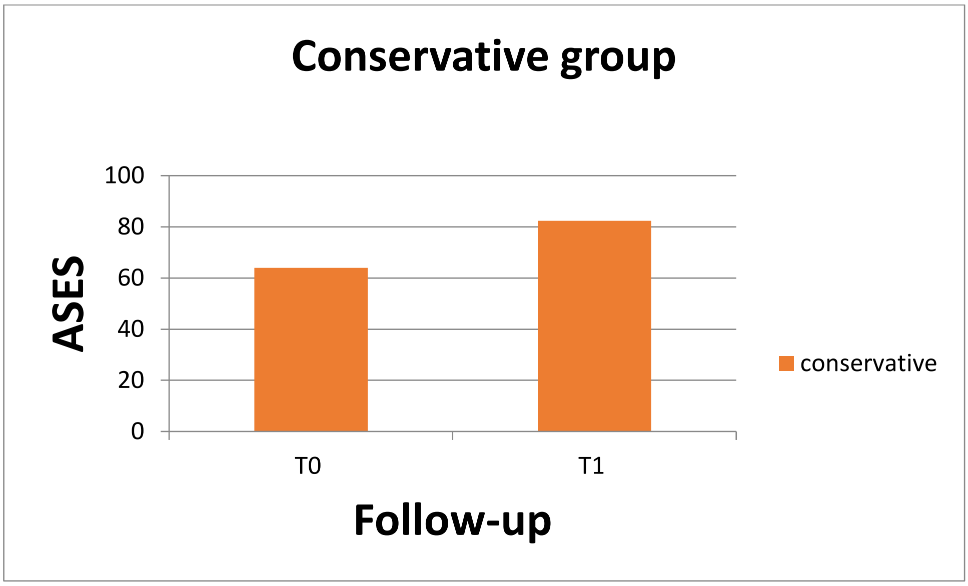

Figure 18: differences in ASES between T0 and T1 in the conservative group

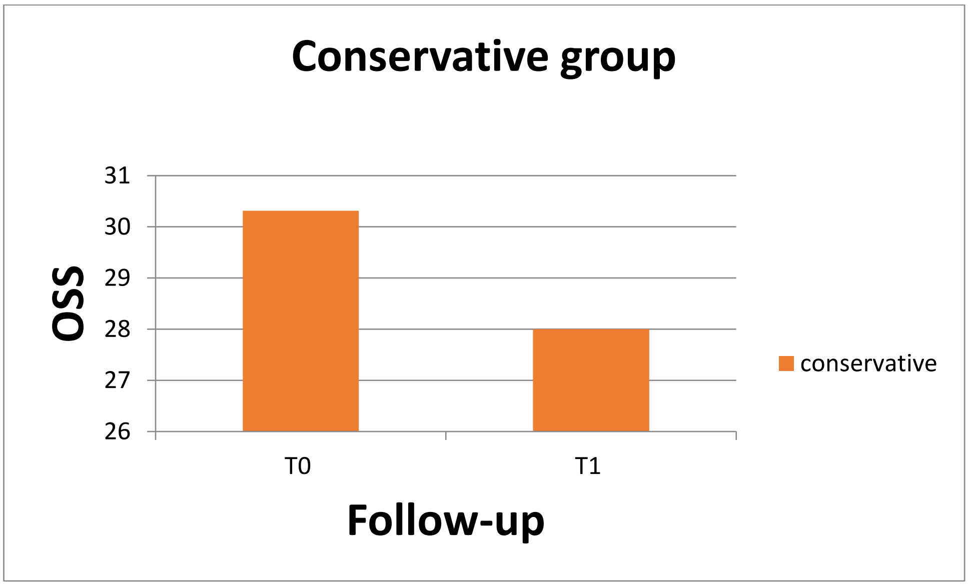

Figure 19: differences in OSS between T0 and T1 in the conservative group

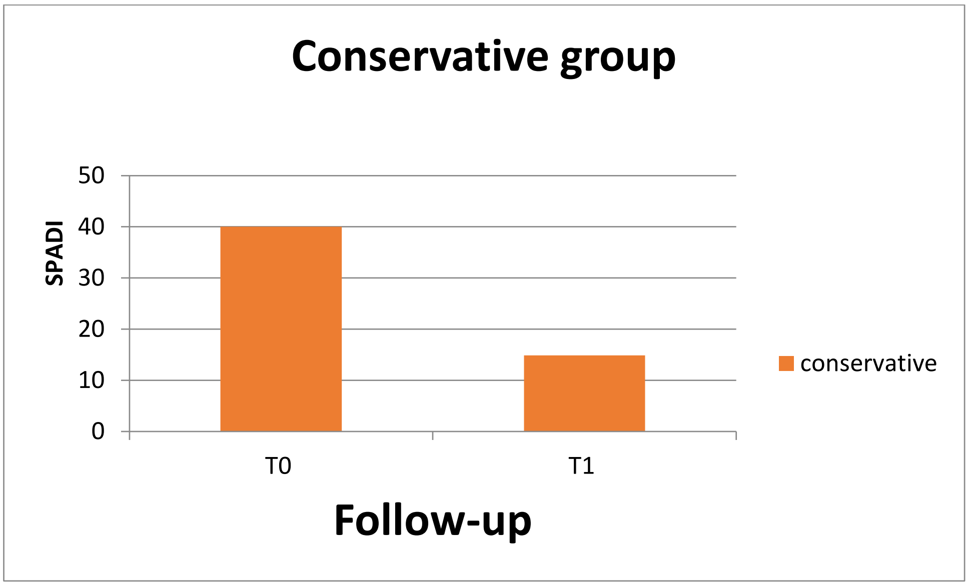

Figure 20: differences in SPADI between T0 and T1 in the conservative group

Table 3: differences in surgical and conservative group between T0 and T1

	Surgical			Conservative		
	T0	T1	P	T0	T1	p
CMS	42,9	64	< 0.00001*	52,8	62,5	0.02382
ASES	41,5	84,2	0.0006*	63,9	82,3	0.11642
VAS	6,6	2	< 0.00001*	4,9	2,8	0,0093*
OSS	38	25,6	< 0.00001*	30,3	28	0.3843
SPADI	64,4	13,6	= 0.12356	40	14,9	0.3843

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3.5.3 Group 1 versus Group2

The differences between the surgical repair and conservative group were not significant in terms of Constant score (p-value = 0.63836) (Figure 21), ASES Shoulder Score (p-value = 0.63836) (Figure 22), VAS (p-value =63836) (Figure 23), Oxford Shoulder Score (p-value = 0.477) (Figure 24), Shoulder pain and disability index (p-value is 0.8414) (Figure 25)

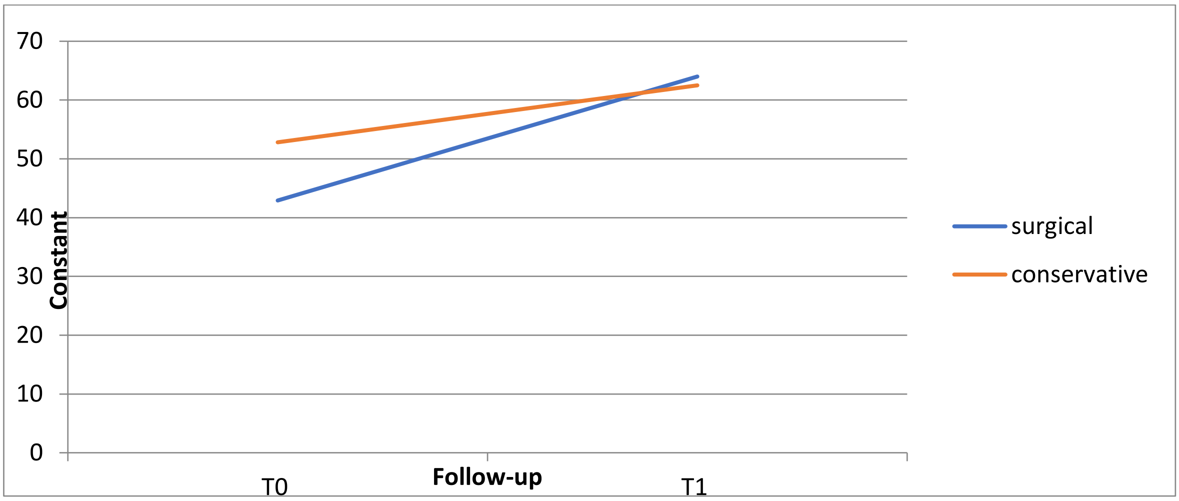

Figure 21: differences between the surgical repair and conservative group in Constant score

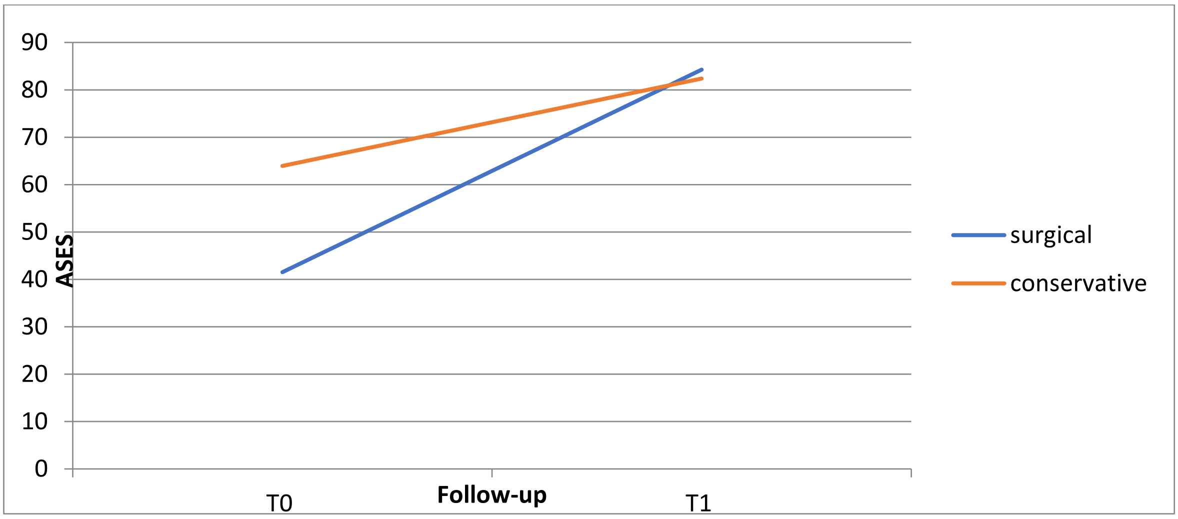

Figure 22: differences between the surgical repair and conservative group in ASES score

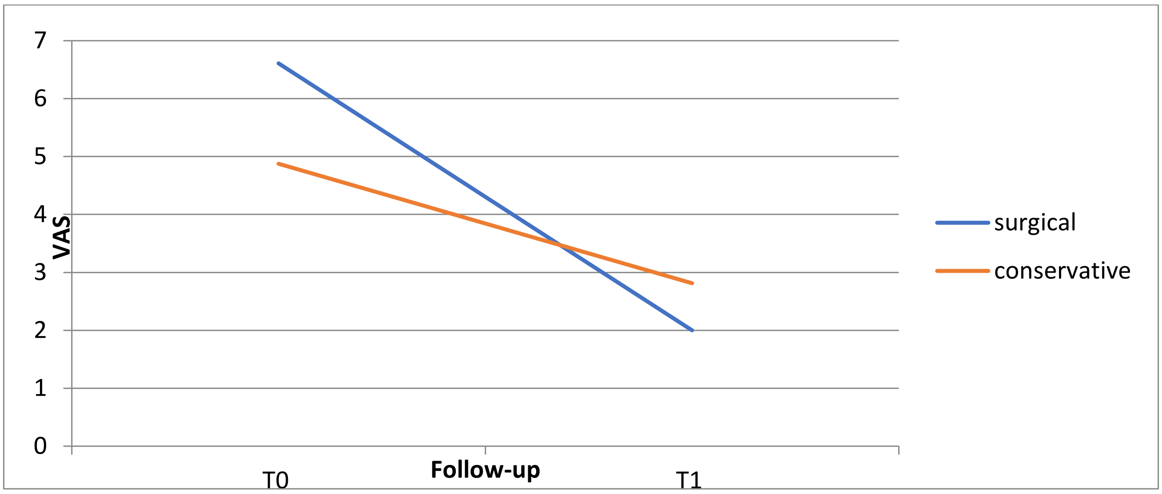

Figure 23: differences between the surgical repair and conservative group in VAS score

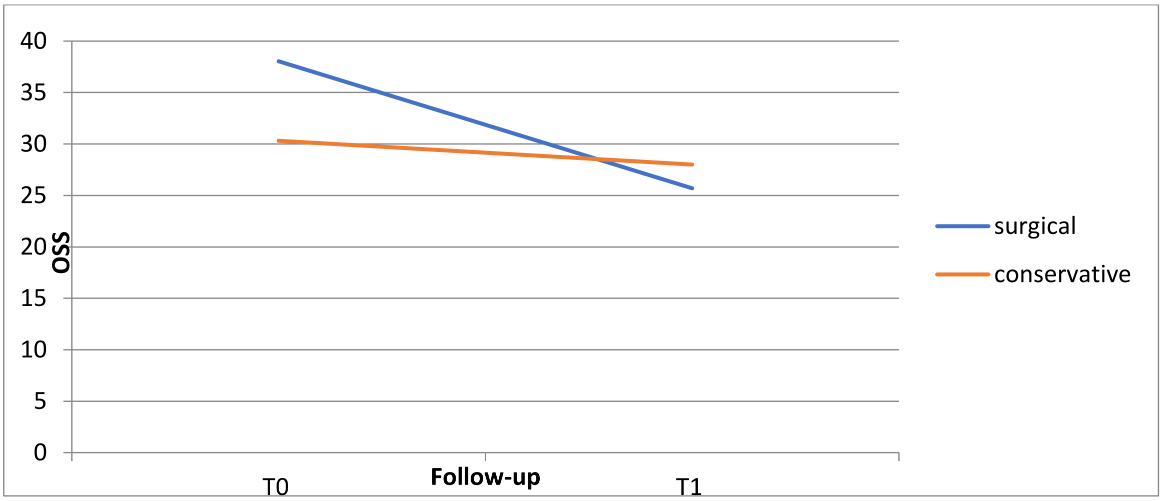

Figure 24: differences between the surgical repair and conservative group in OSS score

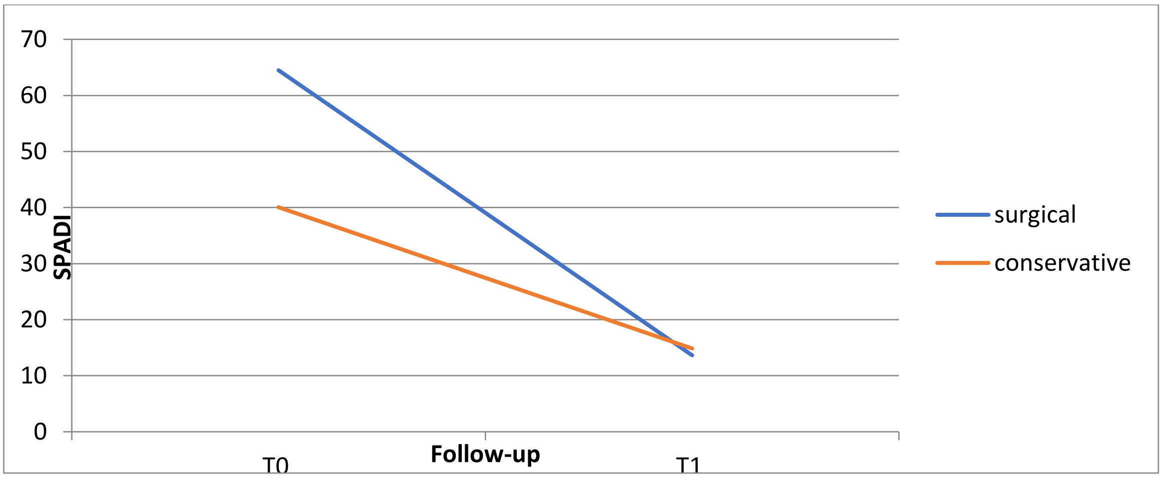

Figure 25: differences between the surgical repair and conservative group in SPADI score

3.6 Differences in Radiological Outcomes outcomes

3.6.1 Group 1

The difference in fatty infiltration and atrophy according to Goutallier classification and Tangent sign, respectively, between T0 and T1 in the surgical repair group was not significant (p-value = 0.83366)

3.6.2 Group 2

The difference in fatty infiltration and atrophy according to Goutallier classification and Tangent sign, respectively, between T0 and T1 in the conservative group was not significant (p-value = 0. 63836)

4 Discussion and conclusion

This randomized controlled trial was designed to compare outcomes after surgical or conservative treatment for degenerative rotator cuff tears.

Six months after surgery we found a significant improvement in clinical outcomes assessed with Constant score, ASES Shoulder Score, VAS and Oxford Shoulder Score. These results can be considered comparable to other studies: several authors [50] [38] found a significant improvement in pain and outcome scores after rotator cuff repair.

On the other side, no significant implementation in clinical outcomes for patients treated with physiotherapy was found. After the rehabilitation protocols patients had a significant improvement in terms of pain, demonstrated by a significant decrease in the VAS scale, and a nonsignificant improvement in clinical outcomes.

The literature reported good clinical outcomes for patients with massive rotator cuff tears treated only with rehabilitation [22,26]. However, those conclusions were supported by prospective studies without a control group, focused on showing the benefits of a good rehabilitation protocol, rather than comparing surgical and conservative treatments. A good rehabilitation protocol could be useful and is certainly raccommodated rather than nothing.

No significant differences between T0 and T1 in terms of fatty degeneration and muscle atrophy in both groups were found.

Moreover, no significant differences in terms of clinical outcomes between the conservative and surgical groups at 6 months were found.

Our results can be considered comparable to other similar randomized clinical trials.

Kukkonen et al [23] concluded that surgical treatment yields no significantly better CMS than conservative treatment.

Moosmayer et al [40] found better results for the surgery group at one and ten years of follow-up [41]. However, the difference between the 2 groups at 5 years of follow-up was small (5 points), which is below the clinically important level [42].

To choose the best treatment between physiotherapy and surgery, it is of vital importance to know the natural history of rotator cuff tears if treated non-operatively. Full-thickness tears do not heal without surgical intervention [49].

Non-surgical treatment may predispose patients to continued irreversible tissue degeneration with muscle atrophy and fatty degeneration over time, with primarily repairable tears progressing to irreparable tears [49].

Ranebo et al [49], in a retrospective analysis of a consecutive series of 69 patients treated between 1989 and 1993 with acromioplasty without cuff repair, found that, at a mean of 22 years of follow-up, 17 of 23 patients with a full-thickness tear had developed cuff tear arthropathy (Hamada ≥2) and 20 had progressed in tear size. Of the 43 patients with partial-thickness tears, 3 had developed cuff tear arthropathy and 16 had tear progression. They concluded that most unrepaired full-thickness tears will, in the long-term, increase in size and be accompanied by cuff tear arthropathy changes. Most partial-thickness tears remain unchanged.

Moosmayer et al [39], in a retrospective study, analyzed 89 small to medium-sized full-thickness tears of the rotator cuff treated with physiotherapy. 23 of 89 tears were later repaired surgically. 49 of those tears treated with physiotherapy, were re-examined after 8.8 months of follow-up (37 patients with MRI, the others with ultrasonography): mean tear size increased by 8.3 mm in the anterior-posterior plane and by 4.5 mm in the medial-lateral plane. Muscle atrophy and fatty degeneration progressed in 18 and 15 of the 37 patients, respectively.

Kim et al [20] analyzed 122 patients (34 with a full-thickness tear and 88 with a partial-thickness tear) treated conservatively with a mean follow-up period was 24.4 ± 19.5 months and found that tear size increased for 28/34 (82.4%) patients with full-thickness tears and 23/88 (26.1%) patients with partial-thickness tears.

Similarly, in another study, over 50% of full-thickness tears treated non-operatively increased in size at a minimum follow-up of 6 months [36].

In a prospective case-control study of 174 patients conducted by Yamamoto et al [56], it was found that 47% of shoulders with symptomatic rotator cuff tears experienced tear enlargement over an average follow-up period of 19 months, with a rate of growth of 3.8mm in length and 2mm in width per year. The study determined that tear progression was more likely to occur in medium-sized tears, full-thickness tears, and among smokers. Those evidences underline that medium and large full-thickness rotator cuff tears progress over time. However, the question is: have patients with tear progression worst outcome compared to patients surgically treated? To answer this question it is important to analyze the systematic review on long-term outcomes of Chalmers et al [4]. They compare patient-based outcomes, future surgical intervention, future tear progression or recurrence and tear size, including studies with a minimum follow-up of 5-years and found that there were no differences between the repair and no-repair groups in terms of the Constant score and that the likelihood of failure (repair group) or extension of the tear (no-repair group) was not different between groups.

The results of this study need to be viewed in light of certain limitations. First of all, this is a short time (6 months) follow-up with a small sample size and just a per-protocol analysis. Our reported data are preliminary results at 6 months of follow-up There remains some controversy regarding the relationship between the timing of surgery and outcomes. The most of the studies have focused in acute, traumatic tears rather than degenerative, atraumatic tears. There are poor evidences on degenerative teras. However, Finger et al, in a retrospective cohort study, found that delaying surgical treatment for 1 year or more does not appear to significantly impact postoperative outcomes [10].

There are limited high-level studies that compare conservative treatment with physiotherapy.

Kukkonen et al [23] compared, in a clinical trial with two-year follow-up, three groups of patients with rotator cuff tears treated with physiotherapy (Group 1); acromioplasty and physiotherapy (Group 2); rotator cuff repair, acromioplasty, and physiotherapy group (Group 3). They found no significant difference in clinical outcomes between the three interventions. The limitation of this study is the heterogeneity of patients in therm of tear size.

Moosmayer et al [42], in a randomized clinical trial with a five-year follow-up, compared functional outcomes in 52 patients treated with rotator cuff repair and 51 patients treated by physiotherapy. The results of the study showed that 24% of patients who initially received physiotherapy eventually required additional repair. The final evaluation found that those who underwent primary tendon repair had a significantly greater improvement in their Constant score compared to those who only received physiotherapy. Over a 10-year period, the results of primary tendon repair were better than physiotherapy for treating both small and medium-sized rotator cuff tears [41].

Lambers Heerspink et al [24] compared surgical repair versus physiotherapy combined with subacromial steroid injection and analgesics in 56 patients with degenerative RCT. The surgery group had significantly lower scores for pain and disability. The Constant score was not significantly different between surgery and conservative groups at 12 months of follow-up. Moreover, the retear rate at one year was 74% in the surgical group.

That evidence suggests that clinical outcomes could change in the long time follow-up period.

Chona et al[5] in a meta-analysis of thirteen articles found that retear rates for medium tears increased for approximately 15 months until a retear rate of 20% and that for medium tears increased for approximately 2 months until an upper limit of approximately 40%. The range of retears for massive tears ranged from 20% to 60%.

Patients with a history of trauma who have waited longer than 24 months for surgical repair had higher re-tear rates (20%) than those who had their surgery earlier (13%) [53].

It is important to underline that patients with radiological evidence of a failure of rotator cuff repair could even have an improvement in clinical outcomes.

Jost et al [19] documented that an attempt at rotator cuff repair significantly decreases pain ($p = 0.0026$) and significantly improves function ($p = 0.0005$) and strength ($p = 0.0137$) even if magnetic resonance imaging documents that the repair has failed.

Namdari et al [44] in a retrospective study, found that successful outcomes were achieved in 54% of patients with failed rotator cuff repair.

A systemic review and meta-analysis of 8011 shoulders revealed that patients reported an overall improvement in their condition, regardless of whether the rotator cuff repair was successful in restoring tendon integrity [37].

In this study, in 8% of surgically treated patients, a retear of the rotator cuff was diagnosed on MRI after six months. This is only the preliminary follow up, that will be updated on the basis of further follow up. However the four patients with rotator cuff retear had a poor adherence to post-operadive prescriptions and rehabilitation program.

In licterature the retear rate of rotator cuff repair can vary depending on several factors such as the size of the tear, the quality of the repair, the age and health of the patient, and post-operative rehabilitation. However, studies suggest that the retear rate of rotator cuff repair is generally between 20% to 30%. [5,43,45]. Factors that can increase the risk of retear include larger tears, poor tissue quality, advanced age, smoking, and a delay in surgery. On the other hand, factors that can decrease the risk of retear include the use of modern surgical techniques, better quality of tendon and bone healing, and adherence to a comprehensive rehabilitation program.

Several authors evaluated the prevalence and clinical impact of osteoarthritis following rotator cuff repair. Herve et al reported a rate of osteoarthritis of 29%, 20 years following rotator cuff repair. Massive rotator cuff tears were significantly associated with a higher rate of osteoarthritis. Less osteoarthritis was observed when suprasupinatus healed [17]. Age, male gender, initial tear severity, and the pain and mobility components of the preoperative Constant score were found to be risk factors for gleno-humeral osteoarthritis after rotator cuff repair a in retrospective multicentre study of patients who underwent rotator cuff repair in 2003 and were re-evaluated at least 10 years later [12]. Collin et al made a 20-year follow-up of 127 patients operated for massive rotator cuff tears and found that nine patients (17%) had cuff tear arthropathy (Hamada stage 4)[6]. On the other side Ranebo et al [49], reported that, at a mean of 22 years of follow-up, 17 of 23 patients with a full-thickness tear had developed cuff tear arthropathy (Hamada ≥ 2). However, the relationship between shoulder osteoarthritis and rotator cuff tear is unclear.

In conclusion, significant differences in functional outcome 6 months after surgery were observed but comparing surgical and conservative treatment no statistically significant differences were found. Patients treated with surgery had better outcomes compared with patients treated with physiotherapy. On the other side, physiotherapy could significantly improve pain. Additional research and follow–up are needed to establish a recommendation for conservative or surgical treatment for individual patients.

5 References

1. Antoni M, Klouche S, Mas V, et al. Return to recreational sport and clinical outcomes with at least 2years follow-up after arthroscopic repair of rotator cuff tears. *Orthopaedics & traumatology, surgery & research : OTSR.* 2016;102(5):563-567.
2. Candela V, Longo UG, Di Naro C, et al. A Historical Analysis of Randomized Controlled Trials in Rotator Cuff Tears. *International journal of environmental research and public health.* 2020;17(18).
3. Castricini R, Longo UG, De Benedetto M, et al. Arthroscopic-Assisted Latissimus Dorsi Transfer for the Management of Irreparable Rotator Cuff Tears: Short-Term Results. *The Journal of bone and joint surgery American volume.* 2014;96(14):e119.
4. Chalmers PN, Ross H, Granger E, et al. The Effect of Rotator Cuff Repair on Natural History: A Systematic Review of Intermediate to Long-Term Outcomes. *JB & JS open access.* 2018;3(1):e0043.
5. Chona DV, Lakomkin N, Lott A, et al. The timing of retears after arthroscopic rotator cuff repair. *Journal of shoulder and elbow surgery.* 2017;26(11):2054-2059.
6. Collin P, Betz M, Herve A, et al. Clinical and structural outcome 20 years after repair of massive rotator cuff tears. *J Shoulder Elbow Surg.* 2020;29(3):521-526.
7. Collin P, Matsumura N, Ladermann A, Denard PJ, Walch G. Relationship between massive chronic rotator cuff tear pattern and loss of active shoulder range of motion. *Journal of shoulder and elbow surgery.* 2014;23(8):1195-1202.
8. Collin PG, Gain S, Nguyen Huu F, Ladermann A. Is rehabilitation effective in massive rotator cuff tears? *Orthopaedics & traumatology, surgery & research : OTSR.* 2015;101(4 Suppl):S203-205.
9. Ellman H. Diagnosis and treatment of incomplete rotator cuff tears. *Clinical orthopaedics and related research.* 1990(254):64-74.
10. Finger L, Dunn R, Hughes J, Lesniak B, Lin A. Clinical outcomes secondary to time to surgery for atraumatic rotator cuff tears. *J Shoulder Elbow Surg.* 2022;31(6S):S18-S24.
11. Flurin PH, Hardy P, Abadie P, et al. Arthroscopic repair of the rotator cuff: prospective study of tendon healing after 70 years of age in 145 patients. *Orthopaedics & traumatology, surgery & research : OTSR.* 2013;99(8 Suppl):S379-384.

12. Flurin PH, Hardy P, Valenti P, et al. Osteoarthritis after rotator cuff repair: A 10-year follow-up study. *Orthop Traumatol Surg Res.* 2017;103(4):477-481.
13. Franceschi F, Longo UG, Ruzzini L, et al. The Roman Bridge: a "double pulley - suture bridges" technique for rotator cuff repair. *BMC musculoskeletal disorders.* 2007;8:123.
14. Fuchs B, Weishaupt D, Zanetti M, Hodler J, Gerber C. Fatty degeneration of the muscles of the rotator cuff: assessment by computed tomography versus magnetic resonance imaging. *Journal of shoulder and elbow surgery.* 1999;8(6):599-605.
15. Gerber C, Fuchs B, Hodler J. The results of repair of massive tears of the rotator cuff. *The Journal of bone and joint surgery American volume.* 2000;82(4):505-515.
16. Goutallier D, Postel JM, Bernageau J, Lavau L, Voisin MC. Fatty muscle degeneration in cuff ruptures. Pre- and postoperative evaluation by CT scan. *Clinical orthopaedics and related research.* 1994(304):78-83.
17. Herve A, Thomazeau H, Favard L, et al. Clinical and radiological outcomes of osteoarthritis twenty years after rotator cuff repair. *Orthop Traumatol Surg Res.* 2019;105(5):813-818.
18. Hsu J, Keener JD. Natural History of Rotator Cuff Disease and Implications on Management. *Operative techniques in orthopaedics.* 2015;25(1):2-9.
19. Jost B, Pfirrmann CW, Gerber C, Switzerland Z. Clinical outcome after structural failure of rotator cuff repairs. *The Journal of bone and joint surgery American volume.* 2000;82(3):304-314.
20. Kim YS, Kim SE, Bae SH, et al. Tear progression of symptomatic full-thickness and partial-thickness rotator cuff tears as measured by repeated MRI. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2017;25(7):2073-2080.
21. Klouche S, Lefevre N, Herman S, Gerometta A, Bohu Y. Return to Sport After Rotator Cuff Tear Repair: A Systematic Review and Meta-analysis. *The American journal of sports medicine.* 2016;44(7):1877-1887.
22. Kuhn JE, Dunn WR, Sanders R, et al. Effectiveness of physical therapy in treating atraumatic full-thickness rotator cuff tears: a multicenter prospective cohort study. *Journal of shoulder and elbow surgery.* 2013;22(10):1371-1379.
23. Kukkonen J, Joukainen A, Lehtinen J, et al. Treatment of Nontraumatic Rotator Cuff Tears: A Randomized Controlled Trial with Two Years of Clinical and Imaging Follow-up. *The Journal*

of bone and joint surgery American volume. 2015;97(21):1729-1737.

24. Lambers Heerspink FO, van Raay JJ, Koorevaar RC, et al. Comparing surgical repair with conservative treatment for degenerative rotator cuff tears: a randomized controlled trial. *Journal of shoulder and elbow surgery.* 2015;24(8):1274-1281.
25. Lee CS, Davis SM, Doremus B, Kouk S, Stetson WB. Interobserver Agreement in the Classification of Partial-Thickness Rotator Cuff Tears Using the Snyder Classification System. *Orthopaedic journal of sports medicine.* 2016;4(9):2325967116667058.
26. Levy O, Mullett H, Roberts S, Copeland S. The role of anterior deltoid reeducation in patients with massive irreparable degenerative rotator cuff tears. *Journal of shoulder and elbow surgery.* 2008;17(6):863-870.
27. Longo UG, Berton A, Ahrens PM, Maffulli N, Denaro V. Clinical tests for the diagnosis of rotator cuff disease. *Sports medicine and arthroscopy review.* 2011;19(3):266-278.
28. Longo UG, Berton A, Papapietro N, Maffulli N, Denaro V. Epidemiology, genetics and biological factors of rotator cuff tears. *Medicine and sport science.* 2012;57:1-9.
29. Longo UG, Candela V, De Salvatore S, et al. Arthroscopic Rotator Cuff Repair Improves Sleep Disturbance and Quality of Life: A Prospective Study. *International journal of environmental research and public health.* 2021;18(7).
30. Longo UG, Carnevale A, Massaroni C, et al. Personalized, Predictive, Participatory, Precision, and Preventive (P5) Medicine in Rotator Cuff Tears. *Journal of personalized medicine.* 2021;11(4).
31. Longo UG, Lamberti A, Rizzello G, Maffulli N, Denaro V. Synthetic augmentation in massive rotator cuff tears. *Medicine and sport science.* 2012;57:168-177.
32. Longo UG, Margiotti K, Petrillo S, et al. Genetics of rotator cuff tears: no association of col5a1 gene in a case-control study. *BMC medical genetics.* 2018;19(1):217.
33. Longo UG, Mazzola A, Carotti S, et al. The role of estrogen and progesterone receptors in the rotator cuff disease: a retrospective cohort study. *BMC musculoskeletal disorders.* 2021;22(1):891.
34. Longo UG, Salvatore G, Rizzello G, et al. The burden of rotator cuff surgery in Italy: a nationwide registry study. *Archives of orthopaedic and trauma surgery.* 2017;137(2):217-224.

35. Maffulli N, Longo UG, Berton A, Loppini M, Denaro V. Biological factors in the pathogenesis of rotator cuff tears. *Sports medicine and arthroscopy review.* 2011;19(3):194-201.
36. Maman E, Harris C, White L, et al. Outcome of nonoperative treatment of symptomatic rotator cuff tears monitored by magnetic resonance imaging. *The Journal of bone and joint surgery American volume.* 2009;91(8):1898-1906.
37. McElvany MD, McGoldrick E, Gee AO, Neradilek MB, Matsen FA, 3rd. Rotator cuff repair: published evidence on factors associated with repair integrity and clinical outcome. *The American journal of sports medicine.* 2015;43(2):491-500.
38. Millett PJ, Horan MP, Maland KE, Hawkins RJ. Long-term survivorship and outcomes after surgical repair of full-thickness rotator cuff tears. *Journal of shoulder and elbow surgery.* 2011;20(4):591-597.
39. Moosmayer S, Gartner AV, Tariq R. The natural course of nonoperatively treated rotator cuff tears: an 8.8-year follow-up of tear anatomy and clinical outcome in 49 patients. *Journal of shoulder and elbow surgery.* 2017;26(4):627-634.
40. Moosmayer S, Lund G, Seljom U, et al. Comparison between surgery and physiotherapy in the treatment of small and medium-sized tears of the rotator cuff: A randomised controlled study of 103 patients with one-year follow-up. *The Journal of bone and joint surgery British volume.* 2010;92(1):83-91.
41. Moosmayer S, Lund G, Seljom US, et al. At a 10-Year Follow-up, Tendon Repair Is Superior to Physiotherapy in the Treatment of Small and Medium-Sized Rotator Cuff Tears. *The Journal of bone and joint surgery American volume.* 2019;101(12):1050-1060.
42. Moosmayer S, Lund G, Seljom US, et al. Tendon repair compared with physiotherapy in the treatment of rotator cuff tears: a randomized controlled study in 103 cases with a five-year follow-up. *The Journal of bone and joint surgery American volume.* 2014;96(18):1504-1514.
43. Moraiti C, Valle P, Maqdes A, et al. Comparison of functional gains after arthroscopic rotator cuff repair in patients over 70 years of age versus patients under 50 years of age: a prospective multicenter study. *Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association.* 2015;31(2):184-190.

44. Namdari S, Donegan RP, Chamberlain AM, et al. Factors affecting outcome after structural failure of repaired rotator cuff tears. *The Journal of bone and joint surgery American volume.* 2014;96(2):99-105.
45. Park JG, Cho NS, Song JH, et al. Rotator Cuff Repair in Patients over 75 Years of Age: Clinical Outcome and Repair Integrity. *Clinics in orthopedic surgery.* 2016;8(4):420-427.
46. Patte D. Classification of rotator cuff lesions. *Clinical orthopaedics and related research.* 1990(254):81-86.
47. Petrillo S, Longo UG, Margiotti K, et al. Genetic factors in rotator cuff pathology: potential influence of col 5A1 polymorphism in outcomes of rotator cuff repair. *BMC medical genetics.* 2020;21(1):82.
48. Petrillo S, Longo UG, Papalia R, Denaro V. Reverse shoulder arthroplasty for massive irreparable rotator cuff tears and cuff tear arthropathy: a systematic review. *Musculoskeletal surgery.* 2017;101(2):105-112.
49. Ranebo MC, Bjornsson Hallgren HC, Norlin R, Adolfsson LE. Clinical and structural outcome 22 years after acromioplasty without tendon repair in patients with subacromial pain and cuff tears. *Journal of shoulder and elbow surgery.* 2017;26(7):1262-1270.
50. Robinson HA, Lam PH, Walton JR, Murrell GAC. The effect of rotator cuff repair on early overhead shoulder function: a study in 1600 consecutive rotator cuff repairs. *Journal of shoulder and elbow surgery.* 2017;26(1):20-29.
51. Salvatore G, Longo UG, Candela V, et al. Epidemiology of rotator cuff surgery in Italy: regional variation in access to health care. Results from a 14-year nationwide registry. *Musculoskeletal surgery.* 2020;104(3):329-335.
52. Schmidt CC, Morrey BF. Management of full-thickness rotator cuff tears: appropriate use criteria. *Journal of shoulder and elbow surgery.* 2015;24(12):1860-1867.
53. Tan M, Lam PH, Le BT, Murrell GA. Trauma versus no trauma: an analysis of the effect of tear mechanism on tendon healing in 1300 consecutive patients after arthroscopic rotator cuff repair. *Journal of shoulder and elbow surgery.* 2016;25(1):12-21.
54. Tashjian RZ. AAOS clinical practice guideline: optimizing the management of rotator cuff problems. *J Am Acad Orthop Surg.* 2011;19(6):380-383.

55. Tsuchiya S, Davison EM, Rashid MS, et al. Determining the rate of full-thickness progression in partial-thickness rotator cuff tears: a systematic review. *Journal of shoulder and elbow surgery*. 2021;30(2):449-455.
56. Yamamoto N, Mineta M, Kawakami J, Sano H, Itoi E. Risk Factors for Tear Progression in Symptomatic Rotator Cuff Tears: A Prospective Study of 174 Shoulders. *The American journal of sports medicine*. 2017;45(11):2524-2531.
57. Zanetti M, Gerber C, Hodler J. Quantitative assessment of the muscles of the rotator cuff with magnetic resonance imaging. *Investigative radiology*. 1998;33(3):163-170.
58. Zhao J, Pan J, Zeng LF, et al. Risk factors for full-thickness rotator cuff tears: a systematic review and meta-analysis. *EFORT open reviews*. 2021;6(11):1087-1096.