TREATMENT OF CONSERVATIVE THERAPY RESISTANT CALCIFYING TENDINITIS OF THE SHOULDER

Evaluation of minimal invasive and surgical treatment options

Freek U. Verstraelen

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PROEFSCHRIFT

Voor het behalen van de graad van Doctor aan
de Universiteit Maastricht,
onder gezag van Rector Magnificus, prof. dr. Pamela Habibović,
overeenkomstig met het besluit van het College van Decanen, te verdedigen in het
openbaar op
vrijdag 5 april 2024 om 13.00 uur

door

Freek Urbaan Verstraelen
Geboren op 09 december 1987 te Venlo

Design: Ilse Modder | www.ilsemodder.nl
Layout: Ilse Modder | www.ilsemodder.nl
Printed by: Gildeprint Enschede | www.gildeprint.nl
ISBN: 978-94-6496-050-1

Financial support for the publication of this thesis was provided by: Maastricht University, Nederlandse Orthopaedische Vereniging, Anna Fonds|NOREF, Màxima MC Academie, Kenniscentrum Orthopedie ZZV.

Promotor:
Prof. dr. L.W. van Rhijn

Copromotoren:
dr. E.J.P. Jansen
dr. M.C. van der Steen

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CONTENTS

ABBREVIATIONS

ACI	acromial coverage index
AHD	acromial humeral distance
AP	anteroposterior
ASES	American shoulder and elbow score
BMI	body mass index
CMS	Constant-Murley score
CSA	critical shoulder angle
CT	calcifying tendinitis
DASH	disability of arm, shoulder and hand score
ESWT	extracorporeal shockwave therapy
HADS	hospital anxiety and depression scale
IQR	interquartile range
ISP	infraspinatus tendon
NACD	needle aspiration of the calcific deposits
NRS	numerous rating scale
PCS	pain catastrophizing scale
RCT	randomized controlled trial
ROM	range of motion
SAPS	subacromial pain syndrome
SSC	subscapularis tendon
SSP	supraspinatus tendon
SST	simple shoulder test
VAS	visual analog scale

CHAPTER 1

General introduction and research aims of the thesis

INTRODUCTION

Calcifying tendinitis of the shoulder is a disease in which one or multiple calcific deposits are located within one or more tendons of the rotator cuff (Figure 1). [1] The rotator cuff is a complex cooperation between four muscles which originate on the scapula and attach at different sites on the proximal humeral bone. [2] This vulnerable complex functions as a dynamic stabiliser of the intrinsically unstable shoulder joint. Conditions of the rotator cuff, such as rotator cuff tears and tendinopathies, are a common cause of shoulder complaints. [3] The presence of subacromial calcifications are first described by Painter in 1907 as a radiological finding. At that time, the hypothesis was that these calcific deposits were located in the subacromial bursa. [4] Codman was in 1941 the first to acknowledge that the calcific deposits did not arise from the subacromial bursa but from the tendon underneath it. In addition, Codman noticed that the supraspinatus tendon was most often affected. [5] In 1941 a large cohort study of 12.122 shoulders was published by Bosworth. [6] The hypothesis of Bosworth was that calcifying tendinitis of the shoulder could be a degenerative disease. The calcific deposits were hypothesized to be the result of repetitive trauma causing micro tears within the rotator cuff. These micro trauma were hypothesized to be caused by conditions such as subacromial impingement. [6] In 1997, Uhthoff and Loehr hypothesized that calcifying tendinitis could be an inflammatory and self-limiting disease, which did not have a relation with degenerative disease. Although Uhthoff and Loehr described the naturel course of the disease, the exact mechanism of triggering this process and thus the aetiology of calcifying tendinitis of the shoulder still is not fully understood. [7]

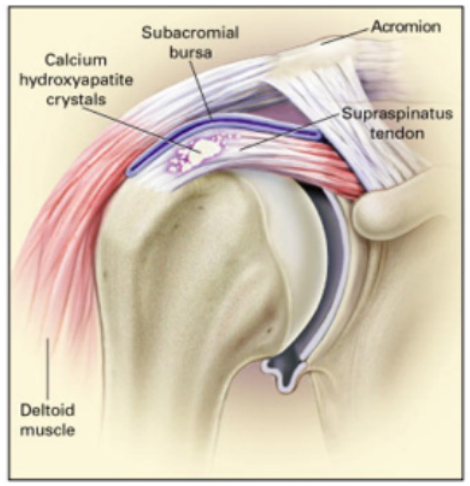

Figure 1. Presence of calcific deposits within rotator cuff. (reproduced with permission from Speed et all [16], Copyright Massachusetts Medical Society

Epidemiology

In the general population shoulder disorders are common with an estimated lifetime prevalence of 34%. [3] Calcifying tendinitis is one of the most commonly diagnosed disorders of the shoulder. In the Netherlands, the incidence of shoulder disorders in primary care is nineteen per 1.000 persons-year. [3,8] It affects individuals between 30 and 60 years of age. Women are more frequently affected compared to men with a 2:1 ratio. [6,9]

In 2015 the most recent Dutch epidemiological data on subacromial calcifications were published. [10] In a cohort study 734 radiographs were screened of patients without prior shoulder complaints who were seen at the emergency department with a shoulder trauma (asymptomatic group). Furthermore, 485 patients who were referred to the orthopaedic surgeon with shoulder complaints were evaluated (symptomatic patients). The authors observed a prevalence of subacromial calcifications of 7.8% in asymptomatic people with a mean size of the calcification of 0.42 cm and a prevalence of 42.5% in patients with shoulder complaints with a mean size of 1.16 cm. [10] This is in line with the general thought that larger size calcifications are more likely to cause symptoms. [6,11-13]

Of the four rotator cuff tendons the supraspinatus tendon is most often affected with an incidence of 80%. In 15% the calcific deposit is located in the infraspinatus tendon and in 5% the subscapularis tendon is involved. In about 20% of the patients multiple tendons are affected. Furthermore, calcifying tendinitis can occur bilaterally. [14,15] In the supraspinatus tendon the calcific deposits are typically located 1.5 to 2.0 cm of its insertion on the greater tubercle of the humeral bone. It is assumed that this is related to the fact that this site is poorly vascularised. [15-17]

Natural course and pathophysiology

As mentioned above, Uhthoff and Loehr [7] have proposed a natural course of calcifying tendinitis. It is hypothesized that calcifying tendinitis of the shoulder is a self-limiting disease, and it passes several consecutive stages (Figure 2).

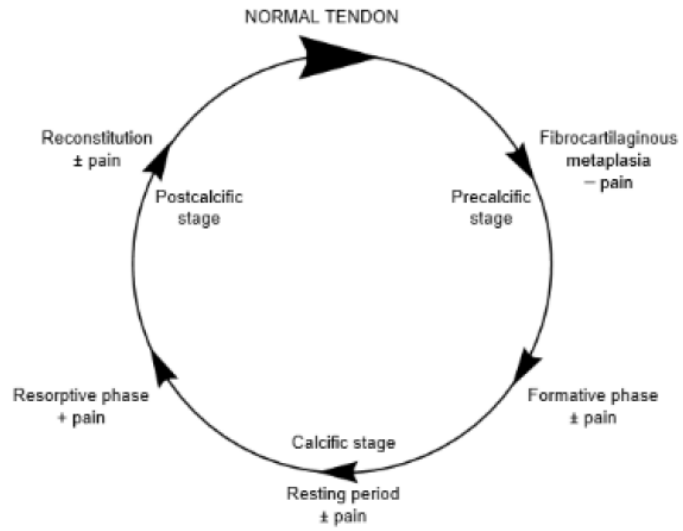

Figure 2. Proposed natural course of calcifying tendinitis of the shoulder. (adapted from Diehl et al. [14])

In the precalcific stage metaplasia takes place from tenocytes to chondrocytes which is accompanied by metachromasia. The second stage is the calcific stage. This can be subdivided into three distinct phases. The first phase is the formative phase. In this phase calcium or carbonated crystals are deposited in a matrix to form a calcific deposit in which the deposit is chalk-like and contains several septa. As time passes the septa diminish and the deposit can increase in size. The second phase is a resting phase. At this point no significant changes appear in the calcific deposits. Inflammation and vascular channels are not apparent. The duration of these first two phases can vary tremendously. The final phase of the calcific stage is the resorptive phase. During this phase vascular channels starting from a peripherical zone become apparent. With this appearance, macrophages and multinucleated giant cells can come into action. Factors which trigger the resorption phase remain unknown. In this final phase the calcific deposit has a toothpaste like appearance. Phagocytosis of the calcific deposit takes place, leaving some scar tissue at the site of the prior calcifications. The postcalcific stage is characterized by replacement of this scar tissue (type III collagen) into normal tendon tissue (type I collagen). The entire natural course of calcifying tendinitis can take up to three to five years. [7]

Clinical presentation

The clinical presentation of patients with calcifying tendinitis of the shoulder varies significantly. It depends on the stage of the disease, the size and the location of the calcific deposit. The most frequently observed symptoms are pain and decreased range of motion. [14]

Especially in the resorptive phase the patient can experience a sudden onset of severe symptoms. It can even mimic the symptoms of a septic bursitis or arthritis. This is caused by the eruption of the calcific deposit in the subacromial bursa. [18,19] In the other stages the symptoms are often mild and mostly remain subclinical. [16] Bosworth [6] stated that symptoms are mostly present when calcifications were larger than 1.5cm in diameter. The hypothesis is that larger size calcifications are more likely to cause subacromial impingement resulting in microtrauma to the rotator cuff tendons. [6] Other authors postulate that besides the size, the anatomical location and morphology of the calcific deposit are most related to the presence of symptoms of pain and decreased range of motion. [11,13,20]

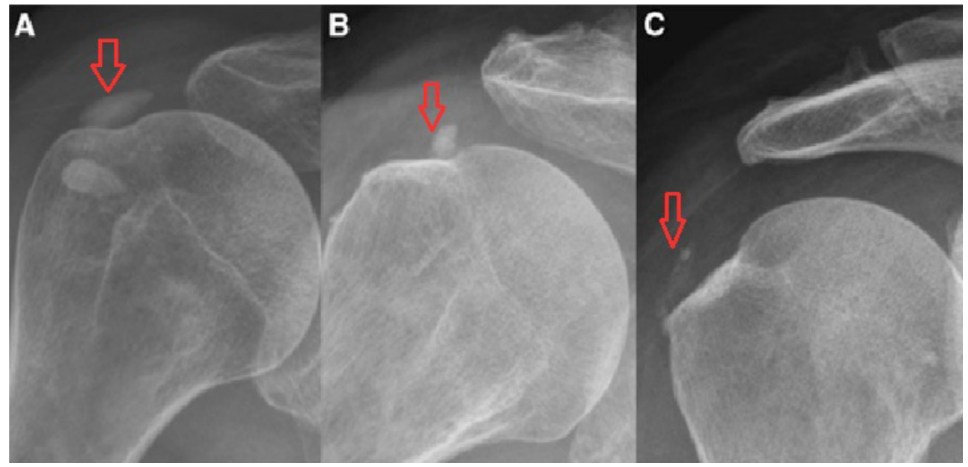

Figure 3. Gartner and Heyer classification of calcifying tendinitis of the shoulder. A shows type I calcification, **B** shows type II calcification, **C** shows type III calcification. (adapted from Brinkman et al. [46])

Radiological evaluation

When calcifying tendinitis of the rotator cuff is expected, radiographs of the affected shoulder should be obtained in three directions: true AP-view, AP-view in internal and external rotation. These standardized radiographs are also valuable during follow-up. Based on standardized radiographs several authors have proposed a classification system. A commonly used classification is the one proposed by Gartner and Heyer [20]. They proposed a classification based on the appearance of the calcific deposits on conventional radiographs (Figure 3). They categorized the subacromial calcifications into three types. Type 1 calcifications have a clearly circumscribed and dense appearance. Type 2 calcifications have a mixed appearance on the radiographs as they are partly clearly circumscribed but are less dense than a type 1 calcifications. Type 3 calcifications have a cloudy and translucent appearance. Type 3 calcifications are thought to be related to the resorptive phase and have a high potency for spontaneous resolution. Type 1 and 2 calcifications are thought to be related to the formative and resting phase and are less likely to spontaneously dissolve. [20] Another imaging technique valuable to visualise the subacromial calcific deposits is sonography. Sonography is a reliable imaging technique to detect and define the location of the calcific deposits. Farin and Jaroma [21] defined three types of subacromial calcifications based on sonography. Type 1 calcifications have a hyperechoic focus with a well-defined shadow. Type 2 calcifications have a hyperechoic focus with a faint shadow, and type 3 calcifications have a hyperechoic focus without a shadow. However, this classification does not have a correlation with the formative or resorptive phase. [21] Other imaging techniques such as magnetic resonance imaging and computed

tomography are less valuable in diagnosing and treating calcifying tendinitis of the shoulder. However, they can be valuable in ruling out other subacromial or glenohumeral pathology. [14]

TREATMENT OF CALCIFYING TENDINITIS OF THE SHOULDER

Conservative therapy

The initial treatment of calcifying tendinitis of the shoulder consists of conservative measures. Conservative treatment can include exercise therapy, anti-inflammatory drugs, ice therapy and/ or subacromial corticosteroid injections. [11] In the majority of patients this treatment regime is successful. However, nearly 30% of the patients remain symptomatic. [11,13] Several prognostic factors for the outcome of conservative treatment have been recognized. Negative prognostic factors are a more medial extension of the calcific deposit, bilateral and multifocal occurrence, a large volume of the calcific deposit and a more anterior localization within the supraspinatus tendon. Positive prognostic factors are Gärtner type 3 deposits and a lack of sonographic sound extinction (Farin type 3) of the calcific deposit. [11-13]

Treatment options for conservative therapy resistant calcifying tendinitis of the shoulder

If this initial conservative treatment fails the next step treatment remains unclear. [10] Treatment options for conservative therapy resistant can be grouped in either a surgical or a minimal invasive treatment. Surgical treatment shows good and predictable clinical outcomes, but are invasive and desire a prolonged rehabilitation. [22] On the other hand, minimal invasive techniques, such as extracorporeal shockwave therapy (ESWT) or needle aspiration of the calcific deposit (NACD) also show promising clinical outcomes. Though, there is limited long term data, the short-term results are promising. [23,24] Some authors even state that these minimal invasive techniques may show comparable clinical outcomes to the surgical treatment. [25,26]

Surgical treatment options

Historically, surgical treatment has been the next step treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder. [14] Several surgical treatment options are described in orthopaedic literature. The first option is performing only a subacromial decompression and leaving the calcifications untouched. In this procedure the subacromial space is enlarged and by performing an acromioplasty several growth factors are released into the subacromial space. This could potentially stimulate the tendon to start the resorption phase, which is the final phase of the natural course

of calcifying tendinitis. [27] The advantage of this approach is that the rotator cuff is not damaged and as such -in theory- is less prone to develop a rotator cuff tear. [28] The second surgical treatment option is performing only a debridement of the calcific deposits. Debate remains whether to complete removal is necessary or if arthroscopic needling/ partial removal is sufficient. With this latter approach extensive damage to the rotator cuff tendons again can be avoided and rotator cuff repair often is not necessary. [29-31] The third option is a combination of debridement of the calcific deposits and a subacromial decompression. [22,32,33] It is not clear yet whether calcifying tendinitis of the shoulder is related to subacromial impingement and therefore if a subacromial decompression is necessary. The three aforementioned surgical procedures can either be performed arthroscopically or via an open procedure. An arthroscopic procedure is preferred because of the less invasive character and as a result quicker recovery. [32] All three surgical procedures seem to be safe and show low complication rates. [22,27] Adhesive capsulitis is the most common complication in this procedure. Therefore, a rehabilitation protocol including quick return to pain-based movements and limiting the period of immobilisation of the shoulder is advisable. [28,33,34] However, a preferable surgical treatment procedure is not appointed yet.

Minimal invasive treatment options

Several minimal invasive treatment options are currently becoming more and more available, such as needle aspiration of the calcific deposits (NACD), extracorporeal shock wave therapy (ESWT) or platelet enriched plasma therapy (PRP). Of these minimal invasive treatments, NACD and ESWT show the most promising results. [35,36] ESWT has been investigated extensively. Though, the exact working mechanism of ESWT is not yet fully understood. Loew et al [37] postulated a three-way mechanism of action of ESWT; (1) a mechanical effect resulting in fragmentation of the calcific deposit; (2) molecular effect resulting in deposit phagocytosis; and (3) a denervation effect of small nociceptive nerves in the rotator cuff surrounding the calcific deposit. [37]

In clinical practise, there are many different treatment protocols of ESWT used in the treatment of calcifying tendinitis of the shoulder. For example, the shockwaves can be generated by different mechanisms (e.g. piezoelectric, electromagnetic, electrohydraulic). Furthermore, ESWT can be subdivided in focussed and radial ESWT and different intensities of ESWT such as low-, mid- and high-energy ESWT. Moreover, ESWT can be used in many treatment protocols with either a single session of ESWT or multiple sessions. [37] There are numerous studies investigating these different types and treatment protocols of ESWT. [38-40] These studies all emphasize the effectiveness of ESWT. However, no consensus exists on a preferable protocol and more research is needed to appoint an optimal treatment protocol for ESWT. [37,40]

The second minimal invasive treatment option is NACD. This treatment is usually ultrasound guided and also is referred to as ultrasound guided needling (UGN). [35] In this procedure the patient receives under ultrasonic guidance multiple punctures and irrigation of the calcific deposits in the rotator cuff. The aim of this treatment is to mechanically fragment the calcific deposit and also to promote the resorption phase of calcifying tendinitis. [35] In 2014, a systematic review was performed in which in total 908 patients received NACD for conservative therapy resistant calcifying tendinitis of the shoulder. This review showed following NACD marked improvement in clinical score with low complication rates on the short term. [24] However, the mid and long-term evidence on the clinical outcome of NACD as treatment for conservative therapy resistant calcifying tendinitis is still limited. [24] Only one randomized trial is evaluating the midterm results of NACD compared to ultrasound guided subacromial injection. The functional outcome was comparable after five years. However, in patients who only received a subacromial injection significantly more additional treatment were registered (e.g. additional NACD or surgery). [41] Besides this randomized trial, there is only one cohort study reporting comparable results five and ten years after NACD compared to conservative treatment. [42]

To date it is unclear which minimal invasive treatment option leads to the best and most cost-effective results. In 2014, a randomized trial was published in which radial ESWT was compared to NACD. Furthermore, in 2020 the most recent randomized trial was published in which a treatment with multiple sessions of focussed high-energy ESWT was compared to NACD. Both studies showed that both treatment modalities were effective on the short term in the treatment of calcifying tendinitis of the shoulder with low complication rates. However as both studies used markedly different treatment protocols a preferable treatment cannot yet be appointed, and more research is needed. [24,43-45]

AIM OF THE THESIS

The general objective of the present thesis is to outline and enhance the current treatment algorithm for patients with conservative therapy resistant calcifying tendinitis of the shoulder. In order to make this possible, first the following questions need to be answered:

- Do the available surgical procedures lead to different functional outcomes in patients with conservative therapy resistant calcifying tendinitis of the shoulder?
  a) What is the currently available evidence on the surgical treatment?
  b) Is a sole acromioplasty still a relevant surgical treatment option?
  c) Can a preferable surgical treatment option be appointed?

- Do minimal invasive techniques result in comparable functional outcome compared to surgical treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder?

- What is the preferred minimal invasive treatment option for patients with conservative therapy resistant calcifying tendinitis of the shoulder?
  a) What is the preferred intensity for extracorporeal shockwave therapy?
  b) Is there a difference in effectiveness between needle aspiration of the calcific deposits (NACD) compared to Extracorporeal Shockwave therapy (ESWT) regarding functional outcome?

To this end, this thesis is divided in three parts which comprise several studies.

OUTLINE OF THE THESIS

Part 1: Evaluating surgical treatment options for therapy resistant calcifying tendinitis of the shoulder

Surgical treatment is historically considered as a treatment option for patients with conservative therapy resistant calcifying tendinitis of the shoulder. However, the exact preferable surgical treatment procedure is still a matter of dispute. Generally, three different treatment options are known. The first surgical treatment option is performing a subacromial decompression and leaving the calcifications untouched. The second option is debriding the subacromial calcific deposits without an additional subacromial decompression. The third surgical treatment option is combining the aforementioned procedures: debridement of the calcific deposits in combination with a subacromial decompression. **Chapter 2** contains a systematic review of the literature on the clinical and functional outcomes after the three aforementioned surgical procedures for therapy resistant calcifying tendinitis of the shoulder. In **chapter 3** a retrospective study is presented. In this study the mid-term clinical outcomes are evaluated of patients who had a subacromial decompression without debriding the calcific deposits. The primary outcome was the Constant-Murley Score (CMS) three years after treatment and its correlation with any residual calcific deposits in the rotator cuff tendons. In **chapter 4** a randomized controlled trial is described comparing the clinical outcomes of the three aforementioned surgical treatment options for conservative therapy resistant calcifying tendinitis of the shoulder. The primary outcome was the improvement in Visual Analog Scale (VAS) for pain six months after treatment. Secondary outcomes were the Disability of arm, shoulder and hand score (DASH score), the American shoulder and elbow surgeons score (ASES score), additional treatment and the radiological outcome.

Part 2: Evaluating mid-term outcomes of surgical treatment versus minimal invasive treatment for conservative therapy resistant calcifying tendinitis of the shoulder

It remains unclear whether surgery or minimal invasive technique should be preferred as a first step treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder. In **chapter 5** the midterm clinical outcome of the surgical treatment and the NACD treatment of conservative therapy resistant calcifying tendinitis of the shoulder are evaluated in a comparative cohort study. Clinical outcome of thirty-five patients who underwent a surgical treatment were compared to the results of 41 patients who received a NACD treatment. The primary outcome was the improvement in VAS for pain after a mean follow-up of more than five years. Secondary outcomes were DASH score, ASES, EQ-5D, additional treatment and percentage of cross-over to surgical treatment.

Part 3. Evaluating minimal invasive techniques in treatment for conservative therapy resistant calcifying tendinitis of the shoulder

As stated above minimal invasive treatment, especially NACD and ESWT, is a treatment option with promising short-term results for therapy resistant calcifying tendinitis of the shoulder. However, the optimal treatment strategy is still a matter of debate. This concerns both preferable treatment intensity for ESWT as well as which minimal invasive treatment is preferable. In **chapter 6** the results of a meta-analyses of five randomized controlled trials which compared low-energy ESWT to high-energy ESWT are presented. The primary outcome was comparing the short-term improvement of the Constant-Murley Score and the likelihood of significant resorption of the calcific deposit after low-energy ESWT versus high-energy ESWT. In **chapter 7** a study protocol of a randomized trial is presented to establish a preferable minimal invasive treatment. In this study patients are randomly allocated to either NACD or ESWT. The primary outcome is difference in improvement of Constant-Murley Score after 12 months. Secondary outcomes are other clinical outcome score and an extensive cost-effectiveness analyses.

REFERENCES

1. Hurt G, Baker CL Jr (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am, 34(4):567-575.
2. Veeger, HEJ & Van Der Helm, FCT (2007) Shoulder function: the perfect compromise between mobility and stability. Journal of biomechanics, 40(10), 2119-2129.
3. Diercks R, Bron C, Dorrestijn O, Meskers C, Naber R, de Ruiter T, Willems J, Winters J, van der Woude HJ; Dutch Orthopaedic Association (2014) Guideline for diagnosis and treatment of subacromial pain syndrome: a multidisciplinary review by the Dutch Orthopaedic Association. Acta Orthop, 85(3):314-322.
4. Painter CF (1907) Subdeltoid bursitis. Boston Med Surg J, 156:345-349.
5. Codman EA (1934) The shoulder. Boston: Todd
6. Bosworth BM (1941) Calcium deposits in the shoulder and subacromial bursitis. A survey of 12,122 shoulders. JAMA, 116:2477-2482.
7. Uhthoff, HK & Loehr, JW (1997) Calcific Tendinopathy of the Rotator Cuff: Pathogenesis, Diagnosis, and Management. Journal of the American Academy of Orthopaedic Surgeons: 5(4): 183-191
8. Reilingh ML, Kuijpers T, Tanja-Harfterkamp AM, van der Windt DA (2008) Course and prognosis of shoulder symptoms in general practice. Rheumatology (Oxford), 47(5):724-730.
9. Welfing J, Kahn MF, Desroy M, Paolaggi JB, De Sèze S (1965) Les calcifications de l'épaule. II. La maladie des calcifications tendineuses multiples. Rev Rhum Engl Ed, 32:325-334
10. Louwerens JK, Sierevelt IN, van Hove RP, van den Bekerom MP, van Noort A (2015) Prevalence of calcific deposits within the rotator cuff tendons in adults with and without subacromial pain syndrome: clinical and radiologic analysis of 1219 patients. J Shoulder Elbow Surg, 24(10):1588-1593.
11. Drummond Jr M, Ayinon C, Rodosky M, Vyas D, Lesniak B, Lin A (2021) Predictive factors for failure of conservative management in the treatment of calcific tendinitis of the shoulder. JSES Int, 26;5(3):469-473.
12. Oudelaar BW, Huis In 't Veld R, Schepers-Bok R, Ooms EM, Nelissen RGHH, Vochteloo AJH (2020) Prognostic factors for the outcome of needle aspiration of calcific deposits for rotator cuff calcific tendinitis. Eur Radiol, 30(7):4082-4090.
13. Ogon P, Suedkamp NP, Jaeger M, Izadpanah K, Koestler W, Maier D (2009) Prognostic factors in nonoperative therapy for chronic symptomatic calcific tendinitis of the shoulder. Arthritis Rheum, 60(10):2978-2984.
14. Diehl P, Gerdesmeyer L, Gollwitzer H, Sauer W, Tischer T (2011) Die Kalkschulter - Tendinosis calcarea [Calcific tendinitis of the shoulder]. Orthopade,40(8):733-746.
15. Hurt G, Baker CL Jr (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am, 34(4):567-575.
16. Speed CA, Hazleman BL (1999) Calcific tendinitis of the shoulder. N Engl J Med, 20;340(20):1582-1584.
17. Sansone V, Maiorano E, Galluzzo A, Pascale V (2018) Calcific tendinopathy of the shoulder: clinical perspectives into the mechanisms, pathogenesis, and treatment. Orthop Res Rev, 3;10:63-72.
18. Beyth S, Safran O (2021) Acute Calcific Tendonitis of the Shoulder Mimicking Septic Arthritis. Isr Med Assoc J, 23(8):531-533.
19. Oudelaar BW, Van Liebergen MR, Van Arkel ERA (2021) Een vrouw met acuut ontstane schouderklachten [A woman with acute-onset shoulder pain]. Ned Tijdschr Geneeskd, 18;165.
20. Gärtner J, Heyer A (1995) Tendinosis calcarea der Schulter [Calcific tendinitis of the shoulder]. Orthopade, 24(3):284-302.

21. Farin PU, Jaroma H (1995) Sonographic findings of rotator cuff calcifications. J Ultrasound Med, 14(1):7-14.
22. Clement ND, Watts AC, Phillips C, McBirnie JM (2015) Short-Term Outcome After Arthroscopic Bursectomy Debridement of Rotator Cuff Calcific Tendonopathy With and Without Subacromial Decompression: A Prospective Randomized Controlled Trial. Arthroscopy, 31(9):1680-1687.
23. Bazzocchi A, Pelotti P, Serraino S, Battaglia M, Bettelli G, Fusaro I, Guglielmi G, Rotini R, Albisinni U (2015) Ultrasound imaging-guided percutaneous treatment of rotator cuff calcific tendinitis: success in short-term outcome. Br J Radiol, 89(1057):20150407.
24. Gatt DL, Charalambous CP (2014) Ultrasound-guided barbotage for calcific tendonitis of the shoulder: a systematic review including 908 patients. Arthroscopy, 30(9):1166-1172.
25. Castillo-González, FD, Ramos-Álvarez, JJ, Rodríguez-Fabián, G, González-Pérez, J, Calderón-Montero, J (2014) Treatment of the calcific tendinopathy of the rotator cuff by ultrasound-guided percutaneous needle lavage. Two years prospective study. Muscles, ligaments and tendons journal, 4(2), 220–225.
26. Randelli P, Margheritini F, Cabitza P, Dogliotti G, Corsi MM (2009) Release of growth factors after arthroscopic acromioplasty. Knee Surg Sports Traumatol Arthrosc, 17(1):98-101.
27. Hofstee DJ, Gosens T, Bonnet M, De Waal Malefijt J (2007) Calcifications in the cuff: take it or leave it? Br J Sports Med, 41(11):832-835.
28. Castagna A, DE Giorgi S, Garofalo R, Conti M, Tafuri S, Moretti B (2016) Calcifying tendinitis of the shoulder: arthroscopic needling versus complete calcium removal and rotator cuff repair. A prospective comparative study. Joints, 3(4):166-172.
29. El Shewy MT (2011) Arthroscopic removal of calcium deposits of the rotator cuff: a 7-year follow-up. Am J Sports Med, 39(6):1302-1305.
30. Seil R, Litzenburger H, Kohn D, Rupp S (2006) Arthroscopic treatment of chronically painful calcifying tendinitis of the supraspinatus tendon. Arthroscopy, 22(5):521-527.
31. Balke M, Bielefeld R, Schmidt C, Dedy N, Liem D (2012) Calcifying tendinitis of the shoulder: midterm results after arthroscopic treatment. Am J Sports Med, 40(3):657-661.
32. Rubenthaler F, Ludwig J, Wiese M, Wittenberg RH (2003) Prospective randomized surgical treatments for calcifying tendinopathy. Clin Orthop Relat Res, (410):278-284.
33. Merolla G, Singh S, Paladini P, Porcellini G (2016) Calcific tendinitis of the rotator cuff: state of the art in diagnosis and treatment. J Orthop Traumatol, 17(1):7-14.
34. ElShewy MT (2016) Calcific tendinitis of the rotator cuff. World J Orthop, 7(1):55-60.
35. Louwerens JK, Veltman ES, van Noort A, van den Bekerom MP (2016) The Effectiveness of High-Energy Extracorporeal Shockwave Therapy Versus Ultrasound-Guided Needling Versus Arthroscopic Surgery in the Management of Chronic Calcific Rotator Cuff Tendinopathy: A Systematic Review. Arthroscopy, 32(1):165-175.
36. Oudelaar BW, Huis In 't Veld R, Ooms EM, Schepers-Bok R, Nelissen RGHH, Vochteloo AJH (2021) Efficacy of Adjuvant Application of Platelet-Rich Plasma After Needle Aspiration of Calcific Deposits for the Treatment of Rotator Cuff Calcific Tendinitis: A Double-Blinded, Randomized Controlled Trial With 2-Year Follow-up. Am J Sports Med, 49(4):873-882.
37. Loew M, Jurgowski W, Mau HC, Thomsen M (1995) Treatment of calcifying tendinitis of rotator cuff by extracorporeal shock waves: a preliminary report. J Shoulder Elbow Surg, 4(2):101-106.

38. Gerdesmeyer L, Wagenpfeil S, Haake M, Maier M, Loew M, Wörtler K, Lampe R, Seil R, Handle G, Gassel S, Rompe JD (2003) Extracorporeal shock wave therapy for the treatment of chronic calcifying tendonitis of the rotator cuff: a randomized controlled trial. JAMA, Nov 19;290(19):2573-2580.
39. Huisstede BM, Gebremariam L, van der Sande R, Hay EM, Koes BW (2011) Evidence for effectiveness of Extracorporal Shock-Wave Therapy (ESWT) to treat calcific and non-calcific rotator cuff tendinosis--a systematic review. Man Ther, 16(5):419-433.
40. Ioppolo F, Tattoli M, Di Sante L, Venditto T, Tognolo L, Delicata M, Rizzo RS, Di Tanna G, Santilli V (2013) Clinical improvement and resorption of calcifications in calcific tendinitis of the shoulder after shock wave therapy at 6 months' follow-up: a systematic review and meta-analysis. Arch Phys Med Rehabil, 94(9):1699-1706.
41. de Witte PB, Kolk A, Overes F, Nelissen RGHH, Reijnierse M (2017) Rotator Cuff Calcific Tendinitis: Ultrasound-Guided Needling and Lavage Versus Subacromial Corticosteroids: Five-Year Outcomes of a Randomized Controlled Trial. Am J Sports Med, 45(14):3305-3314.
42. Serafini G, Sconfienza LM, Lacelli F, Silvestri E, Aliprandi A, Sardanelli F (2009) Rotator cuff calcific tendonitis: short-term and 10-year outcomes after two-needle us-guided percutaneous treatment-nonrandomized controlled trial. Radiology, 252(1):157-164.
43. Rompe JD, Bürger R, Hopf C, Eysel P (1998) Shoulder function after extracorporal shock wave therapy for calcific tendinitis. J Shoulder Elbow Surg, 7(5):505-509.
44. Kim YS, Lee HJ, Kim YV, Kong CG (2014) Which method is more effective in treatment of calcific tendinitis in the shoulder? Prospective randomized comparison between ultrasound-guided needling and extracorporeal shock wave therapy. J Shoulder Elbow Surg, 23(11):1640-1646.
45. Louwerens JKG, Sierevelt IN, Kramer ET, Boonstra R, van den Bekerom MPJ, van Royen BJ, Eygendaal D, van Noort A (2020) Comparing Ultrasound-Guided Needling Combined With a Subacromial Corticosteroid Injection Versus High-Energy Extracorporeal Shockwave Therapy for Calcific Tendinitis of the Rotator Cuff: A Randomized Controlled Trial. Arthroscopy, 36(7):1823-1833.
46. Brinkman JC, Zaw TM, Fox MG, Wilcox JG, Hattrup SJ, Chhabra A, Neville MR, Hartigan DE (2020) Calcific Tendonitis of the Shoulder: Protector or Predictor of Cuff Pathology? A Magnetic Resonance Imaging-Based Study. Arthroscopy, 36(4):983-990.

PART I

Optimizing surgical treatment

CHAPTER 2

Surgery for calcifying tendinitis of the shoulder: a systematic review

Verstraelen FU
Fievez E
Janssen L
Morrenhof W

2017 World J Orthop;8(5):424-430

ABSTRACT

Aim

To systematically search literature and determine a preferable surgical procedure in patients with failed conservative treatment of calcifying tendinitis of the shoulder.

Methods

The electronic online databases MEDLINE (through PubMed), EMBASE (through OVID), CINAHL (through EBSCO), Web of Science and Cochrane Central Register of Controlled Trials were systematically searched in May 2016. Eligible for inclusion were all available studies with level II and level III evidence (LoE). Data was assessed and extracted by two independent review authors using a specifically for this study designed data extraction form.

Results

Six studies (294 surgically treated shoulders) were included in this review. No significant differences between the three available treatment options (acromioplasty with the removal of the calcific deposits, acromioplasty or solely the removal of the calcific deposits) were detected regarding the functional and clinical outcome. The follow- up ranged from 12 months to 5 years. Complication rates were low. No reoperations were necessary and the only reported complication was adhesive capsulitis, which in all cases could be treated conservatively with full recovery.

Conclusion

We found that all three available treatment options show good functional and clinical outcomes in the short and midterm. However, a favourable procedure is difficult to determine due to the lack of high-quality comparing studies.

Key words

Calcifying tendinitis; Surgery; Systematic review; Acromioplasty; Debridement

INTRODUCTION

Calcifying tendinitis (CT) of the shoulder is a common disease. It is one the most frequent causes of non- traumatic shoulder pain and has a high disease burden. In a healthy population the incidence of subacromial calcific deposits is 2.7%. [1] In patients with shoulder complaints this number rises to 6.8%. CT mainly affects individuals between 30 and 60 years of age. Males and females are equally affected. [1-3] The calcific deposits are most frequently (80%) seen in the supraspinatus tendon, at a typical location of 1.5 to 2.0 cm of its insertion on the major tuberculum. CT is primarily treated conservatively, though in about 10% of the cases this fails. Then often surgery is a last resort. The aetiology of CT remains unclear and is still a matter of dispute. Some authors state that CT is not related to subacromial impingement. [2] This is supported by the histological finding in the study of Uhthoff et al. [4] In this study only minimal signs of inflammation in the rotator cuff of patients with CT were seen. Conversely, other authors observed that there was neovascularization and influx of phagocytes around the calcific deposits. As they state this could lead to subsequent oedema of the rotator cuff and an increase of the intratendineous pressure. This theoretically can lead to secondary subacromial impingement as the thickened and calcified tendon decreases the subacromial space. Others state that impingement causes rotator cuff tendinitis, which when chronically apparent leads to CT, due to decreased local oxygen tension or hypoxia. [1,2,5,6] There are several surgical procedures available, mostly in accordance with the above-mentioned theories. In the current orthopaedic literature three major surgical strategies have been postulated. The first is an acromioplasty in combination with removal of the calcific deposits, the second is an acromioplasty without removing the calcific deposits and the third surgical procedure is to solely debride the calcific deposits and leave the acromion untouched. However, there is still some debate what the most preferable procedure is. It remains unclear whether the calcific deposits need to be, completely or partially, removed and if an additional acromioplasty is beneficial. Therefore, the objective of this study is to determine if there is a preferable surgical procedure in patients with conservative treatment resistant CT. We performed a systematic review with two clear research questions: (1) Is there a difference in functional and clinical outcomes after debridement of the calcifications in comparison with debridement and additional acromioplasty on the short- and mid-term; and (2) Is there a difference in the functional and clinical outcomes after acromioplasty compared to acromioplasty with debridement of the calcifications on the short- and mid-term?

MATERIALS AND METHODS

This review was performed and written down following the principles of the PRISMA statement. [7] Five relevant electronical databases (MEDLINE through PubMed, EMBASE

through OVID, CINAHL through EBSCO, Web of Science and Cochrane Central Register of Controlled Trials) were systematically searched by one review author (FV) in May 2016 for studies in English, German and Dutch. Furthermore, the reference lists of the included articles and available reviews were crosschecked for possible relevant studies.

Table 1. PICO search strategy

Population	Patients with radiographically confirmed symptomatic tendinitis calcarea of the shoulder (search terms: shoulder joint, rotator cuff, shoulder, supraspinatus, infraspinatus, subscapular or teres, impingement syndrome, tendinopathy, tendonitis or tendinitis, tendinosis, calcinosis, calcifying, calcification, calcified, calcific, calcarea)
Intervention	Surgery (search terms: surgery, surgical, orthopaedic surgery, shoulder surgery, acromioplasty, debridement, bursectomy, arthroscopic, Neer)
Comparison	Surgery (search terms: surgery, surgical, orthopaedic surgery, shoulder surgery, acromioplasty, debridement, bursectomy, arthroscopic, Neer)
Outcome	functional and clinical outcome
Limits	Language: English, German, Dutch Publication year: 1996-2016 Human

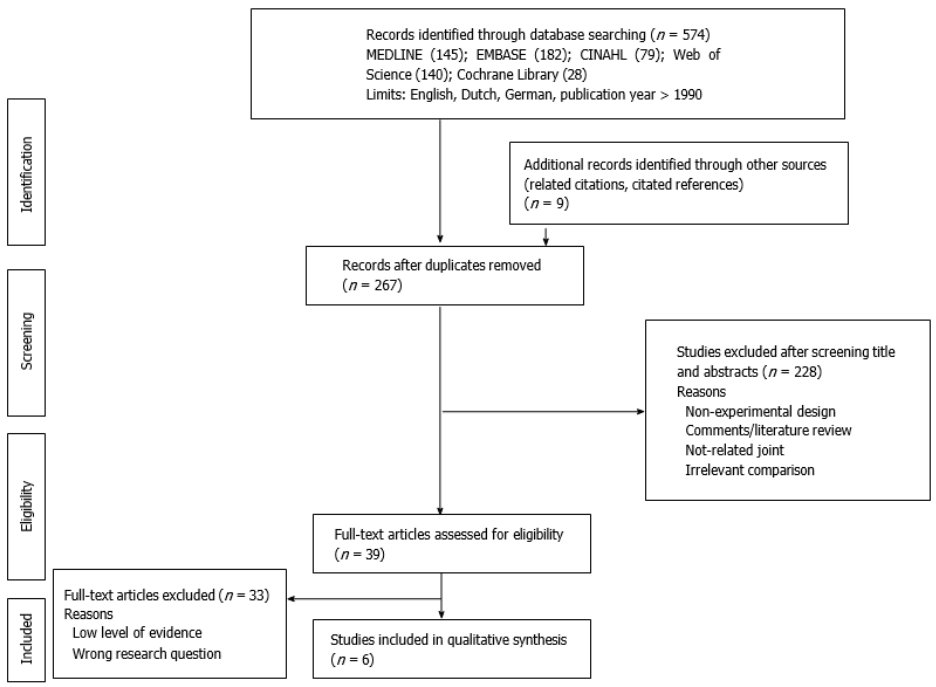

Figure 1. PRISMA flow diagram

The search was set up using a PICO format [patient (or disease), intervention (drug or treatment), comparison (another drug of treatment) and outcome], from which search terms were deduced, as can be seen in Table 1. Studies eligible for inclusion were Level of Evidence (LoE) II (randomized controlled trials) and LoE III (comparative cohort studies) that compared different surgical procedures for CT of the shoulder. From the selected articles, the authors, their institutions and the journal name were masked, a few weeks before data assessment took place.

Data assessment and management

Risk of bias and the quality of the included studies were assessed independently by two authors (FV, EF). The included RCTs and quasi-RCTs were assessed using the twelve quality criteria of Furlan et al (2008). High-Quality was defined as a "yes" score in ≥ 50% of all items. [8] The non- randomized studies were assessed using the Newcastle- Ottawa assessment scale. [9] Disagreements were resolved by consensus, or when necessary a third review author (JWM) was consulted. Data was independently extracted by two reviewers (FV, EF) and crosschecked for accuracy. The reviewers were blinded to the authors of the included articles, their institutions, and the journals in which they were published. Data from each individual study was extracted in a standardized way using a specifically designed extraction form (appendix 1 in supplemental material). Discrepancies were resolved by scrutinizing the original article until a consensus was reached. Extracted data included information such as inclusion and exclusion criteria, inclusion period, method of randomization, specific characteristics of the patient groups, specific surgical information, primary and secondary outcomes, baseline characteristics, statistics used, results and complications (appendix 2 in supplemental material). In case of missing information, we tried to contact the authors of the identified studies.

Data analysis

Whenever possible data was pooled. When pooling was not possible, due to clinical heterogeneity of the included studies based on the included intervention and/or study population, data is presented in a quality synthesis.

RESULTS

Using the above-mentioned search strategy (appendix 3 in supplemental material) 574 potential relevant studies were identified (Figure 1); of which 267 remained after removing the duplicates. After screening of the titles and abstracts 228 studies were excluded. The main reasons for exclusion were that the studies did not concern the shoulder, were non-experimental studies, or made an irrelevant comparison. The full texts were read in 39 studies. Finally, six studies were included in this review, concerning

294 surgically treated shoulders with CT.

Characteristics

Study characteristics of the included studies are summarized in Table 2. Of these six studies there were two were RCTs (118 participants), one quasi-RCT (40 participants) and three comparative cohort studies (136 participants). The data could not be pooled because of the incompleteness of the extracted data and owing to the diversity in timing of the outcome moments (range, 6 wk-5 years).

Data assessment

The risk of bias was assessed by two independent review authors (FV, EF). Three studies were evaluated with the twelve criteria of Furlan et al[8], and three studies were evaluated with the Newcastle-Ottawa scale. [9] Two RCTs were assessed as high-quality RCTs (Table 3), whereas in the non-randomized group one study received the maximum score and the other two studies had a near to maximum score (Table 4). Results of the functional outcome are presented using different outcome measures, namely the Constant-Murley score (CMS), Patte score and the University of California-Los Angeles score (UCLA). The results of the clinical outcome are presented with various outcomes measures, including the Disabilities of Arm, Shoulder and Hand score (DASH) and return to work, as can be seen in Table 2.

Debridement vs debridement with additional acromioplasty

The studies of Rubenthaler et al[10], Clement et al[11], Marder et al[12] and Maier et al[13] aided in answering the first research question (Figure 2). *Functional outcome:* For the comparison of the functional outcome on the short and midterm only the RCT of Clement et al[11] reported data 6 weeks and 12 months after debridement vs debridement with acromioplasty. They reported no significant difference after 6 weeks (mean CMS 62.2 vs 64.1) and 12 months (mean CMS 82.4 vs 77.5). Rubenthaler et al[10] reported the results after debridement with acromioplasty in an open vs arthroscopic procedure (mean CMS 86.0 vs 85.3). Marder et al[13] and Maier et al[15] reported data of debridement vs debridement with acromioplasty after 5 years and 34 months, respectively. The mean UCLA of 32.0 vs 32.4 after 5 years did not differ significantly and the mean CMS of 74.9 vs 73.4 after 34 months did not differ either. *Clinical outcome*: The clinical outcome was reported by Clement et al[11] and Marder et al[13] using the DASH score and QuickDASH score. The clinical outcome did not differ significantly on the short and midterm (6 weeks: mean DASH 24.5 vs 24.0 and 12 months: mean DASH 14.5 vs 14.0). After 5 years the mean QuickDASH did not differ significantly either (6.3 vs 11.1).

Table 2. Characteristics of the included studies

Reference	Study design (LoE)	Population	Interventions	Outcome measures	Findings	
					Baseline	**Follow-up**
Rubenthaler et al[10]	RCT (II)	38	Arthroscopic debridement + acromioplasty vs Open debridement + acromioplasty	Patte score, VAS, CMS	No significant baseline differences	16 months: CMS: 86.0 vs 85.3 (NS) VAS: 1.4 vs 1.8 (NS) Patte score: 84.4 vs 84.6 (NS)
Clement et al [11]	RCT (II)	80	Arthroscopic debridement + acromioplasty vs arthroscopic debridement	VAS, DASH, CMS, SF-12	No significant baseline differences	6 weeks: CMS: 62.2 vs 64.1 (NS) DASH: 24.5 vs 24.0 (NS) VAS: 4.4 vs 4.5 (NS) SF-12: 45.7 vs 44.3 (NS) 12 months: CMS: 82.4 vs 77.5 (NS) DASH: 14.5 vs 14.0 (NS) VAS: 1.6 vs 2.5 (NS) SF-12: 43.0 vs 42.5 (NS)
Hofstee et al [12]	Quasi-RCT (III)	40	Arthroscopic debridement + acromioplasty vs arthroscopic debridement	DASH, VAS, satisfaction, ROM	No significant baseline differences	36 months: DASH: 3.14 vs 3.04 (NS) VAS: 4.3 vs 4.2 satisfied, yes: 80 vs 75%
Marder et al [13]	Retrospective case-control study (III)	50	Arthroscopic debridement vs arthroscopic debridement + acromioplasty	QuickDASH, RTW, UCLA	No significant baseline differences	6 weeks: RTW: 60 vs 20% (p= 0.004) 5 years: QuickDASH: 6.3 vs 11.1 (NS) VAS: not well recorded UCLA: 32.0 vs 32.4 (NS)
Tillander et al [14]	Matched pair analysis (III)	50	Arthroscopic acromioplasty in patients with vs without CT	CMS, satisfaction, radiological	No significant baseline differences	24 months: CMS: 78 vs 79 (NS) Satisfaction, yes: 72 vs 80% (NS)
Maier et al [15]	Comparative cohort study (III)	36	Open debridement vs open debridement + acromioplasty	CMS	No significant baseline differences	34 months: CMS: 74.9 vs 73.4 (NS)

RCT = randomized controlled trial; CMS = Constant-Murley score; DASH = Disabilities of Arm, Shoulder and Hand score; VAS = Visual Analog Scale for pain; UCLA = University of California-Los Angeles score; RTW = return to work.

Table 3. Methodological quality scores of the individual included RCT's and qausi-RCT

	12 quality criteria of Furlan et al.[8]							
Reference	**Adequate randomization?**	**Allocation concealment?**	**Blinding patients?**	**Blinding caregiver?**	**Blinding outcome assessors?**	**Incomplete outcome data addressed? dropouts**	**Incomplete outcome data? ITT-analysis?**	**No selective outcome reporting?**
Rubenthaler et al [10]	+	+	+	-	?	+	-	+
Clement et al[11]	+	+	+	-	+	+	-	+
Hofstee et al.[12]	-	-	?	-	?	+	-	+

12 quality criteria of Furlan et al.[8]							
Reference	**Similarity baseline characteristics?**	**Co-interventions avoided or similar?**	**Compliance acceptable in all groups?**	**Timing of the outcome assessments similar?**	**Score Maximum**	**Score Study**	**Percentage**
Rubenthaler et al [10]	+	-	+	+	12	8	67%
Clement et al[11]	+	+	+	+	12	10	83%
Hofstee et al[12]	+	+	+	+	12	6	50%

+,Yes =1 point; -,No=0 points; ?,unclear/unsure=0 points
High-Quality = >50%, Low-Quality = <50%

	Newcastle-Ottawa Scale[9]		
Reference	Selection (max = ****)	Comparability (max =**)	Exposure (max =***)
Marder et al[13]	***	**	***
Tillander et al[14]	****	**	***
Maier et al[15]	***	**	***

Acromioplasty vs acromioplasty with additional debridement

The studies of Hofstee et al[12] and Tillander et al[14] were helpful in answering the second research question. There was no information available for the comparison of the results in the short term.

Functional outcome: Tillander et al[14] reported results of the functional outcome after 24 months after solitary acromioplasty in patients with and without CT. The mean CMS was 78.0 and 79.0, respectively. As an indication of the functional outcome Hofstee et al[12] reported the ROM after 36 months. In all six planes the ROM did not differ significantly between patients after acromioplasty in comparison with patients after acromioplasty with debridement. *Clinical outcome*: Hofstee et al[12] reported a DASH score of 3.1 vs 3.0 after 36 months of surgery which was not significantly different.

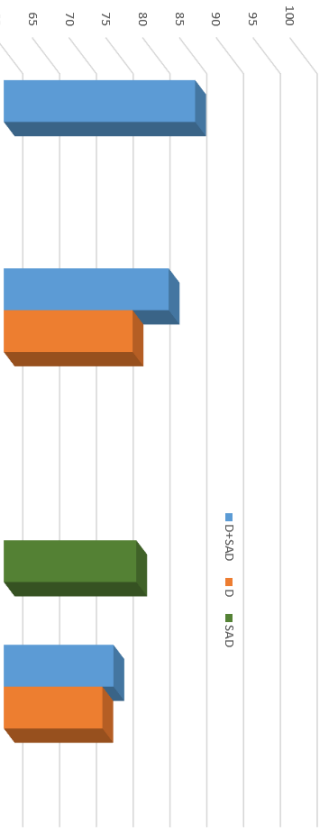

Figure 2. Constant-Murley score after treatment.
D: Debridement; SAD: Subacromial decompression.

Complications

Four of the included six studies reported information about adverse events or complications. [10,11,13,15] There were no intraoperative complications reported, none of the included patients required reoperation. The only complication reported was adhesive capsulitis. In the studies of Clement et al[11] and Marder et al[13], one patient (1.3%) and three patients (6%) showed signs of adhesive capsulitis. These patients all could be treated conservatively and showed full recovery at the end of the follow-up.

DISCUSSION

CT is often a self-limiting disease which in the majority of the patients can be managed with conservative measures, such as physical therapy, subacromial infiltrations, shock wave therapy or needling. However, in some patients these conservative measures fail and surgery is needed. Based on the results of this systematic review of LoE II and III evidence, we found that all three available treatment options show good functional and clinical outcomes in the short and midterm. However, a favoured procedure is difficult to determine due to the lack of high-quality comparing studies. Regarding the first research question four studies aided in answering this "question". [10,11,13,15] The functional and clinical outcome did not differ after debridement vs debridement with an additional acromioplasty. It could be postulated that CT is not correlated with subacromial impingement and an acromioplasty does not seem to be beneficial. This supports the aforementioned theory of Gärtner et al.[2] Of the other outcomes extracted from the included studies, only in the study of Marder et al[13] did significantly more patients return to work after six weeks (Table 2). In the included RCT [11] an additional acromioplasty was not found to be beneficial. Though, in this study the (patho)anatomy (e.g., classification of Bigliani[16]) of the acromion was not considered. It has been postulated that if there are any radiological or intraoperative signs of impingement an acromioplasty can be performed.[16,17] The studies of Hofstee et al[12] and Tillander et al[14] aided in answering the second research question. They found good functional and clinical results 24 and 36 months after an acromioplasty and an acromioplasty with an additional debridement of the calcifications. They found no significant differences. Short term results were not available. Other variables (VAS and satisfaction) also did not differ significantly. These results support the correlation between CT and subacromial impingement. Whereas, this suggests that the complete or partial debridement of the calcific deposits is not necessary. All three available treatment options are safe; the complication rates are low and the reported complications were treated conservatively and showed full recovery. In the included studies in which a debridement was performed the rotator cuff defect was not sutured afterwards, even though no rotator cuff tears were seen in our entire study population. Some limitations apply to this systematic review. The main limitation is the lack of high-quality, preferably randomized, comparing trials between the different treatment options. Two high-quality RCTs were included of which one did not make the exact comparison in which we were interested. The other one was valuable; however the follow-up was rather short (one year). Therefore, there is a need for more research on this topic. The data could not be pooled due to heterogeneity of the included studies and therefore no quantitative analysis could be made. We analysed the causes of this heterogeneity. But we could not improve this sufficiently; therefore data is presented in a narrative fashion. On the other hand, we were able to detect all relevant LoE II and III evidence regarding the surgical treatment options of CT and describe their results in this concise review. All three available surgical treatment options for patient with conservative therapy resistant CT of the shoulder show good functional and clinical outcome and are safe procedures. Based on this systematic review a preferable treatment option could not be appointed and therefore recommendations cannot be made. Future research should be aimed at comparing all three available options. This is preferably done in a randomized fashion including a short-, mid- and long-term follow-up.

REFERENCES

1 Diehl P, Gerdesmeyer L, Gollwitzer H, Sauer W, Tischer T (2011) [Calcific tendinitis of the shoulder]. Orthopade; 40: 733746

2 Gärtner J, Heyer A (1995) [Calcific tendinitis of the shoulder]. Orthopade; 24: 284302

3 Mouzopoulos G, Stamatakos M, Mouzopoulos D, Tzurbakis M (2007) Extracorporeal shock wave treatment for shoulder calcific tendonitis: a systematic review. Skeletal Radiol; 36: 803881

4 Uhthoff HK, Sarkar K (1991) Classification and definition of tendinopathies. Clin Sports Med; 10: 707720

5 Hurt G, Baker CL (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am; 34: 567575

6 Speed CA, Hazleman BL (1999) Calcific tendinitis of the shoulder. N Engl J Med; 340: 15821584

7 Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med; 6: e1000097

8 Furlan AD, Pennick V, Bombardier C, van Tulder M; Editorial Board, Cochrane Back Review Group (2009) 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine (Phila Pa 1976); 34: 19291941

9 Pastorino R, Milovanovic S, Stojanovic J, Efremov L, Amore R, Boccia S (2016) Quality Assessment of Studies Published in Open Access and Subscription Journals: Results of a Systematic Evaluation. PLoS One; 11: e0154217

10 Rubenthaler F, Ludwig J, Wiese M, Wittenberg RH (2003) Prospective randomized surgical treatments for calcifying tendinopathy. Clin Orthop Relat Res; (410): 278284

11 Clement ND, Watts AC, Phillips C, McBirnie JM (2015) ShortTerm Outcome After Arthroscopic Bursectomy Debridement of Rotator Cuff Calcific Tendonopathy With and Without Subacromial Decompression: A Prospective Randomized Controlled Trial. Arthroscopy; 31: 16801687

12 Hofstee DJ, Gosens T, Bonnet M, De Waal Malefijt J (2007) Calcifications in the cuff: take it or leave it? Br J Sports Med; 41: 832835

13 Marder RA, Heiden EA, Kim S (2011) Calcific tendonitis of the shoulder: is subacromial decompression in combination with removal of the calcific deposit beneficial? J Shoulder Elbow Surg; 20: 955960

14 Tillander BM, Norlin RO (1998) Change of calcifications after arthroscopic subacromial decompression. J Shoulder Elbow Surg; 7: 213217

15 Maier M, Krauter T, Pellengahr C, Schulz CU, Trouillier H, Anetzberger H, Refior HJ (2002) [Open surgical procedures in calcifying tendinitis of the shoulder concomitant pathologies affect clinical outcome]. Z Orthop Ihre Grenzgeb; 140: 656661

16 Seil R, Litzenburger H, Kohn D, Rupp S (2006) Arthroscopic treatment of chronically painful calcifying tendinitis of the supraspinatus tendon. Arthroscopy; 22: 521527

17 Balke M, Bielefeld R, Schmidt C, Dedy N, Liem D (2012) Calcifying tendinitis of the shoulder: midterm results after arthroscopic treatment. Am J Sports Med; 40: 657661

18 Merolla G, Bhat MG, Paladini P, Porcellini G (2015) Complications of calcific tendinitis of the shoulder: a concise review. J Orthop Traumatol; 16: 175183

19 Gosens T, Hofstee DJ (2009) Calcifying tendinitis of the shoulder: advances in imaging and management. Curr Rheumatol Rep; 11: 129134

20 ElShewy MT (2016) Calcific tendinitis of the rotator cuff. World J Orthop; 7: 5560

CHAPTER 3

Isolated acromioplasty for calcific tendinitis produces good results at 3-year follow-up: Clinical outcome is not correlated to presence of residual calcifications

Verstraelen FU
Glimmerveen ND
Fievez E
Janssen L
Morrenhof W

2015 Curr Orthop Practice;26: 363-366

ABSTRACT

Background
The surgical procedure for calcific tendinitis of the shoulder remains a matter of dispute. Some advocate complete removal of the calcium deposits. The aim of this study was to investigate the midterm clinical outcome of an isolated acromioplasty with a secondary aim to investigate the relationship between the persisting presence of the calcifications and the midterm clinical outcome.

Method
Records of all patients who underwent an acromioplasty in 2 consecutive years were reviewed. Patients were included if calcifications on preoperative radiographs were seen. These patients were followed-up, and the Constant-Murley score (CMS) and Shoulder Disability Questionnaire (SDQ) were administered.

Results
Seventy-five patients met the inclusion criteria. Eleven patients were lost to follow-up and 14 patients were excluded. In our study population (n=50, mean follow-up 2.9 yr) the calcium deposits were not present in 52% of the shoulders. There were no differences in the CMS between patients with or without calcifications with 83.9 (SD 14.8) and 86.0 (SD 17.3), respectively. The SDQ did not show any differences between the two groups with 34.3 (SD 30.0) and 23.2 (SD 32.1), respectively.

Conclusions
This retrospective cohort study demonstrates good clinical results in patients with calcific tendinitis refractory to conservative measures treated with a Neer acromioplasty alone in the midterm (mean follow-up of 2.9 yr). This study suggests that the presence of residual calcifications is not a risk factor for a poorer clinical outcome after acromioplasty for calcific tendinitis.

Key Words
Tendinitis; calcifications; acromioplasty; clinical outcome; midterm

INTRODUCTION

Calcific tendinitis of the shoulder is a common disease in which chronic inflammation of the rotator cuff tendons causes calcium particles to deposit. This results in a pattern of pain and decreased range of motion. In an asymptomatic population, intratendineous calcifications are seen in about 2.7% of the people. [1] When considering patients with shoulder complaints, this incidence rises to 6.8-54.0%. [1-3] Calcific tendinitis mainly affects individuals between 30-60 years of age. Men and women are equally affected. The disease usually is self-limiting, but the complaints can last 3-5 yr. [3] In about 80% the calcium deposits are located in the tendon of the supraspinatus, with a typical location of 1.5-2.0 cm of its insertion at the greater tuberosity of the humeral bone. [1,3] The aetiology of calcium deposits in the rotator cuff is still a matter of dispute. It has been suggested that it is related to a decreased local oxygen tension or hypoxia. [4] The disease usually passes through four stages in the following order:

1. pre-calcific stage, in which fibrocartilaginous metaplasia within the tendon is seen.
2. formative stage, in which calcific deposit formation is seen in the fibrocartilaginous matrix
3. resorptive stage, in which a cell-mediated resorption takes place that results in the disappearance of the calcium deposits
4. restitution stage, in which the calcium deposits are resorbed and the tendon heals. [3,5]

The calcific deposits can be subdivided based on their appearance on radiographs using the classification of Gartner et al. [6] In this classification the calcifications are subdivided into three groups: type I, clearly circumscribed and dense; type II, clearly circumscribed, translucent, cloudy, and dense; type III, cloudy and translucent. [6] The disease is primarily treated conservatively, with measures such as with anti-inflammatory drugs, ice therapy, physiotherapy, corticosteroid injections, needling, or extracorporeal shock wave therapy and this is successful in up to 90% of the patients. [7] However, when this fails, surgery often is the next step treatment. [8] The exact surgical treatment is still a matter of debate. There are three options when considering surgery for calcific tendinitis. The first one is to perform an acromioplasty according to Neer (including the removal of the anterior edge and undersurface of the anterior part of the acromion with the attached coracoacromial ligament in combination with a bursectomy). The second is the same acromioplasty but in combination with debridement of the calcifications, and the last option is to solely debride the calcifications. All surgical treatment options have shown good to excellent results in several retrospective studies; however, there are few high-quality comparative studies available. [9-14] In particular, the role of an acromioplasty remains a matter of debate. Some studies argue that it

is not necessary to remove the calcification when performing an acromioplasty. [9,12] While other authors state that the functional outcome is inversely related to the residual calcifications and that all effort should be made to remove all calcifications. [10,11] Others state that beneficial results are achieved when the calcifications are solely debrided. [12,15] Therefore, in our opinion the question remains: what is the effect of an acromioplasty alone on rotator cuff calcifications? In this study, the aim was to determine the midterm clinical outcome of an isolated acromioplasty for calcific tendinitis with a secondary aim to investigate the relationship between the presence of rotator cuff calcifications and the midterm clinical outcome. Our hypothesis is that an isolated acromioplasty has good clinical results and that the presence of residual calcifications is not related to the clinical outcome.

MATERIALS AND METHODS

Approval for the study was obtained from the institutional review board (METC Venlo). All patients were informed and consented to providing data for anonymous use. At our institution calcific tendinitis of the shoulder refractory to conservative therapies is treated with an acromioplasty without the removal of the calcium deposits. The conservative therapy includes a variety of treatments including anti-inflammatory drugs, physical therapy, corticosteroid injections, needling, or extracorporeal shock wave therapy for at least 6 months. The radiographs of all patients who had an acromioplasty at our institution in 2 consecutive years were investigated for the presence of calcifications preoperatively. Included and contacted were patients in whom the calcifications, cumulatively larger than five mm, were shown on preoperative radiographs. The indication for surgery (Neer acromioplasty) in all patients was subacromial pain syndrome refractory to conservative measures, not regarding the presence of rotator cuff calcifications on the preoperative radiographs. Excluded were patients who had other previous surgery before or combined with the acromioplasty, patients who had clinical suspicion of shoulder instability, or patients who had full-thickness rotator cuff tears. All patients had a preoperative shoulder radiograph taken (anteroposterior view with the arm in internal and external rotation and an axillary view). MRI was not performed preoperatively routinely. Sonography was done when a full- thickness lesion was clinically suspected. The Constant-Murley score (CMS) of both shoulders was assessed postoperatively. The CMS is an outcome score to assess the functional outcome; it combines patient-reported outcome measures and clinical outcomes measurements including the range of motion. [16-18] Patients were also asked to fill out the Shoulder Disability Questionnaire (SDQ) to assess the impairments in daily living. [19-21] Furthermore, demographic data were assembled and the calcifications were subdivided using the Gartner classification. [6] Four experienced orthopaedic surgeons performed an open or arthroscopic

acromioplasty. The procedure chosen was to the surgeon's preference. In all shoulders the calcium deposits were left untouched. [22] During the arthroscopic procedure there were no other significant side pathologies seen and no full-thickness rotator cuff lesions were apparent. A standardized postoperative rehabilitation protocol was applied, including early passive mobilization and anti- inflammatory drugs for 2 weeks. The additional conservative therapies were not registered postoperatively. All data were computed with the statistical software program SPSS. The baseline characteristics and outcome measures were compared with t-tests for continual variables and x^2-tests for nominal and ordinal variables. All variables were normally distributed.

RESULTS

Of 276 patients who had an acromioplasty at our institution in 2 consecutive years, a total of 75 patients had rotator cuff calcifications on preoperative radiographs and were invited for follow-up. Sixty-four patients were available for follow- up. The other 11 patients either refused or could not be contacted. Furthermore, 14 patients were excluded according to the previous described exclusion criteria. This resulted in a study population of 50 patients (Figure 1). The study population consisted of 21 men and 29 women. Two women had bilateral surgery. Baseline characteristics of the included patients are presented in Table 1.

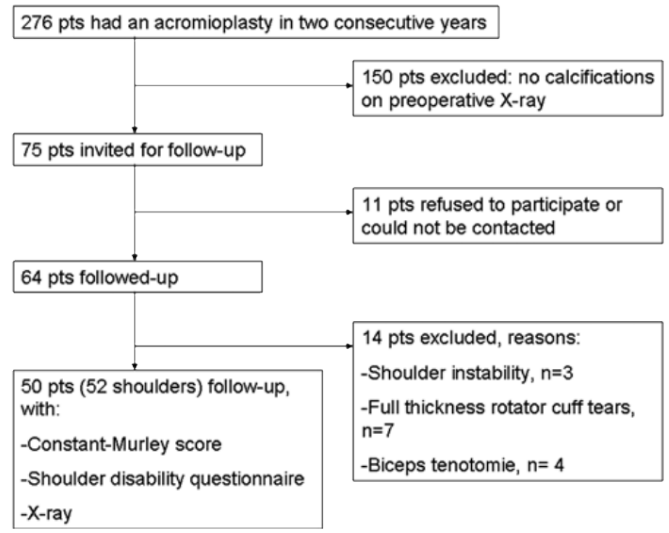

Figure 1. Flow Chart of patients through study

All calcifications were located in the tendon of the supraspinatus, the infraspinatus, or both as confirmed on the preoperative radiographs. The preoperative calcium deposits were subdivided using the Gartner classification. There were five shoulders with type I calcium deposits, 27 with type II, and 12 with type III calcium deposits. In the other eight shoulders the calcium deposits could not be classified because the calcifications were too fragmented. All patients with type I calcifications on the preoperative radiographs still had these at follow-up. Of the 27 shoulders with type II calcifications, 14 still had them postoperatively whereas 13 patients did not. In only three of the 12 patients with type III calcifications, the calcifications persisted postoperatively (Table 2). In the whole study population, the calcifications were not present in 52% (27 out of 52 shoulders) of the shoulders after a mean follow-up of 2.9 years (range 2.0-3.9). No significant differences were found in sex, age at operation, and duration of follow-up between patients with or without calcifications on the radiographs at follow-up. No significant differences in Constant-Murley scores were found in shoulders with or without calcifications on the postoperative radiograph (Table 2). The age-related, mean Constant-Murley score in men between 51-60 yr old is 90.0 ± 3.1 and in women 73 ± 2.8.18,19 In our study population, the mean Constant-Murley score in men was 91.3 ± 9.9 and in women 79.4 ± 17.5. No significant differences were found in the presence of calcifications, Constant-Murley scores, or Shoulder Disability Questionnaire between the open (n=19) and the arthroscopic group (n=33). The scores of the Shoulder Disability Questionnaire showed a mean of 29.0 ± 31.2 (a higher score indicating a more symptomatic shoulder). No significant differences were found in these scores between shoulders with or without calcifications on the radiographs at follow-up (Table 3).

Table 1. Baseline characteristics of our study population

Baseline characteristics	
Age in years (SD)	51 (7.94)
Sex (%)	Male: 21 (40.4) Female: 31 (59.6)
Follow-up time in years (SD)	2.86 (0.51)
Affected side (%)	Right: 23 (44.2) Left: 29 (55.8)
Dominant side (%)	Right: 49 (94.2) Left: 3 (5.8)
Type of surgery (%)	Open: 19 (36.5) A'scopic: 33 (63.5)

Table 2. Graph showing the preoperative Gärtner classification and the number of patients at follow up with calcifications

Gärtner type start study	With Calcification	Without Calcification	Total
Type I	5 (100%)	0 (0%)	5
Type II	14 (51.9%)	13 (48.1%)	27
Type III	3 (75.0%)	9 (25.0%)	12
Total	22	22	44

Table 3. Graph showing that there is no relation between the persisting presence of the calcifications at follow up.

	With Calcification (n= 27)	Without Calcification (n=25)	p-value
Age (SD)	50.95 (9.47)	49.17 (5.92)	NS
Sex (%)	Male: 17 (55.6) Female: 12 (44.4)	Male: 10 (40) Female: 15 (60)	NS
CMS (SD)	83.85 (14.79)	85.96 (17.33)	NS
SDQ (SD)	34.33 (29.99)	23.16 (32.09)	NS

NS = Not Significant

DISCUSSION

The exact surgical treatment for calcific tendinitis of the shoulder is still a matter of debate. [4,10,12,22] Therefore, the aim of this study was to investigate the midterm clinical outcomes of an isolated acromioplasty for calcific tendinitis with a secondary aim to investigate the relationship between the presence of rotator cuff calcifications and the midterm clinical outcomes. Our hypothesis was that an isolated acromioplasty would provide good clinical results and that the presence of residual calcifications are not related to the clinical outcome. In our study population 52% of the calcifications disappeared after a mean follow-up of 2.9 years (range 2.0-3.9). No significant differences were found in Constant-Murley scores. This suggests that the presence of residual calcifications is not a risk factor for a poorer clinical outcome after acromioplasty for calcific tendonitis. These findings are in line with results reported in some of the current literature. [9,11,12,22] Tillander and Norlin [12] reviewed 50 patients in a matched pair analysis two years after acromioplasty (without removal of the calcific deposits). The first group of patients had calcifications on preoperative radiographs; the second group did not. After 2 years most (79%) calcifications had regressed or disappeared on the radiographs. The postoperative functional outcomes of patients with unchanged calcifications were not significantly different compared with patients in whom the calcifications resolved or significantly decreased. In 2007, Hofstee et al [9] did not report better functional outcomes in patients who underwent an acromioplasty in combination with the removal of the calcifications compared to patients who had an acromioplasty alone. These two studies postulated

that rotator cuff calcifications on radiographs are insignificant and transient findings. Marder et al [13] on the contrary, stated that the 'time to return to pain-free activity' was shorter when debridement alone was performed than when an additional acromioplasty was performed. The long-term Disability of the Arm, Shoulder and Hand (DASH) scores did not differ significantly. Some limitations may apply to our study in concordance to its retrospective design. First, the preoperative CMS were not available. Although it is obvious when reading many other studies that do have preoperative data, it is likely that the average CMS in patients with calcific tendinitis is significantly lower than the CMS at follow-up. [11,22-25] It is also not likely to be different between the two groups, although this could not be statistically proven. The results could be different if the calcifications were subdivided according to the size of the deposits; however, the size of the study population did not allow such analysis. This retrospective cohort study demonstrates good mid- term (mean follow-up 2.9 yr) clinical results in patients with calcific tendinitis refractory to conservative measures treated with a Neer acromioplasty alone. In 52% of the shoulders, the rotator cuff calcifications were not present at follow-up. There was no correlation found between the persisting presence of calcifications and the clinical outcome at midterm follow-up. Bearing in mind that this study has limitations, we concluded that there is no need to remove the calcium deposits. However, we do believe further prospective comparative trials are needed to determine the best surgical treatment for calcific tendinitis of the shoulder.

REFERENCES

1. Speed CA, Hazleman BL (1999) Calcific tendinitis of the shoulder. N Eng J Med;340:1582-1586
2. Rupp S, Seil R, Kohn D (2000) [Tendinosis calcerea of the rotator cuff]. Orthopade; 29:852-867
3. Diehl P, Gerdesmeyer L, Gollwitzer H, et al (2011) [Calcific tendinitis of the shoulder]. Der Orthopade.; 40:733-746
4. Gosens T, Hofstee DJ (2009 Calcifying tendinitis of the shoulder: advances in imaging and management. Cur Rheum Rep; 11:129-134
5. Hurt G, Baker CL (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am; 34:567-575
6. Gartner J, Heyer A (1995) [Calcific tendinitis of the shoulder]. Der Orthopaede;24:284--302
7. Lam F, Bhatia D, Van Fooyen K, et al (2006) Modern management of calcifying tendinitis of the shoulder. Current Orthopaedics; 20:445-452
8. Verstraelen FU, in den Kleef NJHM, Janssen L, Morrenhof W (2014) High-energy versus low-energy extracorporeal shock wave therapy for calcifying tendinitis of the shoulder: which is superior? a meta-analysis. Clin Orthop Relat Res; 472:2816-2825
9. Hofstee DJ, Gosens T, Bonnet M, et al (2007) Calcifications in the cuff: take it or leave it? Br J Sports Med; 41:832-837
10. Porcellini G, Paladini P, Campi F, et al (2004) Arthroscopic treatment of calcifying tendinitis of the shoulder: clinical and ultrasonographic follow-up findings at two to five years. J Shoulder Elbow Surg; 13:503-511
11. Rizello G, Fransceschi F, Longo UG, et al (2009) Arthroscopic management of calcific tendinopathy of the shoulder. Bull NYU Hospital Joint Diseases; 67:330-333
12. Tillander B, Norlin RO (1998) Change of calcifications after arthroscopic subacromial decompression. J Shoulder Elbow Surg; 7:213-220
13. Marder RA, Heiden EA, Kim S (2011) Calcific tendonitis of the shoulder: is subacromial decompression in combination with removal of the calcific deposit beneficial? J Shoulder Elbow Surg; 20:955-960
14. Balke M, Bielefeld R, Schmidt C, et al (2012) Calcifying tendinitis of the shoulder:midterm results after arthroscopic treatment. Am J Sports Med; 40:657-661
15. Maier D, Jaeger M, Izadpanah K, et al (2013) Rotator cuff preservation in arthroscopic treatment of calcific tendinitis. Arthroscopy; 29:824-831
16. Conboy VB, Morris RW, Kiss J, et al (1996) An evaluation of the Constant-Murley shoulder assessment. J Bone Joint Surg Br; 78:229-232
17. Constant CR, Murley AH (1987) A clinical method of functional assessment of the shoulder. Clin Orthop Relat Res; 214:160-164
18. Constant CR, Gerber C, Emery RJ, et al (2008) A review of the Constant score: modifications and guidelines for its use. J Shoulder Elbow Surg; 17:355-361
19. van der Windt DA, van der Heijden GJ, de Winter AF, et al (1998) The responsiveness of the Shoulder Disability Questionnaire. Ann Rheum Dis; 57:82-89
20. Paul A, Lewis M, Shadforth MF, et al (2004) A comparison of four shoulder-specific questionnaires in primary care. Ann Rheum Dis; 63:1293-1302
21. van der Heijden GJ, Leffers P, Bouter LM (2000) Shoulder disability questionnaire design and responsiveness

of a functional status measure. J Clin Epidemiol; 53:29-38

22. Jacobs R, Debeer P (2006) Calcifying tendinitis of the rotator cuff: functional outcome after arthroscopic treatment. Acta Orthop Belg; 72:276-281
23. Neer CS (1972) Anterior acromioplasty for the chronic impingement syndrome in the shoulder: a preliminary report. J Bone Joint Surg. Am; 54:41-50
24. Jerosch J, Strauss JM, Schmiel S (1998) Arthroscopic treatment of calcific tendinitis of the shoulder. J Shoulder Elbow Surg; 7:30-37
25. Hughes PJ, Bolton-Maggs B (2002) Calcifying tendinitis. Curr Orthop; 16:389-394

CHAPTER 3

3

CHAPTER 4

Comparison of clinical and radiological outcomes after three different surgical treatments for resistant calcifying tendinitis of the shoulder: a short-term randomized controlled trial

Verstraelen FU
Schotanus MGM
Klemann-Harings SEJM
Lambers Heerspink FO
Jansen EJP

2022 J Orthop Surg Res;17:480

ABSTRACT

Background

A preferable surgical treatment for patients with conservative therapy-resistant calcifying tendinitis of the shoulder is still a matter of debate. Therefore, the purpose of this study was to evaluate and compare short-term clinical and radiological results of three surgical treatment options for these patients.

Methods

A multicenter randomized trial was conducted. Sixty-nine patients were randomly assigned to receive 1. subacromial decompression (Group SAD), 2. debridement of calcifications (Group D), or 3. debridement of calcifications with SAD (Group D + SAD). Stringent inclusion and exclusion criteria were used. The primary outcome was an improvement in VAS for pain (pVAS) 6 months postoperatively. Secondary outcomes were an improvement in pVAS 6 weeks postoperatively, functional outcomes (CMS, DASH, ASES), radiological outcome, additional treatments, and complications.

Results

The improvement in pVAS was significant in all groups ($p < 0.001$) and did not differ between the groups after 6 months. Six weeks postoperatively, the improvement in pVAS was significantly ($p = 0.03$) less in Group SAD compared to Group D + SAD (16.5 mm, SD 19.3 mm vs 33.1 mm, SD 19.7 mm, respectively). The mean size of calcifications decreased significantly in all groups ($p < 0.0001$). In Group SAD, the size of the calcifications decreased less ($p = 0.04$) compared to Group D and Group D + SAD after 6 weeks. Group SAD received more additional treatments ($p = 0.003$) compared to Group D + SAD (9 vs 1), which were mainly subacromial cortisone injections.

Conclusions

All patient groups showed significant pain relief and an improvement in shoulder function 6 months after surgery. However, patients in Group SAD showed inferior pain relief and less improvement in DASH score after 6 weeks. Furthermore, this group required more postoperative additional treatments. No significant differences in clinical and radiological outcomes were observed between patients in Group D compared to Group D + SAD. Therefore, an arthroscopic debridement without subacromial decompression seems to be advisable for patients with therapy resistant calcifying tendinitis of the shoulder.

Key word

Calcifying tendinitis; shoulder; debridement; subacromial decompression; surgical treatment

INTRODUCTION

Calcifying tendinitis of the shoulder is a common shoulder disease that often leads to long-lasting pain and loss of function. [1–3] The supraspinatus tendon is the most affected rotator cuff tendon. [1,2] The exact aetiology of calcifying tendinitis of the shoulder remains unclear. [3–6] The initial treatment of calcifying tendinitis of the shoulder is with conservative or minimal invasive measures (such as shock wave therapy or needle aspiration of calcific deposit (NACD). However, about 10% of the patients require surgical treatment. [6–9] Several surgical treatment options are shown to be effective. [10,11] However, the most effective surgical treatment procedure has not been appointed yet. [10] In general, there are three surgical treatment options available. The first is to perform an arthroscopic subacromial decompression without debridement of the calcifications. [12–14] The second option is to perform an arthroscopic debridement of the calcifications without subacromial decompression, and the third option is to perform an arthroscopic debridement of the calcifications combined with subacromial decompression. It is not known which of these surgical treatment procedures is the most effective concerning short-term pain relief and functional outcomes. [10,11,15,16] Therefore, the purpose was to compare these three surgical treatment procedures regarding pain relief and functional outcomes 6 months after surgical treatment. We hypothesized that all three procedures have comparable effectiveness concerning pain relief and functional outcome.

MATERIALS AND METHODS

After approval of the medical ethics review committee (METC) of both centres (number: 14-T-112) and registration in the Dutch clinical trial registry (number: NL 4974), an open-label dual-centre randomized clinical trial was conducted between September 2015 and June 2020. Patients were randomly assigned by computer into three treatment groups: 1. arthroscopic subacromial decompression without debridement of the calcifications (Group SAD), 2. arthroscopic debridement of the calcifications without subacromial decompression (Group D), and 3. arthroscopic debridement of the calcifications combined with subacromial decompression (Group D + SAD).

Patient eligibility

All patients were recruited by experienced orthopaedic shoulder surgeons in two different hospitals (SK and EJ in Zuyderland MC and OLH in Viecuri MC). Patients with a prolonged course of calcifying tendinitis of the shoulder in which surgical treatment was chosen as a treatment were considered for eligibility. Inclusion criteria were failed conservative treatment (including at least a subacromial injection (SAI) in combination

with exercise therapy and/or nonsteroidal anti-inflammatory drugs (NSAIDs) for at least 6 months, type I or II subacromial calcifications according to the Gartner classification[4] (Fig. 1), calcifications with diameter more than 5 mm (Bosworth Grade 2–3) [17], unrestricted range of motion (> 150° abduction/anteflexion and > 70° external rotation) and able and willing to participate in the study. Exclusion criteria were signs of adhesive capsulitis, symptomatic degenerative diseases of the acromioclavicular joint, full-thickness rotator cuff lesions, fibromyalgia, rheumatoid arthritis, surgical history of the affected shoulder, perioperative findings of significant intraarticular pathology (e.g., biceps pathology or acromioclavicular/glenohumeral osteoarthritis), and Gartner type III subacromial calcifications.

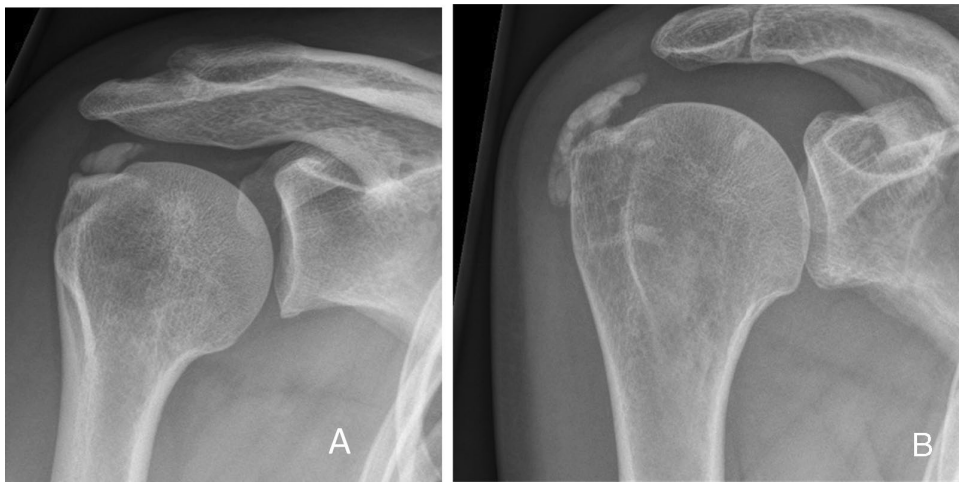

Figure 1. Gartner type I and II calcifications. A Clearly circumscribed, dens subacromial calcification (Gartner type I) on shoulder AP view; **B** partially clearly circumscribed, partially heterogeneous, partially dens subacromial calcification (Gartner type II) on shoulder AP view

Operative technique and rehabilitation protocol

All surgical procedures were performed by experienced shoulder surgeons (EJP, OLH, SK). After general and/ or regional anaesthesia a standardized diagnostic glenohumeral arthroscopy was performed to assess possible intraarticular and full-thickness rotator cuff lesions. Then a subacromial bursectomy was performed. In patients allocated to Group D and Group D + SAD, the calcification was located using an 18-gauge needling technique described by Ellman. [18] A small bursal-sided partial- thickness rotator cuff defect was made (Ellman grade 1–2) in line with the tendon fibres and a calcific deposit was arthroscopically debrided by applying pressure using a curette and shaver (Fig. 2). [18] Rotator cuff repair was not deemed necessary in any of the patients. In patients allocated to Group SAD and D + SAD, an arthroscopic SAD was performed as described by

Caspari and Thal (Fig. 3). [19] The rehabilitation protocol was the same in all groups and consisted of a sling for several days, pain- based movements and NSAIDs as necessary for 2 weeks.

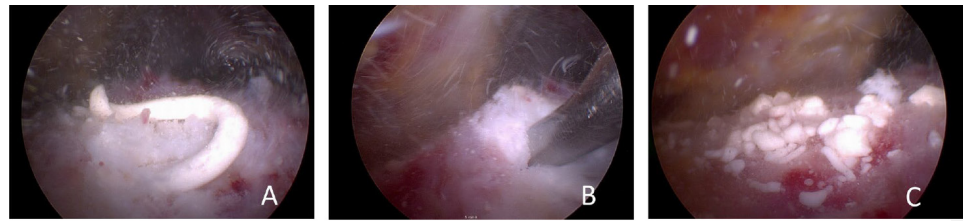

Figure 2. Arthroscopic debridement of calcifications. A After needling with 18-gauge needle, a toothpaste-like calcification discharges; **B** after a small bursal side in line with the tendon fibres incision and calcific deposit is arthroscopically debrided by applying pressure using a curette and a shaver; **C** after debridement of the calcification the subacromial space is extensively rinsed to eliminate as much calcific deposit particles as possible

Outcome measures

Patients were invited for clinical and radiological evaluation at the orthopaedic outpatient department 6 weeks and 6 months after surgery.

Primary outcome

Visual analog scale

The primary outcome was the difference in an improvement in the visual analog scale for pain (pVAS) 6 months after surgical treatment between the three groups. The pVAS was recorded at the start of the study, 6 weeks and 6 months after surgery. [20]

Secondary outcomes

Functional outcome

The functional outcome was assessed preoperatively, 6 weeks and 6 months after surgery using Constant-Murley Score (CMS) [21], Disability of Arm, Shoulder and Hand score (DASH) [22], and American Shoulder and Elbow Surgeons score (ASES). [23]

Radiological outcome

Preoperatively, 6 weeks and 6 months postoperatively standardized radiographs were taken. Radiological evaluation was done by one author (FV) and consisted of an evaluation of plain radiographs taken in three directions: true anteroposterior view, anteroposterior view with arm in internal rotation, and anteroposterior view with arm in external rotation. Using these radiographs, calcifications were classified using Gartner classification [4] and Bosworth classification. [17] Furthermore, the size and location of the calcifications were measured. Results of additional imaging techniques (e.g., MRI

or sonography) were retrieved from electronic patient files. Six weeks and 6 months postoperatively, the size of residual calcification was measured by the same author (FV). In the case of multifocal or heterogeneous calcifications, the size was added up and presented as the sum of the sizes of the calcifications.

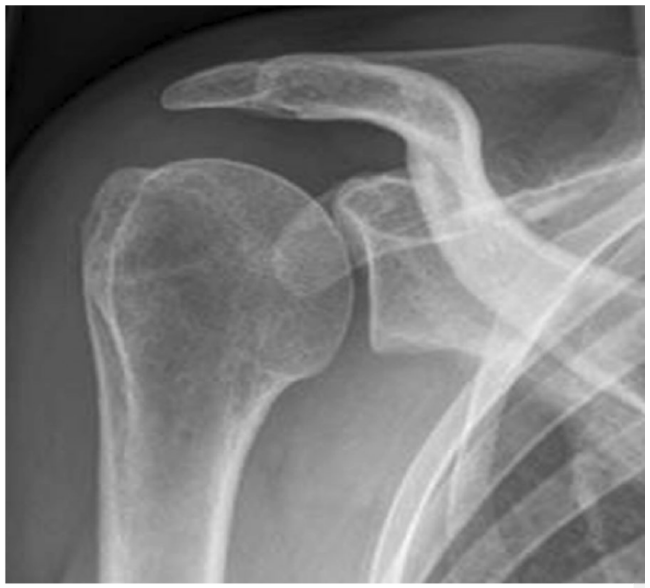

Figure 3. Postoperative status after subacromial decompression

Additional treatments and complications

Complications such as postoperative adhesive capsulitis and infection were registered. Furthermore, any proto- col violations such as additional treatments (e.g., subacromial injections and number of needle aspirations of calcific deposit procedures) were recorded. The decision to perform additional treatments was made after deliberation of the treating physician with the research team and the patient. It was documented and retrieved from the electronic patient files. When the decision was made to perform an additional treatment, adverse events such as rotator cuff lesions (confirmed on ultrasound or MRI) and adhesive capsulitis were first ruled out. Failure to treatment was defined as a decrease in VAS of less than 20 mm 6 months postoperatively. [24]

Sample size calculation and power analysis

The study was designed using an equivalence model. The trial was powered to detect a difference of 15 mm on the pVAS between the three treatment groups, since 15 mm was the minimal clinically important difference in patients after rotator cuff surgery in

the study of Kim et al. [24] The sample size calculation estimated that we needed to include 34 patients per group using an alpha of 0.05. This would provide a power of 90%. Considering that 10% of patients would be lost to follow-up, the study population needed to consist of 114 patients.

Statistical analyses

The data were analysed using SPSS version 26.0 (IBM Corp., Armonk, NY). The data were analysed using an intention-to-treat analysis (ITT analysis). Furthermore, a per-protocol analysis (PP analysis) was performed. Data of the ITT analysis are presented. In the cases of statistically significant differences between the ITT analysis and PP analysis, data for both analyses are presented. Normally distributed data are presented as a mean with standard deviation. Non-normally distributed data are presented as a median and range. Differences in baseline characteristics were analysed with a one-way ANOVA test for continuous variables and chi-square test for categorical variables for normally distributed data. Non-normally distributed data were analysed with a Kruskal–Wallis one-way ANOVA for non-normally dis- tributed data. The outcomes were analysed using a one-way ANOVA (with a Tukey's adjustment for multiple testing). $p \leq 0.05$ was considered statistically significant for all tests.

RESULTS

Study population

As can be seen in the CONSORT Flowchart, 77 patients were considered eligible and were randomized into three treatment groups (Fig. 4). Four patients were excluded because of significant other intraarticular pathology (e.g., two patients with significant acromioclavicular osteo- arthritis and two patients with biceps pathology). Two patients were excluded from further analyses because the calcification could not be located at the time of the intervention and thus could not be debrided. These two patients received subacromial decompression without debridement of the calcifications. The mean follow-up was 6.4 months (SD, 1.3 months). The overall follow-up rate after 6 weeks and 6 months was 97.1% and 89.9%, respectively. Thus, seven patients were lost to follow-up. These patients were contacted by phone and stated they did not receive other treatments for the affected shoulder. The baseline characteristics are given in Table 1. Baseline characteristics did not differ statistically significantly between groups. In 52 patients (83.9%), pre- operative additional imaging tests were performed. In 50 patients (80.6%), an ultrasound was performed and two patients had an additional MRI scan. No partial or full-thickness rotator cuff lesions were observed preoperatively. Data from the ITT analyses are presented since no significant differences were apparent between the ITT analysis and the PP analyses.

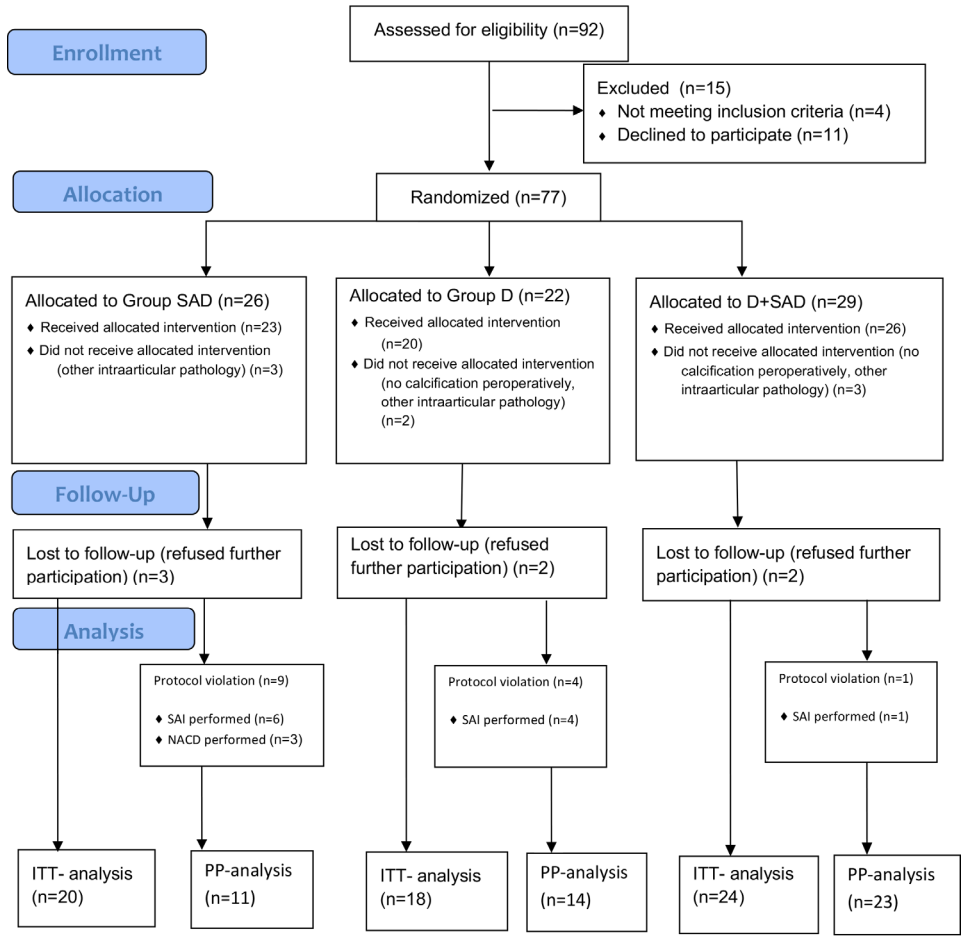

Figure 4. CONSORT Flowchart. Group SAD arthroscopic subacromial decompression, Group D arthroscopic debridement, Group D + SAD arthroscopic subacromial decompression and debridement. NACD needle aspiration of the calcific deposit, SAI subacromial injection, ITT analysis intention-to-treat analysis, PP analysis per-protocol analysis

Table 1. Baseline characteristics

	Complete study population (*n* = 62)	**Group SAD (*n* = 20)**	**Group D (*n* = 18)**	**Group D + SAD (*n* = 24)**	***p* value**
Age in years (SD)	53.5 (9.0)	52.7 (10.1)	54.9 (7.7)	53.2 (8.8)	0.82
Gender male (%)	21 (33.9)	7 (35.0)	3 (16.7)	11 (45.8)	0.13*
Affected side Right (%)	47 (75.8)	15 (75.0)	16 (88.9)	16 (66.7)	0.24*
Dominant side Right (%)	46 (74.2)	14 (70.0)	16 (88.9)	16 (66.7)	0.20*
Smoking status smoking (%)	18 (29.0)	6 (20.0)	3 (16.7)	9 (37.5)	0.48*

Table 1. Continued.

	Complete study population (*n* = 62)	**Group SAD (*n* = 20)**	**Group D (*n* = 18)**	**Group D + SAD (*n* = 24)**	***p* value**
ASA category					
1 (%)	26 (41.9)	8 (40.0)	8 (44.4)	10 (41.7)	0.99*
2 (%)	32 (51.6)	10 (50.0)	11 (61.1)	11 (45.8)	
3 (%)	4 (6.5)	1 (5.0)	1 (5.6)	2 (8.3)	
BMI Mean (SD)	26.7 (4.3)	26.4 (4.5)	26 (3.5)	27.3 (4.7)	0.78
Comorbidities					
Pulmonary (%)	12 (19.4)	4 (20.0)	1 (5.6)	7 (29.2)	0.21
Cardiovascular (e.g., HT, hyperlipidaemia)	9 (14.5)	2 (10.0)	3 (16.7)	4 (16.7)	0.91
Thyroid dysfunction	2 (3.2)	0	1 (5.6)	1 (4.2)	NA
Diabetes mellitus	1 (1.6)	0	0	1 (4.2)	NA
Duration of symptoms in months (range)	22.2 (6–120)	17.1 (6–120)	20.3 (6–120)	24.7 (6–120)	0.57+
Size of deposit in mm	23.0 (7.6)	23.4 (6.0)	24.7 (7.3)	21.3 (8.6)	0.34
Bosworth grade					
II, medium (%)	5 (8.1)	1 (5)	0	4 (16.7)	0.34
III, large (%)	57 (91.9)	19 (95)	18 (100.0)	20 (83.3)	
Gartner type					
Type I (%)	39 (62.9)	15 (75.0)	11 (61.1)	13 (54.2)	0.62*
Type II (%)	23 (37.1)	5 (25.0)	7 (38.9)	11 (45.8)	
Location of deposit					
SSP (%)	54 (87.1)	17 (85.0)	16 (88.9)	21 (87.5)	0.87*
ISP (%)	8 (12.9)	3 (15.0)	2 (11.1)	3 (12.5)	
SSC (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

SAD subacromial decompression, *D* debridement of calcifications, *D + SAD* debridement and subacromial decompression; *, x^2 test; +, Kruskal–Wallis test; *ASA* American Society of Anaesthesiologists Physical Status, *BMI* Body Mass Index, *HT* hypertension, *NA* not applicable, *SSP* supraspinatus, *ISP* infraspinatus, *SSC* subscapularis; (_), standard deviation

Primary outcome

Visual analog scale after 6 months

Patients in all groups showed a statistically significant improvement in pVAS 6 months after surgical intervention ($p < 0.001$), and it did not differ statistically significantly between groups (Table 2).

Secondary outcomes

Visual analog scale after 6 weeks

An improvement in pVAS was significantly more ($p = 0.03$) in Group D + SAD (33.1 mm; SD, 19.7 mm) compared to Group SAD (16.5 mm; SD, 19.3 mm) (Fig. 5). Six weeks and 6 months after treatment, no statistically significant differences between Group D and Group D + SAD were observed.

Table 2. Outcome score after surgery

	Group SAD	Group D	Group D+SAD	P value
VAS for pain				
Baseline	58.8 (15.3)	61.6 (16.3)	58.1 (13.7)	0.74
6 weeks	42.3 (17.0)	30.6 (16.8)	25.1 (19.0)	0.03*
6 months	17.0 (16.0)	12.2 (11.7)	11.4 (14.6)	0.57
CMS				
Baseline	43.0 (13.9)	45.1 (10.3)	51.0 (12.9)	0.10
6 weeks	66.3 (18.0)	72.1 (22.8)	79.3 (16.0)	0.77
6 months	84.8 (18.0)	89.7 (9.6)	91.8 (11.2)	0.84
DASH				
Baseline	49.2 (21.9)	45.0 (21.1)	45.2 (13.6)	0.80
6 weeks	37.6 (20.8)	24.9 (16.5)	14.7 (13.7)	0.02*
6 months	16.3 (14.1)	10.1 (11.5)	8.2 (14.4)	0.89
ASES				
Baseline	41.5 (18.0)	40.4 (12.9)	44.8 (12.5)	0.63
6 weeks	62.5 (21.2)	71.9 (16.2)	77.1 (18.7)	0.21
6 months	83.2 (15.0)	88.9 (10.7)	85.9 (19.3)	0.50
Size of calcification				
Baseline	23.4 (6.0)	24.7 (7.3)	21.3 (8.6)	0.34
6 weeks	14.2 (9.4)	10.3 (7.6)	8.1 (6.1)	0.02*
6 months	6.1 (8.9)	1.0 (3.0)	1.0 (2.7)	0.03*

SAD, subacromial decompression; D, debridement of calcifications; D+SAD, debridement and subacromial decompression; VAS, mean visual analog scale; CMS, mean Constant-Murley score; DASH, mean disability of arm, shoulder and hand score; ASES, mean American shoulder and elbow surgeons score;, statistically significant (e.g. p<0.05) between group D+SAD and SAD; (_), standard deviation*

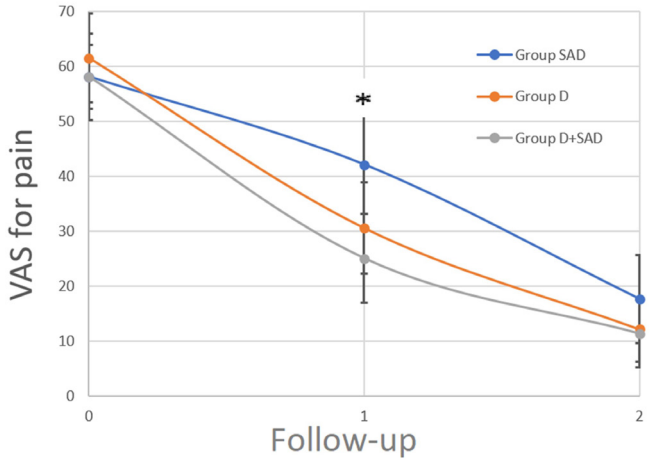

Figure 5. Estimates of pain scores (measured with pVAS) during the follow-up.
SAD subacromial decompression; *D* debridement of calcifications; *D + SAD* debridement and subacromial decompression; *VAS* mean visual analog scale; follow-up 1, 6 weeks; follow-up 2, 6 months; *, statistically significant differences (e.g., $p < 0.05$) between Group D + SAD and SAD

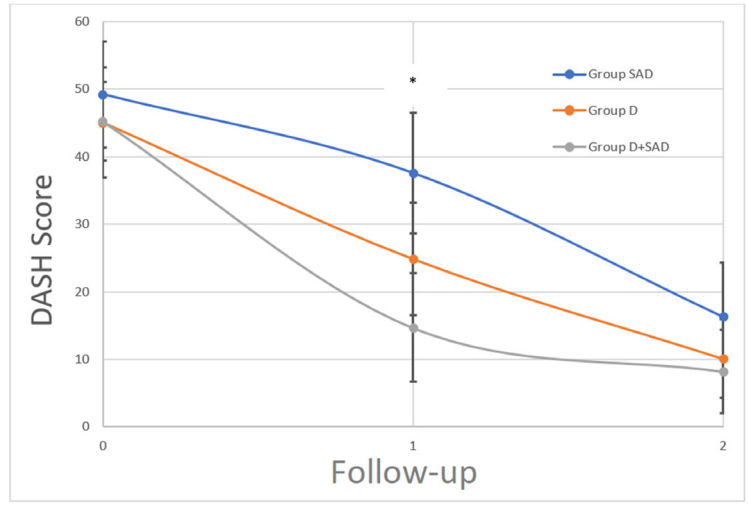

Figure 6. DASH score during follow-up.
SAD subacromial decompression; *D* debridement of calcifications; *D + SAD* debridement and subacromial decompression; *VAS* mean visual analog scale; follow-up 1, 6 weeks; follow-up 2, 6 months; *, statistically significant differences (e.g., $p < 0.05$) between Group D + SAD and SAD

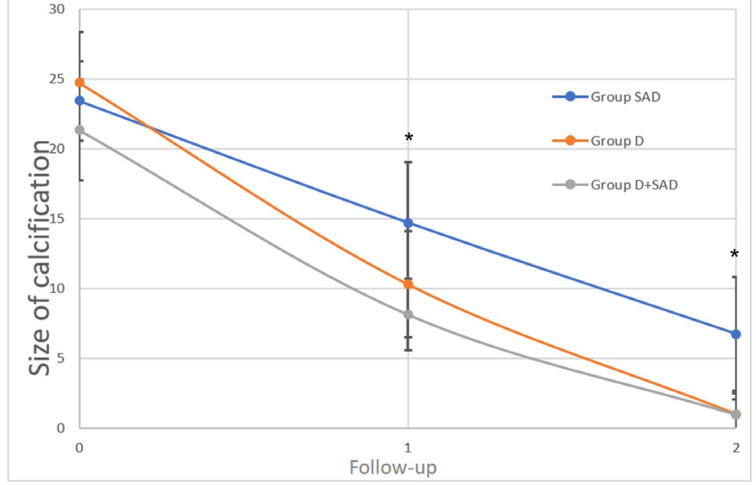

Figure 7. Size of calcification during follow-up.
SAD subacromial decompression; *D* debridement of calcifications; *D + SAD* debridement and subacromial decompression; follow-up 1, 6 weeks; follow-up 2, 6 month additional treatments and complications.

Functional outcome

In Table 2, the functional outcome scores are summarized. In all three groups, the CMS improved significantly ($p < 0.0001$). Six weeks and 6 months after treatment, no statistically significant differences between the groups were observed. The DASH score in all patient groups decreased statistically significantly during the study period ($p < 0.0001$). Six months after treatment, no statistically significant differences between the groups were observed (Fig. 6). At 6 weeks postoperatively, the improvement in DASH score was significantly higher ($p = 0.02$) in Group D + SAD (30.6; SD 17.8) compared to Group SAD (11.6; SD 24.3). Six weeks and 6 months after treatment, no statistically significant differences between Group D and Group D + SAD were observed. In all three groups, ASES improved significantly ($p < 0.0001$). Six weeks and 6 months after treatment, no statistically significant differences between the groups were observed.

Radiological outcome

All three groups showed a statistically significant ($p < 0.0001$) decrease in the size of the calcification from 23.1 mm (SD, 7.6 mm) to 2.3 mm (SD, 5.6 mm) at the 6 months of evaluation (Fig. 7). The decrease was statistically significant less ($p = 0.04$) in Group SAD compared to Group D after 6 weeks and 6 months. The difference in the decrease in the calcification between Group SAD and Group D + SAD was near significant ($p = 0.06$) after 6 months and significant after 6 weeks ($p = 0.04$). Six weeks and 6 months after treatment no statistically significant differences between Group D and Group D + SAD were observed. The clinical outcome did not differ significantly between patients with and without the presence of any residual subacromial calcifications (VAS for pain, $p = 0.96$; CMS, $p = 0.82$; DASH, $p = 0.64$; ASES, $p = 0.94$). In Table 3, the additional treatments and complications are summarized. No reoperations were performed, and no full-thickness rotator cuff lesions were documented during the follow-up. In Group SAD, 45.0% (n = 9) received additional treatments during follow-up: three patients received an additional NACD because of unchanged symptoms of pain and impaired shoulder function between four and 6 months after the initial treatment. Six patients received a subacromial injection with lidocaine and a corticosteroid (SAI). This was significantly more compared to Group D + SAD ($p = 0.003$). The complication rate in Group SAD was 10.0%. Two patients (10%) developed an adhesive capsulitis. This did not differ significantly between the three treatment groups ($p = 0.73$). Three patients (15.0%) showed pain relief less than 20 mm and were therefore classified as a failure to treatment. This did not differ significantly between the three treatment groups ($p = 0.54$). In Group D, 22.2% (n = 4) received additional treatments during follow-up: four patients received a SAI 4 to 6 months after surgery due to persisting pain. The com- plication rate in Group D was 5.5%. One patient developed an adhesive capsulitis two months after treatment, which was resolved at the final follow-up. In Group D + SAD, 4.2% (n = 1) received additional treatments during follow-up: one patient received a SAI 3 months after surgery. The complication rate in Group D + SAD was 4.2%. One patient developed an adhesive capsulitis 3 months after treatment, which was resolved at final follow-up.

Post hoc sample size calculation and power analysis

An interim analysis was performed after the recruitment came to a halt due to the COVID-19 pandemic. With the results of the interim analysis, actual standard deviations of the primary outcome (21.2 mm) were calculated. The post hoc sample size calculation showed that we would need to include 121 patients per group using an alpha of 0.05. This would provide a power of 80%. This was not deemed feasible, and after deliberation among the authors and the local ethical board the study was stopped before the required sample size was achieved at a number of 77 patients (67.5%).

DISCUSSION

This is the first multicenter randomized clinical trial that compares three surgical treatment procedures for therapy-resistant calcifying tendinitis of the shoulder. In this study, all patient groups showed significant pain relief and improvement in shoulder function 6 months after surgery. However, patients who had a SAD showed inferior improvement in pVAS and DASH score after 6 weeks. Furthermore, this group required more post- operative additional treatments. No significant differences were observed between patients in Group D and D + SAD. Therefore, an arthroscopic debridement with- out subacromial decompression seems to be advisable. Whether or not to debride the calcifications is still a matter of dispute. [12–14] The present study is the first to compare the short-term effectiveness of these procedures in a randomized clinical trial. Previous studies on this topic have a retrospective or a non-randomized design. [10] Hofstee et al [12] reported results of a pseudorandomized study. No differences in the functional out- come were observed between patients who had a SAD compared to patients who had a D + SAD after a mean follow-up of 36 months. Furthermore, Tillander et al [13] reported a cohort study in which patients were reviewed 24 months after SAD alone. The two groups in this study were patients with calcifying and non-calcifying tendinitis of the rotator cuff and no differences were apparent in the functional outcome. In both studies, complete disappearance or significant decrease in size of the calcifications was frequently observed. [12,13,25] Therefore, it can be hypothesized that the surgical procedure with the SAD serves as a stimulus for the tendon to return to the resorption phase. This resorption phase is known to cause symptoms of pain and impaired function. [26] Even a chemical subacromial bursitis can occur caused by erupting hydroxyapatite crystals. [27] In the present study, calcifications dis- appeared in almost half of the patients during the follow-up. This aforementioned resorption process might explain why significantly

more postoperative additional treatments were necessary for patients in Group SAD. Hence, these additional treatments (e.g., SAIs and NACDs) were performed between four to 6 months after the initial surgical treatment. One can hypothesize that the actual clinical outcomes are worse in patients who had a SAD as they were influenced by these additional treatments. Therefore, based on the finding that more additional treatments were necessary and worse pVAS and DASH scores when the calcifications were left untouched it seems that debridement of the calcifications is preferential. In the present study, a SAD did not seem to be beneficial in addition to debridement of the calcifications. After a mean follow-up of 6 months, the primary out- come and all secondary outcomes did not differ between patients in Group D compared to D + SAD. These findings are in line with the randomized controlled study of Clement et al. [11] They found that after a mean follow-up of 12 months pain relief and improvement in shoulder function were not influenced by the additional SAD. This is in contradiction with the study of Balke et al. [15] In this study, patients received an additional SAD if perioperative signs of subacromial impingement were observed. Patients who received an additional SAD showed superior scores on the 'pain' component of both the CMS and the ASES scores. [15] Though the difference was small, the clinical relevance can be questioned since it did not exceed the minimal clinical difference (MCID). Furthermore, in contrast to our study these patients were not randomized for an additional SAD and therefore selection bias could have occurred. In the present randomized clinical trial, no between-group differences were observed between patients in Group D and D + SAD. However, in Group D + SAD four patients failed to have satisfactory pain relief at the final follow-up compared to an only patient in Group D. It can be hypothesized that the recovery pat- tern is more prolonged by performing an additional sub- acromial decompression because it is a more extensive procedure. These findings are in line with the study of Cho et al. [28] Therefore, based on these short-term findings an additional subacromial decompression does not seem to be beneficial.

Limitations

Some limitations apply to the current study. Firstly, since the study was terminated prematurely it could be underpowered, which could lead to sampling bias and underestimation of the between-group differences. This should be considered when interpreting the results. Secondly, the lack of a control group in which a sham operation or no surgical treatment was performed. This was left out because of ethical considerations. The aim of this study was to compare the short-term effectiveness of three surgical treatment procedures and not to assess the efficacy of surgery. Several previous studies have been published that assure that a surgical treatment is a safe and effective treatment option with good short- and midterm radio- logical and clinical outcomes. [9,10,29,30] Thirdly, a follow-up of 6 months can be criticized for being too short since the recovery period after shoulder surgery can be prolonged. However, in the

study of Yoo et al. [31] 85.7% of the patients' maximal pain relief was achieved within 6 months after surgery. [31] It was assumed that if differences in the effectiveness between treatment groups would be present they most likely could be detected in the short term. Moreover, with this short-term follow-up the impact of the natural course of calcifying tendinitis of the shoulder on the outcome scores was reduced. Finally, the lack of control group in which complete debridement of the calcifications with additional rotator cuff repair was performed which is advocated by some authors. [31,32] However, an additional rotator cuff repair is also reported to be a negative prognostic factor and a frequently seen complication is adhesive capsulitis with reported incidences as high as 29%. [28,31] Postoperative immobilization after rotator cuff repair is a known risk factor for the development of adhesive capsulitis. [31] Therefore, the investigated surgical procedures were favoured by the authors. This made rehabilitation possible with the usage of a sling for a few days and immediate pain-based movements to decrease the likelihood of an adhesive capsulitis. This surgical technique is supported by other studies. [12,26,28,31]

CONCLUSIONS

All patient groups showed significant pain relief and an improvement in shoulder function 6 months after surgery. However, patients in Group SAD showed inferior pain relief and an improvement in DASH score after 6 weeks. Furthermore, this group required more postoperative additional treatments. No significant differences in clinical and radiological outcomes were observed between patients in Group D compared to Group D + SAD. Therefore, an arthroscopic debridement without subacromial decompression seems to be advisable for patients with therapy resistant calcifying tendinitis of the shoulder.

REFERENCES

1. Louwerens JKG, Sierevelt IN, van Hove RP, van den Bekerom MPJ, van Noort A (2015) Prevalence of calcific deposits within the rotator cuff tendons in adults with and without subacromial pain syndrome: clinical and radiologic analysis of 1219 patients. J Shoulder Elb Surg;24:1588–1593
2. Welfing J (1981) Die Entfacherung der sogenannten: Periarthritis der schulter. Orthopäde;10:187–190
3. Di Cesare A, Giombini A, Dragoni S, Agnello L, Ripani M, Saraceni VM, Maffulli N (2008) Calcific tendinopathy of the rotator cuff. Conservative management with 434 Mhz local microwave diathermy (hyperthermia): a case study. Disabil Rehabil;30(20–22):1578–1583
4. Gärtner J, Heyer A (1995) Calcific tendinitis of the shoulder. Orthopäde;24:284–302
5. Hurt G, Baker CL Jr (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am.;34:567–75
6. Speed CA, Hazleman BL (1999) Calcific tendinitis of the shoulder. N Engl J Med;340:1582–1584
7. Ogon P, Suedkamp NP, Jaeger M, Izadpanah K, Koestler W, Maier D (2009) Prognostic factors in nonoperative therapy for chronic symptomatic calcific tendinitis of the shoulder. Arthritis Rheum;60:2978–2984
8. Drummond M Jr, Ayinon C, Rodosky M, Vyas D, Lesniak B, Lin A (2021) Predictive factors for failure of conservative management in the treatment of calcific tendinitis of the shoulder. JSES Int;5:469–473
9. Frizziero A, Vittadini F, Barazzuol M, Gasparre G, Finotti P, Meneghini A, Maffulli N, Masiero S (2017) Extracorporeal shockwaves therapy versus hyaluronic acid injection for the treatment of painful non-calcific rotator cuff tendinopathies: preliminary results. J Sports Med Phys Fitness;57(9):1162–1168
10. Verstraelen FU, Fievez E, Janssen L, Morrenhof W (2017) Surgery for calcifying tendinitis of the shoulder: a systematic review. World J Orthop;8:424–430
11. Clement ND, Watts AC, Phillips C, McBirnie JM (2015) Short-Term outcome after arthroscopic bursectomy debridement of rotator cuff calcific tendinopathy with and without subacromial decompression: a prospective randomized controlled trial. Arthroscopy;31:1680–1687
12. Hofstee DJ, Gosens T, Bonnet M, De Waal MJ (2007) Calcifications in the cuff: take it or leave it? Br J Sports Med;41:832–835
13. Tillander BM, Norlin RO (1998) Change of calcifications after arthroscopic subacromial decompression. J Shoulder Elb Surg;7:213–217
14. Schiepers P, Pauwels P, Penders W, Brandelet B, Putz P (2000) The role of arthroscopy in subacromial pathology: retrospective study of a series of arthroscopic acromioplasties. Acta Orthop Belg;66:438–448
15. Balke M, Bielefeld R, Schmidt C, Dedy N, Liem D (2012) Calcifying Tendinitis of the shoulder midterm results after arthroscopic treatment. Am J Sports Med;40:657–661
16. Molé D, Kempf JF, Gleyze P, Rio B, Bonnomet F, Walch G (1993) Results of endoscopic treatment of non-broken tendinopathies of the rotator cuff. Rev Chir Orthop Reparatrice Appar Mot;79:532–541
17. Bosworth DM (1953) Diagnosis and treatment of lesions of the shoulder. R I Med J;36:512–515
18. Ellman H (1988) Shoulder arthroscopy: current indications and techniques. Orthopedics;11:45–51
19. Caspari RB, Thal R (1992) A technique for arthroscopic subacromial decompression. Arthroscopy;8:23–30
20. Van der Kloot WA, Vertommen H (1989) De MPQ-DLV: een standaard Neder- landstalige versie van de Mc Gill Pain Questionnaire: achtergronden en handleiding. Lisse: Swets & Zeitlinger; 57–73.
21. Constant CR, Murley AH (1987) A clinical method of functional assessment of the shoulder. Clin Orthop Relat Res;214:160–164
22. Hudak PL, Amadio PC, Bombardier C (1996) Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder, and hand). Am J Ind Med;29:602–608
23. Felsch QTM, Sievert P, Schotanus MGM, Jansen EJP (2019) The Dutch version of the American shoulder and elbow surgeons standardized shoulder assessment form is a reliable and valid questionnaire for shoulder problems. JSES Open Access;3:213–218
24. Kim DM, Kim TH, Kholinne E, Park JH, Shin MJ, Kim H, Park D, Jeon IH, Koh KH (2020) Minimal clinically important difference, substantial clinical benefit, and patient acceptable symptomatic state after arthroscopic rotator cuff repair. Am J Sports Med;48(11):2650–2659
25. Verstraelen FU, Glimmerveen NW, Janssen L, Morrenhof W (2015) Isolated acromioplasty for calcific tendinitis produces good results at 3-year follow-up: clinical outcome is not correlated to presence of residual calcifications. Curr Orthop Practice;26:363–366
26. Uhthoff HK, Loehr JW (1997) Calcific tendinopathy of the rotator cuff: pathogenesis, diagnosis, and management. J Am Acad Orthop Surg;5:183–191
27. Ark JW, Flock TJ, Flatow EL, Bigliani LU (1992) Arthroscopic treatment of calcific tendinitis of the shoulder. Arthroscopy;8:183–188
28. Cho CH, Bae KC, Kim BS, Kim HJ, Kim DH (2020) Recovery pattern after arthroscopic treatment for calcific tendinitis of the shoulder. Orthop Traumatol Surg Res;106:687–691
29. Seil R, Litzenburger H, Kohn D, Rupp S (2006) Arthroscopic treatment of chronically painful calcifying tendinitis of the supraspinatus tendon. Arthroscopy;22:521–527
30. Rochwerger A, Franceschi JP, Viton JM, Roux H, Mattei JP (1999) Surgical management of calcific tendinitis of the shoulder: an analysis of 26 cases. Clin Rheumatol;18(4):313–316
31. Yoo JC, Park WH, Koh KH, Kim SM (2010) Arthroscopic treatment of chronic calcific tendinitis with complete removal and rotator cuff tendon repair. Knee Surg Sports Traumatol Arthrosc;18:1694–1999
32. Lee TK, Shin SJ (2018) Functional recovery of the shoulder after arthroscopic treatment for chronic calcific tendinitis. Clin Shoulder Elb;21(2):75–81

PART II

Comparing surgical treatment to minimal invasive treatment

CHAPTER 5

Surgery versus minimal invasive treatment for therapy resistant calcifying tendinitis of the shoulder: a comparative cohort study

Verstraelen FU
Bemelmans Y
Lambers Heerspink FO
van der Steen MC
Jong B
Jansen EJP
Schotanus MGM

2023 J Orthop Sci; 18:S0949-2658

ABSTRACT

Purpose

Comparing the midterm clinical outcome of surgical treatment versus ultrasound guided needle aspiration of the calcific deposits (NACD) treatment for conservative therapy resistant calcifying tendinitis of the shoulder. The hypothesis is that both surgical treatment and NACD treatment led to a comparable good clinical outcome.

Methods

A comparative cohort study was performed (n=76). The allocation to surgical group (n=35) or NACD group (n=41) was the result of a shared decision-making strategy. Primary outcome was decrease in VAS for pain (pVAS). Secondary outcomes were EQ-5D index, DASH score, ASES, VAS for satisfaction, recommendation of treatment, adverse events, cross-over between groups, additional treatments, and symptomatology after care as usual.

Results

At midterm follow-up (5.5 years, SD 0.5 years) decrease in pVAS did not differ (p=0.20) between two groups (60.6mm, SD 23.3mm vs 53.4mm, SD 24.2mm). Secondary clinical outcomes were also comparable. In 68.3% surgical treatment was avoided. At final follow-up none of the outcome scores differed significantly between the crossed-over patients (n=13, 31.7%) and the initial surgical group.

Discussion

At midterm follow-up surgical and NACD treatment result in comparable clinical outcomes. In the majority surgical treatment can be avoided. Patients show similar good clinical outcome of surgical treatment after failed NACD treatment. Therefore, it seems that NACD is a valid treatment option for conservative therapy resistant calcifying tendinitis.

Key words

Calcific tendinitis; shoulder; NACD; barbotage; surgical treatment

INTRODUCTION

Calcifying tendinitis (CT) of the shoulder is a common cause for shoulder complaints. It is a condition in which calcium hydroxyapatite particles are deposited in one or more tendons of the rotator cuff. [1] CT mainly affects individuals between 30 and 60 years of age. The condition is more common in women. The supraspinatus tendon is the most involved tendon. [2,3] The initial treatment is with conservative measures with reported success rates of 73%. [4,5]

Historically, surgical treatment is seen as an option for conservative therapy resistant calcifying tendinitis of the shoulder. Surgical treatment shows good and predictable clinical results. The exact surgical procedure has been a matter of dispute, but available options such as debridement of the calcifications with or without an additional subacromial decompression show good functional outcome. [6] However, minimal invasive techniques, such as extracorporeal shockwave therapy (ESWT) or needle aspiration of the calcific deposit (NACD) have emerged and also show promising clinical results, especially on the short-term. [7,8] Some authors state that the results of these minimal invasive techniques might even be comparable to surgical treatment. [8,9] Nonetheless, available evidence on mid and long-term clinical results of these minimal invasive techniques is limited. [10] Furthermore, there are no studies comparing the midterm results of surgical treatment compared to NACD treatment. Therefore, the exact place of minimal invasive techniques in the treatment algorithm of therapy resistant calcifying tendinitis of the shoulder is not clear. [8,9,11,12]

The purpose of this study is to compare the midterm clinical outcome of surgical treatment versus NACD treatment in patients with conservative therapy resistant calcifying tendinitis. The hypothesis is that surgical treatment and NACD treatment led to a comparable clinical outcome. Secondly, it is hypothesized that more additional treatments after the NACD treatment are necessary. Thirdly, it is hypothesized that the clinical outcomes of patients who received surgical treatment after failed NACD treatment are inferior compared to patients who received immediate surgical treatment.

METHODS

This research has been approved by the IRB of the authors' affiliated institutions. The study population consisted of all patients who were treated at the orthopaedic outpatient department for therapy resistant calcifying tendinitis of the shoulder between January 2015 and January 2017. Inclusion criteria were non successful conservative therapy for at least six months, at least one calcification on conventional shoulder radiographs with

a minimal diameter of 10mm classified as type 1 or 2 according to the Gartner and Heyer classification. [13] Exclusion criteria were a frozen shoulder at the start of the treatment, history of surgery of the affected shoulder, rheumatoid arthritis, or fibromyalgia. Furthermore, if perioperative findings of other significant intraarticular pathology (e.g. biceps pathology, full-thickness rotator cuff lesions or acromioclavicular/ glenohumeral osteoarthritis) were encountered patient were excluded from further follow-up. Patients were divided into two groups: patients who only had a surgical treatment ('surgical group') and patients who had a NACD treatment ('NACD group') for the therapy resistant calcifying tendinitis of the shoulder. The decision for surgical or NACD treatment was the result of a shared decision-making strategy based on preference of the patient in collaboration with the orthopaedic surgeon.

Surgical technique and rehabilitation protocol

Three experienced shoulder surgeons performed all surgical procedures. After general anaesthesia and an interscalene nerve block, routine diagnostic glenohumeral arthroscopy was performed to assess possible intra-articular lesions. In case of severe glenohumeral osteoarthritis (e.g., Kellgren-Lawrence grade 3/4 chondropathy) or significant rotator cuff lesions (e.g., any full-thickness rotator cuff lesions) patients were excluded. Subsequently, a subacromial bursectomy was performed after which the calcification was located using a 20-gauge spinal needling technique described by Ellman. [14] A small incision on the bursal side of the tendon was made in line with the tendon fibres. Then, the calcific deposit was arthroscopically debrided by applying pressure using a curette and a shaver. The aim of the debridement was to substantially decrease the size of the calcification and not to fully eliminate the calcification. For the reason that in some patients this would necessitate creating a larger size cuff defect which requires rotator cuff repair. In the entire study population, no rotator cuff repair was performed. In patients with pre- or peroperative signs of subacromial impingement (such as fraying of the coracoacromial ligament or severe acromial spur) an additional arthroscopic subacromial decompression was performed as described by Caspari and Thal. [15] The rehabilitation protocol consisted of a sling for two to four days, immediate pain-based movements and NSAIDs combined with acetaminophen when necessary for two weeks. Six weeks after treatment clinical follow-up was performed at the outpatient department and radiographs were performed if necessary.

Needle aspiration procedure and rehabilitation protocol

Patients in the NACD group received a single session of an ultrasound guided needle aspiration of the calcific deposits by two experienced musculoskeletal radiologists. The aim of this procedure was to fragment and eradicate a substantial portion of the calcific deposit. Furthermore, it served as a stimulus for the tendon to return the resorption phase. After local anaesthesia, a double-needle eradication technique as described by

Sconfienza et al [12] was performed. Under ultrasound guidance the calcific deposit was punctured multiple times and lavage of the calcific deposit with a saline solution was performed. After the completion, in all patients, a mixture of 4mL lidocaine 0.5% and 1mL Depo-Medrol® 40 mg/mL (Pfizer Inc) was injected in the subacromial bursa under ultrasound guidance. The rehabilitation protocol consisted of pain-based movements and NSAIDs combined with acetaminophen when necessary for two weeks. Six weeks after treatment clinical follow-up was performed at the outpatient department and standardized radiographs were performed.

Measurements

Baseline characteristics were collected from the medical files; including age, affected side, dominant side, gender, preoperative duration of symptoms. Besides, several radiological measurements were performed (e.g., the size of calcification, location of calcification and the Gartner and Heyer classification [13] was recorded) . Additionally, the visual analog scale (VAS) for pain, EQ-5D-3L (after which the EQ-5Dindex was calculated) [16] and disability of arm, hand, and wrist (DASH) [17] score were collected at baseline. Patients were contacted through an invitation letter for a final follow-up after a minimal follow-up of three years and asked to complete several patient reported outcome measures (PROMs) including; VAS for pain, EQ-5D-3L (after which the EQ-5Dindex was calculated) [16], DASH, the American Shoulder and Elbow score (ASES) [18], VAS for satisfaction regarding the treatment and whether they would recommend their specific treatment to other patients. Furthermore, adverse events, cross-over between treatment groups and additional treatments were assessed. The decision to cross-over between groups was the result of a shared decision-making strategy, in which persisting symptoms had to be accompanied by an unsatisfactory decrease of the subacromial calcifications on the radiographs.

The short-term result of the treatment during follow-up in context of care as usual (with evaluation of the clinical outcome at the outpatient department at six weeks and six months postoperatively) was extracted from the electronical medical files. This result was categorized into three groups: symptom-free after treatment, unchanged symptoms, and a group in which the complaints improved but still had some residual symptoms. No patient reported outcomes were documented at these consultation moments. The primary outcome was the difference in improvement of VAS for pain between the two groups during follow-up. The VAS for pain was documented as a handwritten mark on a 100mm line that represents a continuum between "no pain" and "worst pain".

Statistical analyses

Statistical analysis was performed using SPSS (IBM Statistics, version 26.0, Armonk, New York). Primary and secondary outcomes were reported as mean with standard

deviation and median with range in case of non-parametric distribution. Categorical outcome variables (e.g., for example adverse events) were reported as frequency with percentage. Between group differences and differences between baseline and final follow-up were analysed for both the primary and secondary outcomes. Continuous outcome variables and their differences were analysed with independent t-tests, unless the data was non-parametrical, in which case Mann-Whitney tests were used. Categorical outcome variables were analysed with chi-square tests. A two-tailed p-value of <0.05 was considered significant.

Sample size calculation

The surgical treatment was set as the reference test, the NACD treatment was compared to this procedure in this non-inferiority study. The VAS for pain was used as our primary outcome. A difference of 15mm in improvement was defined as an important difference between the treatment groups. With an assumed standard deviation of 20mm 34 patients per group are necessary to achieve a power of 90%. The Type I error probability associated with this test of this null hypothesis is 0.05.

RESULTS

Between January 2015 and January 2017 a total 168 patients were treated for therapy resistant calcifying tendinitis at our orthopaedic outpatient department. 105 patients were considered eligible and were invited for final follow-up. The response rate was 72.4% (n=76) after a mean follow-up of 5.5 years (Fig 1). Thirty-five patients were allocated to the surgical group and forty-one patients were allocated to the NACD group. Baseline characteristics are shown in table 1. It shows that the baseline characteristics are comparable, with the exemption of the affected side [significantly more (p>0.001) left shoulders were affected in the surgical group] and gender [significantly less (p=0.005) females were included in the surgical group].

Primary outcome

The improvement during follow-up in VAS for pain did not differ significantly (p=0.20) between the groups; surgical group (60.6mm, SD 23.3mm) compared to NACD group (53.4mm, SD 24.2mm). The mean VAS for pain in the entire study population at final follow-up was significantly lower (p<0.01) than the mean VAS for pain at baseline: from 72.2mm (SD 12.5mm) to 15.5mm (SD 22.6mm) at baseline and at final follow-up, respectively (Fig. 2).

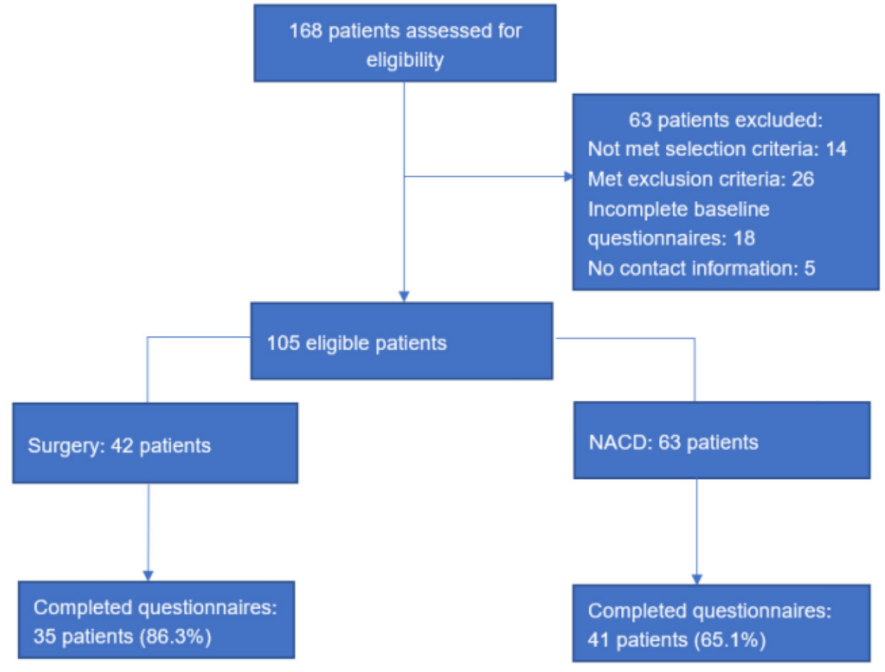

Figure 1. CONSORT Flow-chart of patients through the study

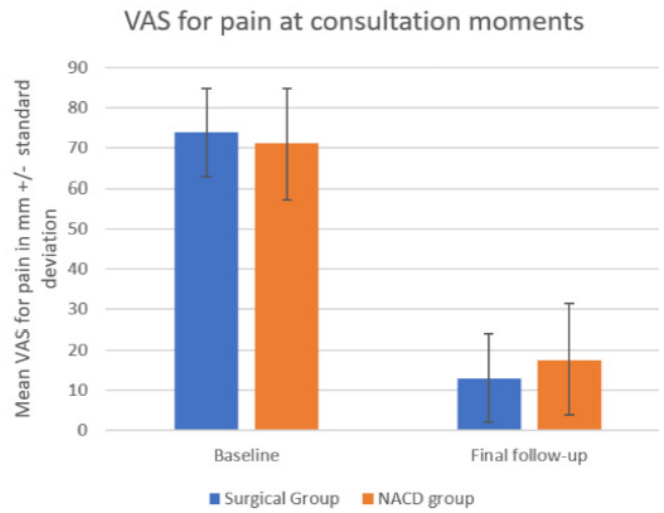

Figure 2. VAS for pain at consultation moments

Table 1. Baseline characteristics

	Complete study population (n=76)	Surgical group (n=35)	NACD group (n=41)	P value
Age in years at time of surgery mean (SD)	54.1 (8.7)	54.3 (9.3)	53.9 (8.3)	0.69
Affected side Right n(%)	41 (54.7)	10 (28.6)	31 (75.6)	**<0.001**+
Dominant side Right n(%)	61 (81.3)	31 (88.6)	31 (75.6)	0.16+
Gender female n(%)	44 (58.7)	14 (40.0)	30 (73.2)	**0.005**+
Duration of symptoms in months median (range)	22 (5-120)	24 (6-120)	18 (5-120)	0.31*
Size of deposit in mm (SD)	20.1 (6.7)	18.7 (8.0)	21.4 (5.2)	0.13
Location of deposit SSP n (%) ISP n (%) SSC n (%)	 64 (84.2) 12 (16.0) 0 (0.0)	 29 (82.9) 6 (17.6) 0 (0.0)	 35 (85.4) 6 (14.6) 0 (0.0)	 0.723+
Gartner and Heyer type: Type I n(%)	 49 (64.5)	 20 (57.1)	 29 (70.7)	 0.28+
VAS in mm (SD)	72.2 (12.5)	73.7 (10.6)	71.0 (13.9)	0.28
EQ-5Dindex (SD)	0.57 (0.29)	0.51 (0.30)	0.62 (0.26)	0.08
DASH (SD)	43.7 (16.2)	45.5 (17.1)	42.1 (15.4)	0.30

*+ = Chi square test, * = Mann-Whitney U test, NACD = Needle Aspiration of Calcific Deposit, SSP = Supraspinatus tendon, ISP = Infraspinatus tendon, SSC = Subscapularis tendon, VAS = Visual Analog Scale, DASH = Disability of Arm, Hand, and Shoulder score*

Secondary outcomes

Patient reported outcomes (PROMs)

Patient reported outcomes at final follow-up are summarized in table 2. The improvement in EQ-5Dindex was less (p=0.04) in the NACD group; surgical group (0.39, SD 0.30) compared to NACD group (0.24, SD 0.32). The improvement in the EQ-5Dindex was calculated by subtracting the EQ-5Dindex at the start of the study from the EQ-5Dindex at final follow-up.

At final follow-up, the reported DASH scores did not differ significantly (p=0.26) between the two groups, nor did the decrease between the two groups differ significantly (p=0.18). The ASES at final follow-up did not differ significantly between the two groups (p=0.17).

Adverse events, additional treatments and cross-over

The secondary and short-term outcomes administered within the context of care as usual which were extracted from the electronical medical files are summarized in table 3.

Table 2. Patient reported outcomes at final follow-up

	Complete study population (n=76)	Group Surgical treatment (n=35)	Group NACD (n=41)	P value
EQ5Dindex	0.86 (0.22)	0.87 (0.21)	0.85 (0.23)	0.73
DASH	11.1 (14.8)	9.1 (16.2)	12.9 (13.4)	0.26
ASES	86.0 (18.9)	89.3 (18.8)	83.2 (18.7)	0.17
VAS for satisfaction in mm	86.0 (16.0)	87.0 (15.0)	86.0 (17.0)	0.77
Recommend treatment Yes (%)	71 (93.4)	33 (94.3)	38 (92.7)	0.78+

+ = Chi square test, NACD = Needle Aspiration of Calcific Deposit, DASH = Disability of Arm, Hand, and Shoulder score, ASES = American Shoulder and Elbow Score, VAS = Visual Analog Scale.

Surgical group

In the surgical group three adverse events (8.6%) were registered. Two patients (5.7%) showed signs of an adhesive capsulitis which recovered, with additional pain treatment of an anaesthesiologist and adjustment of the rehabilitation protocol. Furthermore, one patient had persisting symptoms of pain based on large residual subacromial calcification and recovered after an additional NACD treatment four months after the initial treatment. Besides these three patients with adverse events another four patients received a subacromial cortisone injection to relieve symptoms of pain due to a subacromial bursitis. Cumulatively, in the surgical group 7 of the 35 patients (20%) received an additional treatment.

Table 3. Outcomes administered from electronical medical files

	Complete study population (n=76)	Surgical group (n=35)	NACD group (n=41)	P value
Adverse events Yes n (%)	21 (27.6)	3 (8.6)	18 (43.9)	0.001+
Additional treatments Yes n (%)	37 (48.7)	7 (20.0)	30 (73.2)	<0.001+
Cross-over n (%)	14 (18.4)	1 (2.9)	13 (31.7)	0.001+
Outcome after treatment within care as usual: symptom-free n (%) unchanged symptoms n (%) improved symptoms n (%)	 47 (56.6) 15 (19.7) 14 (18.4)	 26 (74.3) 1 (2.9) 8 (22.9)	 21 (51.2) 14 (34.1) 6 (14.6)	 <0.001+

+ = Chi square test, NACD = Needle Aspiration of Calcific Deposit.

NACD group

In the NACD group more (p=0.001) adverse events (n=18, 43.9%) were registered compared to the surgical group. Four patients (9.8%) showed signs of an adhesive capsulitis which recovered with additional pain treatment of an anaesthesiologist and adjustment of the rehabilitation protocol. Furthermore, fourteen (34.1%) patients had

unchanged symptoms of pain on the short term in combination with an unsatisfactory decrease of the subacromial calcifications on the radiographs. Thirteen patients (31.7%) patients decided to cross-over to the surgical treatment group. In this particular group, the mean residual size of the subacromial calcifications at time of the surgical treatment was 13mm (SD 5.9mm). The median time to cross-over was 0.5 years (range 0.2-2.1 years). The Gartner and Heyer type at the time of surgery was type 1 in five patients, type 2 in five patients and type 3 in three patients. At final follow-up none of the outcome scores differed significantly between these thirteen patients and the original surgical group (table 4).

Table 4. Comparison between surgical group and surgery after failed NACD group

	Surgical group (n=35)	Group surgery after failed NACD (n=13)	P value
VAS for pain in mm	13.1 (24.9)	19.6 (17.6)	0.40
EQ-5D index	0.87 (0.21)	0.85 (0.25)	0.71
DASH	9.1 (16.2)	14.9 (17.2)	0.28
ASES	89.3 (18.8)	80.9 (20.4)	0.18
VAS for satisfaction in mm	87.0 (15.0)	80.4 (26.7)	0.31

NACD = Needle Aspiration of Calcific Deposit, VAS = Visual Analog Scale, DASH = Disability of Arm, Hand, and Shoulder score, ASES = American Shoulder and Elbow Score, ( ) = standard deviation.

One patient (2.4%) opted for a second NACD treatment two months after the initial treatment after which the symptoms resolved (VAS 10.0mm, DASH 9.2, ASES 90.3 at final follow-up). On the other hand, at final follow-up none of the outcomes score differed significantly between patients who only had the NACD treatment (n=28, 68.3%) comparted to the original surgical group (table 5). Cumulatively, thirty patients (73.2%) in the NACD group required additional treatments. Besides the aforementioned additional treatments another twelve patients had a subacromial cortisone injection after a mean follow-up of 0.20 years (SD 0.13 years).

Table 5. Comparison between surgical group and only NACD group

	Surgical Group (n=35)	Group only NACD (n=28)	P value
VAS for pain in mm	13.1 (24.9)	16.6 (21.9)	0.75
EQ-5D index	0.87 (0.21)	0.85 (0.22)	0.80
DASH	9.1 (16.2)	12.0 (11.4)	0.70
ASES	89.3 (18.8)	84.4 (18.3)	0.18
VAS for satisfaction in mm	87.0 (15.0)	87.9 (11.3)	0.55

DISCUSSION

This is the first cohort study which compares the midterm clinical outcome of surgical treatment and NACD treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder. This study showed that both treatment options result in good clinical outcomes. Though, more additional treatments and a substantial number of cross-over (31.7%) were observed in patients who received the NACD treatment. However, at final follow-up patient who crossed over showed comparable good clinical outcomes. Therefore, it seems that NACD is a valid alternative treatment option. After a mean follow-up of 5.5 years both surgical and NACD treatment resulted in good clinical outcomes for patients with conservative therapy resistant calcifying tendinitis. Recently, the self-limiting character of calcifying tendinitis of the shoulder has been questioned. In a study of de Witte et al [19], a high degree of residual shoulder complaints was reported in patients who had conservative treatment for calcifying tendinitis of the shoulder after a mean follow-up of 14 years. The authors stated that a more aggressive treatment strategy can be beneficial. [19] The evidence reporting the mid and long-term results of surgical treatment of calcifying tendinitis is limited. Balke et al [20] reported acceptable clinical outcome after a mean follow-up of six years with a CMS of 76.2 and an ASES of 81.5. Though, these clinical outcome scores were significantly less compared to the patients' non-affected contralateral shoulder. Lorbach et al [21] reported good to excellent clinical outcome 58.4 months after debridement of the calcifications without and with rotator cuff repair with a CMS of 86.2 vs 80.6, respectively and the ASES score of 98.3 vs 88.9. These clinical outcomes are in line with the current (ASES of 89.3). To our knowledge, only two studies report mid/long-term results of NACD treatment. In the study of Serafini et al [22] results are reported five and ten years after NACD treatment. The authors show good outcomes scores with a VAS for pain of 26.0mm and 25.0mm and a CMS of 90.9 and 91.8 after five and ten years, respectively. Furthermore, de Witte et al [10] also report good results five years after treatment with a CMS of 89.5 and a DASH score 12.7. However, it should be noted that both studies also included patients with Gartner and Heyer type 3 calcifications. This is in contrast with the current study in which only patients with Gartner and Heyer type 1 and 2 calcifications were included. Gartner and Heyer type 3 calcifications have high potency of spontaneous resolution. [13] Therefore, the good clinical outcome in the aforementioned studies may be influenced by this high potency for spontaneous resolution of the calcifications. Still, the previous reported good clinical outcomes are in line with the present study. Cross-over to surgical treatment has not been systematically reported in previous studies investigating results of NACD. In our study 31.7% cross-over to the surgical treatment group because of persisting symptoms of pain after NACD. The median interval between the NACD treatment and the surgical treatment was 0.5 years (range 0.2-2.1 years). Although the subacromial calcifications were reduced in size from 21.4mm to 13.0mm

at time of cross-over to surgical treatment. It is known that larger size calcifications (>10mm) are more likely to continue to cause symptoms and are more prone to fail with conservative measures. [5] Furthermore, Oudelaar et al [23] demonstrated that Gartner and Heyer type 1 calcifications are more likely to fail to a single session of NACD. In the present study, 61.5% of the patient who crossed over to the surgical treatment had a Gartner and Heyer type 1 calcification. This highlights the need for further investigation on the relationship between morphology of the calcification and optimal treatment to improve outcome. Nonetheless, the clinical outcome at final follow-up of the patients who had a surgical treatment after a failed NACD treatment were comparable to the initial surgical treatment group. Nevertheless, the VAS for satisfaction was high in the current study. In addition to cross-over between groups, significantly more additional treatments were necessary in the NACD group which may be caused by a subacromial bursitis. Previous studies report that erupting calcific particles in the subacromial bursa can cause a chemical bursitis. [24,25] It can be hypothesized that these additional treatments (e.g., mainly cortisone injections) were needed to alleviate symptoms caused by the resorption phase of these calcific particles which was initiated by the NACD treatment. Once this resorption phase is completed the tendon will return to normal tendinous tissue and the patients will remain free of symptoms. [1]

This study has some limitations. Firstly, patients were allocated to either surgical or NACD treatment after a shared decision-making strategy and therefore selection bias could be introduced. This could have created an imbalance between the two groups and maybe the cause of more males within the surgical treatment group. However, the baseline PROMs and radiological measurements were all comparable between the two groups. Besides, this study population accurately reflects the patients presented at the outpatient department and therefore represent the actual case mix of patients with therapy resistant calcifying tendinitis of the shoulder. Secondly, a limitation could be that the current study only focuses on PROMs and clinical outcomes. Although these measures indicate treatment results as experienced by the patient, they might be subjected to floor and ceiling effects and socially desirable answering. Ideally, a more objective measurement, for example activity monitor tracking or comparison to the contralateral healthy shoulder, is used to detect differences within and between the treatment groups. Thirdly, some specific patient factors were not collected in the study such as their smoking status or comorbidities. Recent studies have shown that these patient factors can be a negative prognostic factor. [23,26] Therefore, confounding of these patient factors cannot be ruled out.

CONCLUSIONS

After a mean follow-up of 5.5 years both surgical and NACD treatment result good clinical outcomes for patients with conservative therapy resistant calcifying tendinitis of the shoulder. A substantial number of patients cross-over to a surgical treatment after NACD treatment. However, in the majority a surgical treatment can be avoided. Besides, patients who had surgical treatment after failed NACD treatment show similar good outcome. Therefore, it seems that NACD is a valid treatment option, although more research in a randomized fashion is needed.

REFERENCES

1. Uhthoff HK, Loehr JW (1997) Calcific Tendinopathy of the Rotator Cuff: Pathogenesis, Diagnosis, and Management. J Am Acad Orthop Surg;5:183-191
2. Louwerens JKG, Sierevelt IN, van Hove RP, van den Bekerom MPJ, van Noort A (2015) Prevalence of calcific deposits within the rotator cuff tendons in adults with and without subacromial pain syndrome: clinical and radiologic analysis of 1219 patients. J Shoulder Elbow Surg;24:1588-1593
3. Diehl P, Gerdesmeyer L, Gollwitzer H, Sauer W, Tischer T (2011) Calcific tendinitis of the shoulder. Orthopäde;40:733-746
4. Ogon P, Suedkamp NP, Jaeger M, Izadpanah K, Koestler W, Maier D. Prognostic factors in nonoperative therapy for chronic symptomatic calcific tendinitis of the shoulder. Arthritis Rheum 2009;60:2978-2984.
5. Drummond Jr M, Ayinon C, Rodosky M, Vyas D, Lesniak B, Lin A (2021) Predictive factors for failure of conservative management in the treatment of calcific tendinitis of the shoulder. JSES Int;5:469-473
6. Verstraelen FU, Fievez E, Janssen L, Morrenhof W (2017) Surgery for calcifying tendinitis of the shoulder: A systematic review. World J Orthop;8:424-430
7. Bazzocchi A, Pelotti P, Serraino S, Battaglia M, Bettelli G, Fusaro I, Guglielmi G, Rotini R, Albisinni U (2016) Ultrasound imaging-guided percutaneous treatment of rotator cuff calcific tendinitis: success in short-term outcome. Br J Radiol;89: 20150407
8. Gatt DL, Charalambous CP (2014) Ultrasound-guided barbotage for calcific tendonitis of the shoulder: a systematic review including 908 patients. Arthroscopy;30:1166-1172
9. Del Castillo-González F, Ramos-Álvarez JJ, Rodríguez-Fabián G, González-Pérez J, Calderón-Montero J (2014) Treatment of the calcific tendinopathy of the rotator cuff by ultrasound-guided percutaneous needle lavage. Two years prospective study. Muscles Ligaments Tendons J;4: 220–225
10. Witte, de PB, Kolk A, Overes F, Nelissen RGHH, Reijnierse M (2017) Rotator Cuff Calcific Tendinitis: Ultrasound-Guided Needling and Lavage Versus Subacromial Corticosteroids: Five-Year Outcomes of a Randomized Controlled Trial. Am J Sports Med;45:3305-3314
11. Verstraelen FU, In den Kleef NJHM, Jansen L, Morrenhof JW (2014) High-energy versus low-energy extracorporeal shock wave therapy for calcifying tendinitis of the shoulder: which is superior? A meta-analysis. Clin Orthop Relat Res;472:2816-2825
12. Sconfienza LM 1, Viganò S, Martini C, Aliprandi A, Randelli P, Serafini G, Sardanelli F (2013) Double-needle ultrasound-guided percutaneous treatment of rotator cuff calcific tendinitis: tips & tricks. Skeletal Radiol;42:19-24
13. Gärtner J, Heyer A (1995) Calcific tendinitis of the shoulder. Orthopäde;24:284-302
14. Ellman H (1988) Shoulder arthroscopy: current indications and techniques. Orthopedics;11(1):45-51
15. Caspari RB, Thal R (1992) A technique for arthroscopic subacromial decompression. Arthroscopy;8:23-30
16. Van der Kloot WA, Vertommen H (1989) De MPQ-DLV: een standaard Nederlandstalige versie van de Mc Gill Pain Questionnaire: achtergronden en handleiding. Lisse: Swets & Zeitlinger:57-73
17. Hudak PL, Amadio PC, Bombardier C (1996) Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder, and hand) Am J Ind Med;29:602-608
18. Felsch QTM, Sievert P, Schotanus MGM, Jansen EJP (2019) The Dutch version of the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form is a reliable and valid questionnaire for shoulder problems. JSES Open Access;3:213-218
19. Witte, de PB, van Adrichem RA, Selten JW, Nagels J, Reijnierse M, Nelissen RG (2016) Radiological and clinical predictors of long-term outcome in rotator cuff calcific tendinitis. Eur Radiol;26:3401-3411
20. Balke M, Bielefeld R, Schmidt C, Dedy N, Liem D (2012) Calcifying tendinitis of the shoulder: midterm results after arthroscopic treatment. Am J Sports Med;40:657-661
21. Lorbach, O, Haupert A, Berger C, Brockmeyer M (2021) Clinical and Structural Results of Rotator Cuff Repair Compared With Rotator Cuff Debridement in Arthroscopic Treatment of Calcifying Tendinitis of the Shoulder. Am J Sports Med;49:3196-3201
22. Serafini G, Sconfienza LM, Lacelli F, Silvestri E, Aliprandi A, Sardanelli F (2009) Rotator cuff calcific tendonitis: short-term and 10-year outcomes after two-needle us-guided percutaneous treatment--nonrandomized controlled trial. Radiology;252:157-164
23. Oudelaar BW, Ooms EM, Huis In 't Veld R, Schepers-Bok R, Vochteloo AJ (2015) Smoking and morphology of calcific deposits affect the outcome of needle aspiration of calcific deposits (NACD) for calcific tendinitis of the rotator cuff. Eur J Radiol;84:2255-2260
24. Ark JW, Flock TJ, Flatow EL, Bigliani LU (1992) Arthroscopic treatment of calcific tendinitis of the shoulder. Arthroscopy;8:183-188
25. Oudelaar BW, Van Liebergen MR, Van Arkel ERA (2021) A woman with acute-onset shoulder pain. Ned Tijdschr Geneesk;165:D6056
26. Azevedo S, Sousa-Neves J, Leite Silva J, Ramos Rodrigues J, Santos Faria D, Alcino S, Peixoto D, Tavares-Costa J, Afonso C, Teixeira F (2020) Shoulder pain: are there predictive factors of response to treatment and of ultrasound findings? Acta Reumatol Port;45:39-45

PART III

Optimizing minimal invasive treatment

CHAPTER 6

High-energy versus low-energy extracorporeal shock wave therapy for calcifying tendinitis of the shoulder: Which is Superior? A Meta-analysis

Verstraelen FU
In den Kleef NJHM
Jansen L
Morrenhof W

2014 Clin Orthop Relat Res;472(9):2816-25

ABSTRACT

Background
There are several treatment options for calcifying tendinitis of the shoulder. The next step treatment after conservative treatment fails is still a matter of dispute. Extracorporeal shock wave therapy (ESWT) has been shown to be a good alternative to surgery, but the best treatment intensity remains unknown. High-energy ESWT is much more painful, more expensive, and usually is done in an inpatient setting, whereas low-energy ESWT can be performed in an outpatient setting by a physical therapist.

Questions/purposes
A systematic review and meta-ana- lysis of randomized trials was performed to answer two clear research questions: (1) Is there a greater increase in the Constant-Murley score in patients treated with high- energy ESWT compared with those treated with low-energy ESWT by 3 months and by 6 months? (2) Is there a greater chance of complete resorption of the calcifications in patients treated with high-energy ESWT compared with those treated with low-energy ESWT by 3 months and by 6 months?

Methods
Five relevant electronic online databases, Medline (through PubMed), EMBASE (through OVID), Cinahl (through EBSCO), Web of Science, and the Cochrane Central Register of Controlled Trials, were systematically searched. We also crosschecked the reference lists of articles and reviews for possible relevant studies. Eligible for inclusion were all randomized controlled trials (RCTs) that compared high-energy ESWT (>0.28 mJ/mm2) with low-energy ESWT (<0.08 mJ/ mm2). One author examined titles and abstracts of each identified study to assess study eligibility. Two reviewers independently extracted data and assessed the risk of bias and study quality. The primary outcome measure, the Constant-Murley score, was assessed by comparing mean functional outcome scores between the groups. Secondary outcomes were assessed using odds ratios when appropriate data were pooled. Based on this process, five RCTs (359 participants) were included.

Results
All five RCTs showed greater improvement in functional outcome (Constant-Murley score) in patients treated with high-energy ESWT compared with patients treated with low-energy ESWT at 3 and 6 months. The 3-month mean difference was 9.88 (95% CI, 9.04–10.72, p <0.001; 6-month data could not be pooled). Furthermore, high-energy ESWT more often resulted in complete resorption of the deposits at 3 months. The corresponding odds ratio was 3.40 (95% CI, 1.35–8.58) and p = 0.009 (6-month data could not be pooled).

Conclusion
When shock wave therapy is chosen, high- energy shock wave therapy is more likely to result in improved Constant-Murley score and resorption of the deposits compared with low-energy therapy.

INTRODUCTION

Calcifying tendinitis of the shoulder is a common disease of the rotator cuff muscles that results in pain and decreased ROM. The disease mainly affects individuals between 30 and 50 years old, and males and females are equally affected. The calcific material consists of a collection of calcium hydroxyapatite in crystalline or amorphous form. [5,8,14] Approximately 80% the calcium deposits are located in the tendon of the supraspinatus, 15% are in the infraspinatus, and approximately 5% are in the subscapularis tendon. In the supraspinatus tendon, the most affected location is 1.5 to 2.0 cm away from its insertion at the greater tuberosity. [5,8,11,23] The aetiology of the calcium deposits in the rotator cuff is disputed. [9, 20, 23] It has been suggested that it is related to decreased local oxygen tension or hypoxia. [5,8] The calcifications can be subdivided using the classification of Gärtner and Heyer. [8] Their classification is used to describe the radiologic aspect of the calcifications. It subdivides the calcifications into three groups: type I, clearly circumscribed and dense; type II, clearly circumscribed, translucent, cloudy, or dense; and type III, cloudy and translucent. The disease is at first treated nonoperatively, including use of anti-inflammatory drugs, ice therapy, physiotherapy, corticosteroid injections, and/or needling. However, when this fails, extracorporeal shock wave therapy (ESWT) can be a good and less-invasive treatment option before surgery. [10,12] The exact mechanisms of action of the ESWT are largely unknown; Loew et al. [17] postulated that the shock waves lead to a three-way mechanism of action: (1) mechanical effect resulting in deposit fragmentation; (2) molecular effect resulting in deposit phagocytosis; and (3) analgesic effect resulting in denervation of pain receptors. Shock wave therapy can be divided into three categories based on its energy levels: low-energy (< 0.08 mJ/mm2), middle-energy (0.08–0.28 mJ/mm2), and high-energy (> 0.28 mJ/mm2). [1,15,20] High-energy ESWT can induce fragmentation and destruction of solid bodies. For example, high-energy ESWT has a physical effect on kidney stones, gallstones, and bony tissue, causing physical and histologic changes. By contrast it is believed that the therapeutic effect of low-energy ESWT is based on neurophysiologic mechanisms. [18,22] Moreover, different devices are needed to apply different energy intensities. Devices that can generate high-energy ESWT are more expensive than the devices needed for low-energy ESWT. High-energy ESWT is more painful than low-energy and more often requires (intravenous) analgesia. This is why it often is done in an inpatient setting. Low-energy ESWT, on the contrary, usually is performed in an outpatient setting by a physical therapist. [1,9] However, regarding the functional and radiologic outcomes, the optimal therapeutic intensity has to be set and a dose-response relation has to be found. [18] We therefore performed a meta-analysis of randomized trials comparing high- with low-energy ESWT for calcifying tendinitis of the shoulder. We specifically sought to determine (1) if there a greater increase in Constant-Murley score in patients treated with high-energy ESWT compared with those treated with low-energy ESWT in the short term (3 months) and at midterm (6 months), and (2) if there is a greater chance of complete resorption of the calcifications in patients treated with high-energy ESWT compared with those treated with low-energy ESWT in the short term (3 months) and at midterm (6 months)?

MATERIALS AND METHODS

Search Strategy

This review was performed and reported following the principles of the QUORUM statement. [7,19]

We systematically searched five relevant electronic online databases: Medline (through PubMed), EMBASE (through OVID), Cinahl (through EBSCO), Web of Science, and the Cochrane Central Register of Controlled Trials. In addition, the reference lists of articles and reviews were crosschecked for possible relevant studies. The search was set up using the PICO (patient [or disease], intervention [a drug or test], comparison [another drug, placebo or test], and outcome) format, and various medical terms were used for the search (Table 1). Eligible for inclusion were all randomized controlled trials (RCTs) that compared high-energy ESWT (> 0.28 mJ/mm2) with low-energy ESWT (< 0.08 mJ/mm2). This literature search identified 194 potentially relevant studies; 108 studies were excluded after screening the titles and another 73 studies were excluded after reading the abstracts. Reasons for exclusion were that the studies were not RCTs or not concerning the shoulder. After reading the full-text articles, another eight studies were excluded, mainly because the comparison between the groups was not of our interest. The remaining five studies were eligible and are included in this systematic review. For the meta-analysis, the data of three studies was used. The results of the functional and radiologic outcomes after 3 months was pooled (Fig. 1).

Data Management

The data were independently extracted by two of the authors (FUV, NidK) and crosschecked for accuracy. The authors were blinded to the authors of the included articles, their institutions, and the journals in which they were published. Data from each study were extracted in a standardized way using an extraction form specifically designed for this study. Extracted data included inclusion and exclusion criteria, inclusion period, the individual study groups, methods of randomization, blinding, type and brand of shock wave generator, intensities and frequencies of the shocks waves, primary and secondary outcome measurements, statistics used, baseline characteristics, and results (Appendix 1. Supplemental material is available with the online version of CORR).

Discrepancies between the authors were resolved by scrutinizing the original article until a consensus was reached. Authors of the articles of the included studies were contacted for missing information.

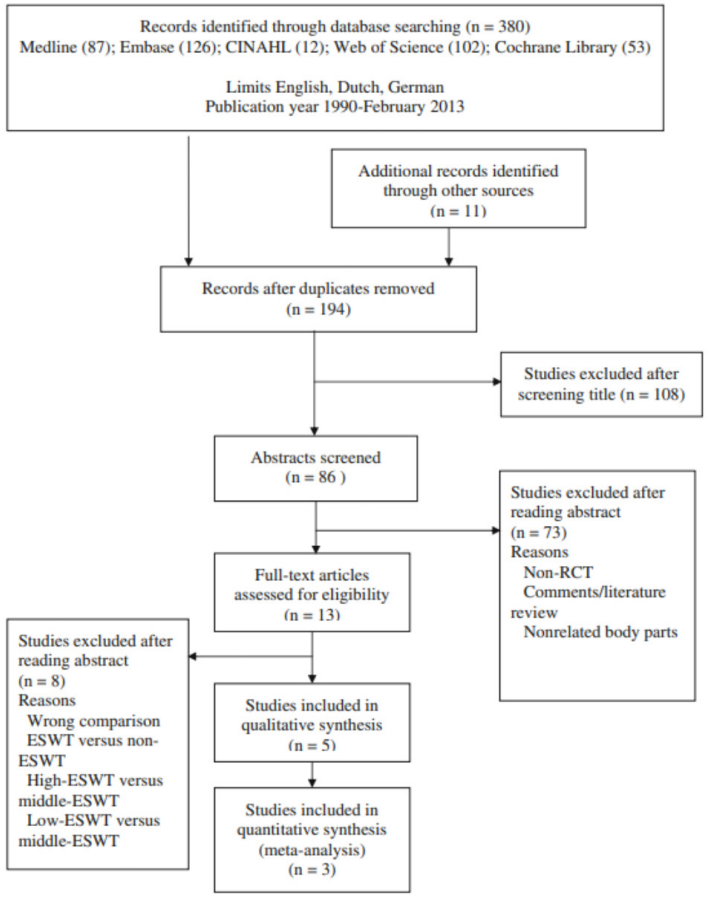

Figure 1. The flowcharat shows the results of the systematic search, including the number of articles identified and excluded at each juncture.

Study Quality

The risk of bias and quality of the individual articles were independently assessed by two of the authors (FUV, NidK) using the criteria of Furlan et al. [7] (Tables 2 and 3). Disagreements were resolved by consensus; a third author (JWM) was consulted if necessary. Three of the five studies qualified as high-quality RCTs. The high-quality studies were those of Albert et al. [1], Gerdesmeyer et al. [9], and Pleiner et al. [21] The low-quality studies were those of Loew et al. [17] and Rompe et al. [22]

Table 1. Search strategy

Population	Patients with radiographically confirmed symptomatic tendinitis calcarea of the shoulder (search terms: shoulder joint, rotator cuff, shoulder, supraspinatus, infraspinatus, subscapular or teres, impingement syndrome, tendinopathy, tendinopathy, tendonitis or tendinitis, tendinosis, calcinosis, calcifying, calcification, calcified, calcific, calcarea)
Intervention	High-energy extracorporeal shock wave therapy (search terms: shock wave, ESWT, ESWL, radiofrequency, HESWT, high- energy, high-intensity, high, high EFD, shock waved therapy, extra corporeal shock wave therapy, radiation nonionizing)
Comparison	Low-energy extracorporeal shock wave therapy (search terms: shock wave, ESWT, ESWL, radiofrequency, LESWT, low- energy, low-intensity, low, low EFD, shock waved therapy, extra corporeal shock wave therapy, radiation nonionizing)
Outcome	Functional outcome and radiologic outcome
Limits	Language: English, German, Dutch Publication years: 1990-February 2013 Study population: humans

ESWT = extracorporeal shock wave therapy; ESWL – extracorporeal shock wave lithotripsy; HESWT = high-energy shock wave therapy; EFD = energy flux density; LESWT = low-energy shock wave therapy.

Characteristics of Included Studies

The total study population from five RCTs of low versus high-energy ESWT consisted of 359 participants (Table 4). All patients were treated with conservative measures for at least 4 months before considering ESWT. No local anaesthetics or corticosteroids were used with the ESWT. The patients were followed up for a minimum of 3 months and a maximum of 12 months. The primary functional outcome measure in all studies was the Constant-Murley score. The Constant-Murley score is used to assess function of the shoulder. [4] This score combines physical tests with subjective evaluations by the patients, for which 35 and 65 points respectively, can be assigned; resulting in a score between 0 (worst) and 100 (most favourable). [2-4] The secondary outcome measures reported in the five studies were more diverse, including the VAS for pain, radiologic outcome, complication rate, and other therapies used. Radiologic resorption of the calcium deposits was subdivided by four studies [1,17,21,22] into complete disappearance, partial disappearance, and no change in the calcific deposits. Gerdesmeyer et al. [9] described the change in calcification in actual mm^2 decrease, thus we did not include this article in the quantitative analysis.

Table 2. Methodologic quality* scores of the included studies (continued)

12 quality criteria of Furlan et al. (2008).								
Reference	**Adequate randomization?**	**Allocation concealment?**	**Blinding patients?**	**Blinding caregiver?**	**Blinding outcome assessors?**	**Incomplete outcome data addressed? dropouts**	**Incomplete outcome data? ITT-analysis?**	**No selective outcome reporting?**
Gerdesmeyer et al. (2003)	+	+	+	-	+	+	-	+
Alberts et al. (2007)	+	+	+	?	?	+	+	+
Pleiner et al. (2004)	?	?	+	-	+	+	-	+
Rompe et al. (1998)	?	?	?	?	?	+	-	+
Loew et al. (1999)	+	?	?	?	?	+	-	+

+,Yes =1 point; -,No=0 points; ?,unclear/unsure=0 points
High-Quality = >50%, Low-Quality = <50%

Table 3. Methodologic quality* scores of the included studies (continued)

12 quality criteria of Furlan et al. (2008).								
Reference	**Similarity baseline characteristics?**	**Co-interventions avoided or similar?**	**Compliance acceptable in all groups?**	**Timing of the outcome assessments similar?**	**Score Maximum**	**Score Study**	**Percentage**
Gerdesmeyer et al. (2003)	?	+	+	+	12	9	75%
Alberts et al. (2007)	+	+	+	-	12	9	75%
Pleiner et al. (2004)	+	+	+	+	12	8	67%
Rompe et al. (1998)	+	+	+	+	12	6	50%
Loew et al. (1999)	?	?	+	+	12	4	33%

Heterogeneity

The extracted data for the increase in the Constant-Murley score after 3 months showed moderate heterogeneity. [7] A random effects model was used to pool the data for the functional outcome after 3 months. The data for the increase in the Constant-Murley score after 6 months could not be pooled because the extracted data were incomplete and owing to the diversity in the timing of the final outcome moment (range, 24-30 weeks), therefore it is presented narratively.

The chance of complete resorption after 3 months showed no heterogeneity and therefore could be pooled using a fixed effect model. The data for the chance of complete resorption after 6 months could not be pooled because the extracted data were incomplete. With only three studies selected for the meta-analysis, we could not perform a meaningful funnel plot analysis to assess for publication bias.

Statistical Analysis

The Cochrane Collaboration's Review Manager (RevMan, http://tech.cochrane.org.mu.idm.oclc.org/revman) was used to pool the data. [11] Mean difference and 95% CIs were calculated to pool the functional outcome.

For the chance of complete resorption, the pooled odds ratio with 95% CI was calculated. For the data that could not be pooled because of heterogeneity and incomplete data in the articles, the results are narratively reported.

RESULTS

Constant-Murley Scores in Patients Treated With High- and Low-energy ESWT

Constant-Murley scores at 3 months improved to a greater degree in patients treated with high-energy ESWT than in patients treated with low-energy ESWT (Fig. 2). Pooled analysis [1,9,17] of the 216 patients showed that patients in the high-energy group improved by a mean of 25.82 points (SD, 10.26 points), compared with 15.94 points (SD, 6.59 points) in the low-energy group (Fig. 3). The mean difference was 9.88 (25.82 versus 15.94, 95% CI, 9.04-10.72; $p < 0.001$). The difference in increase in Constant-Murley scores between high-energy and low-energy ESWT ranged from 16 points [1] to 33 points [17] (Table 5).

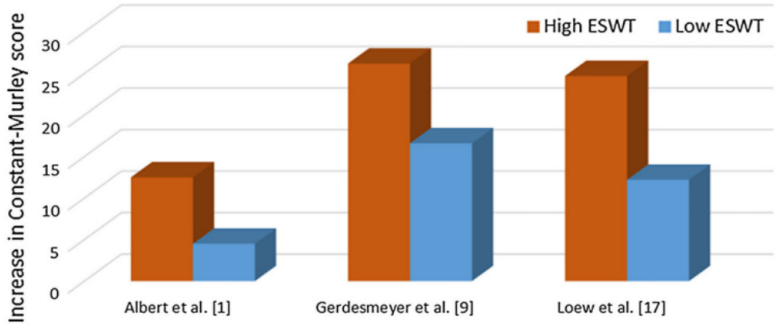

Figure 2. This graph shows the data with the greater increase in Constant-Murley score after 3 months for patients treated with high-energy ESWT compared with those treated with low-energy ESWT.

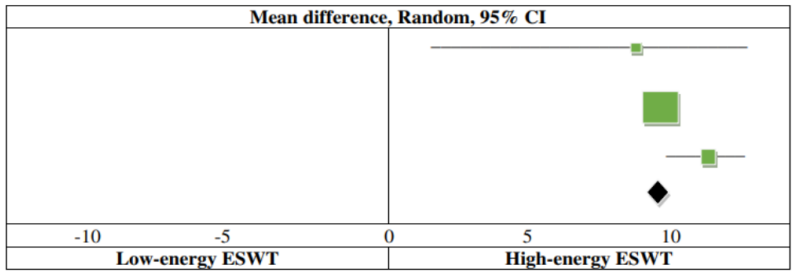

Figure 3. The pooled results of the Constant-Murley scores after 3 months are shown.

For functional outcome after 6 months, three of the five included studies reported results similar to those after 3 months; all individual studies concluded that high-energy showed a greater increase in the functional outcome measured by the Constant-Murley score after 6 months (Fig. 4). This difference in Constant-Murley scores between high-energy and low-energy ESWT ranged from 15 points [22] to 71 points [21] (Table 4). However, these data could not be pooled because the extracted data were incomplete and owing to diversity in the timing of the final outcome moment (range, 24-30 weeks).

Resorption of the Calcifications

The chance of complete resorption of the calcifications at 3 months was greater in patients treated with high-energy ESWT than in patients treated with low-energy ESWT (Fig. 5). Pooled analysis [1,17,21] of the 163 patients showed those in the high-energy group had a greater chance of complete resorption compared with patients in the low-energy group (odds ratio, 3.40; 95% CI, 1.35-8.58; p = 0.009) (Fig. 6). The results of each study showed that high-energy ESWT results in a greater chance of resorption after 3 months. The difference in the rate of complete resorption across the different studies in patients treated with

high-energy ESWT versus low-energy ESWT ranged from 10% [1,21] to 35% [17] (Table 6). Two studies [21,22] showed a greater chance of complete resorption in patients treated with high-energy ESWT compared with those treated with low-energy ESWT after 6 months. The extracted data for the chance of complete resorption after 6 months could not be pooled because of the large amount of incomplete extracted data. The differences in the chance of complete resorption between patients treated with high-energy ESWT and those treated with low-energy ESWT were 11.64% [21] and 6% [22] (Fig. 7).

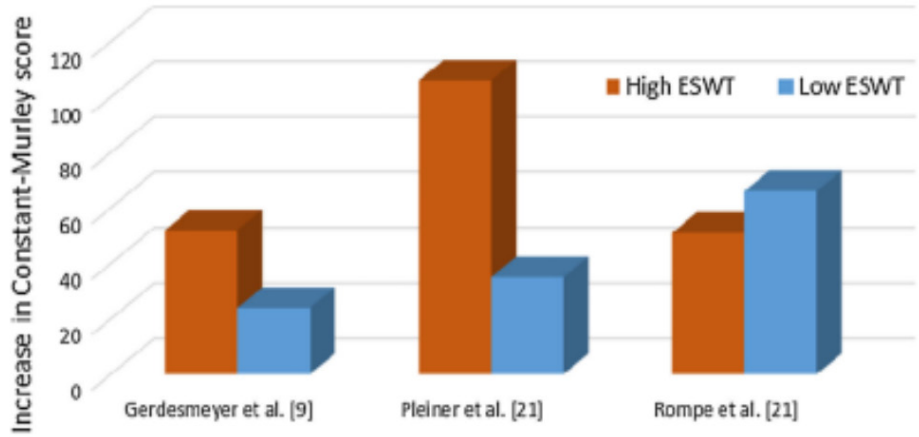

Figure 4. This graph shows the data for greater increase in Constant-Murley scores after 6 months in patients treated with high-energy ESWT compared with those treated with low-energy ESWT.

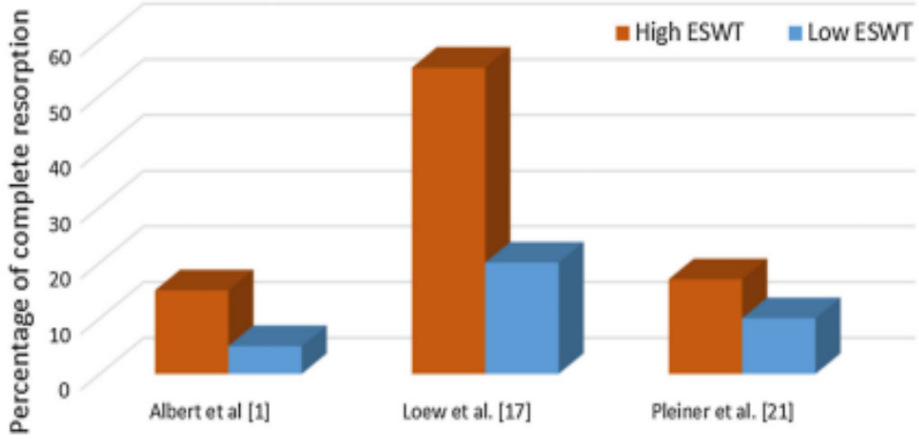

Figure 5. This graph shows the data fot a greater chance of complete resorption after 3 months in patients trwated with high-energy ESWT compared with those treated with low-energy ESWT.

Table 4. Characteristics of the included studies

Study	Study design (level of quality)	Population size	Interventions (low-energy ESWT versus high-energy ESWT)	Outcome measures	Findings		
					3 months	6 months	Radiologic
Albert et al. [1]	RCT (I)	80	< 0.06 mJ/mm^2 versus 0.28-0.45 mJ/mm^2	CMS, VAS for pain, satisfaction, radiologic outcome	Significantly greater increase in high-energy ESWT ($p < 0.0001$) Δ: 16 points	-	3 months: 15% in high-energy ESWT versus 5% in low-energy ESWT
Gerdesmeyer et al. [9]	RCT (I)	144	< 0.08 mJ/mm^2 versus 0.32 mJ/mm^2 versus sham	CMS, radiologic outcome, VAS, side effects	Significantly greater increase in high-energy ESWT ($p = 0.003$) Δ: 18 points	Significantly greater increase in high-energy ESWT ($p < 0.001$) Δ: 28 points	3 months: significantly greater decrease in calcification size in high-energy ESWT ($p = 0.03$)
Pleiner et al. [21]	RCT (I)	46	< 0.07 mJ/mm^2 versus 0.28 mJ/mm^2	CMS, VAS, radiologic outcome	Significantly greater increase in high-energy ESWT ($p < 0.05$) Δ: 13 points	Significantly greater increase in high-energy ESWT ($p < 0.05$) Δ: 71 points	3 months: 13% in high-energy ESWT versus 8% in low-energy ESWT ($p = 0.15$)
Loew et al. [17]	RCT (I)	40	<0.08 mJ/mm^2 versus 0.3 mJ/mm^2	CMS, radiologic outcome	Significantly greater increase in high-energy ESWT Δ: 33 points	-	3 months: 55% in high-energy ESWT versus 20% in low-energy ESWT
Rompe et al. [22]	RCT (I)	100	0.06 mJ/mm^2 versus 0.28 mJ/mm^2		-	Significantly greater increase in high-energy ESWT ($p < 0.01$) Δ: 15 points	6 weeks: 32% in high-energy ESWT versus 8% in low-energy ESWT

ESWT = extracorporeal shock wave therapy; RCT = randomized controlled trial; CMS = Constant-Murley score.

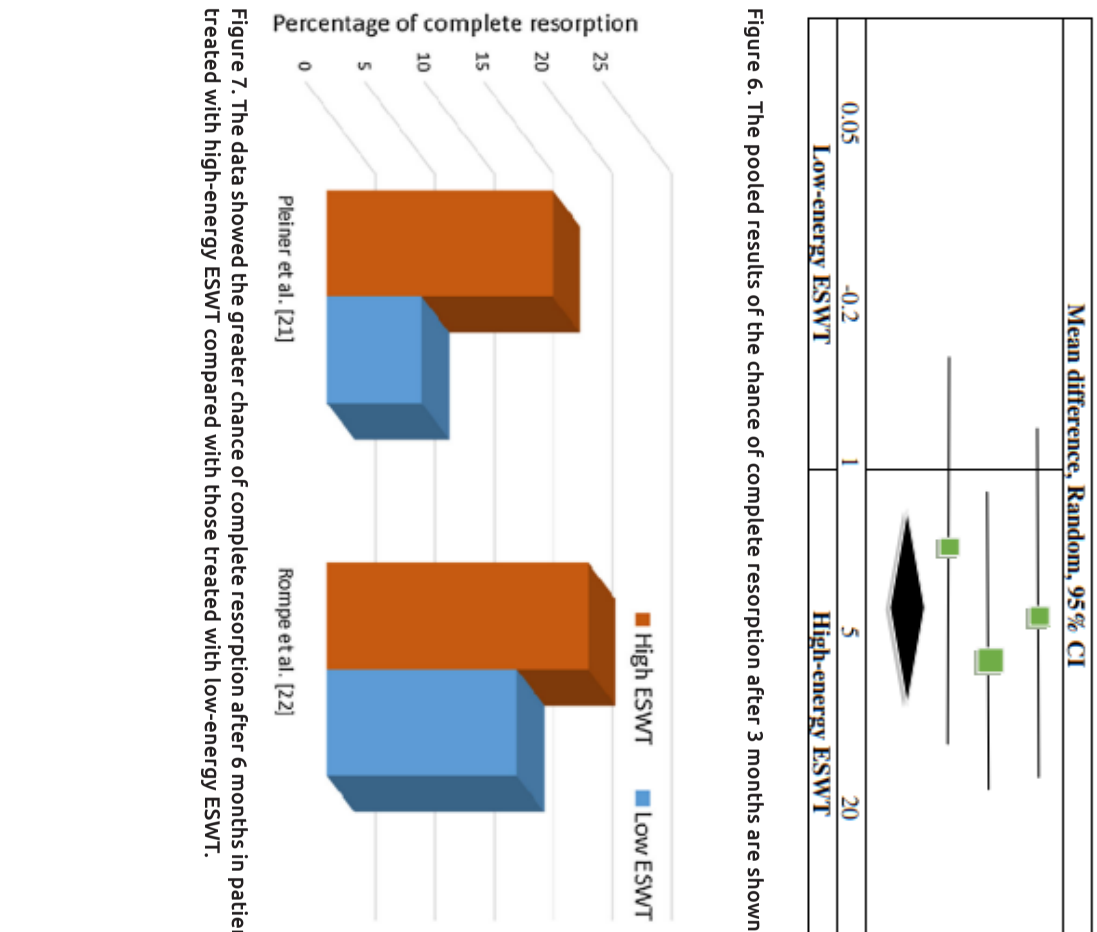

Figure 6. The pooled results of the chance of complete resorption after 3 months are shown.

Figure 7. The data showed the greater chance of complete resorption after 6 months in patients treated with high-energy ESWT compared with those treated with low-energy ESWT.

Table 5. Results of Constant-Murley score (CMS) after 3 months

Study	High-Energy ESWT		Low-energy ESWT			Mean difference (95% CI)
	Mean increase in CMS in individual study group (SD)	Number of participants in individual study group	Mean increase in CMS in individual study group (SD)	Number of participants in individual study group	Weight of individual study within meta-analysis	
Albert et al. [1]	12.5 (16.8)	40	4.5 (14.8)	40	1.5%	8.00 (1.06-14.94)
Gerdesmeyer et al. [9]	26.2 (2.02)	48	16.6 (2.45)	48	88.0%	9.60 (8.70-10.50)
Loew et al. [17]	24.7 (3.57)	20	12.2 (4.74)	20	10.5%	12.50 (9.90-15.10)
Total (95%)		108		108	100%	9.88 (9.04-10.72)

Table 6. Results for complete resorption after 3 months

Study	High-energy ESWT		Low-energy ESWT			Odds ratio (95% CI)
	Events occurred in individual study group	Number of participants in individual study group	Events occurred in individual study group	Number of participants in individual study group	Weight of individual study within meta-analysis	
Albert et al. [1]	6	40	2	40	30.8%	3.35 (0.63-17.74)
Loew et al. [17]	11	20	4	20	43.3%	4.89 (1.20-19.94)
Pleiner et al. [21]	4	23	2	20	25.9%	1.89 (0.31-11.64)
Total (95% CI)	21	83	8	80	100.0%	3.40 (1.35-8.58)

DISCUSSION

ESWT has been proven to be an effective treatment option after failed nonoperative treatment of calcifying tendinitis for at least 4 months. [20] It is a safe treatment option. It has few adverse events and minor side effects such as bruising and hematoma often are short-lived. [9,22] Two cases of humeral head osteonecrosis have been reported. [6] In one case the causative relationship was questionable and in the second case the indication for ESWT was questionable. [6] There are high- and low-energy options, but the best treatment intensity has not been set yet. [20, 24] High-energy ESWT is much more painful and more expensive, and usually is done in an inpatient setting, whereas low-energy ESWT can be performed in an outpatient setting by a physical therapist. [9, 21] Therefore, we hoped to answer two research questions by a systematic review and meta-analysis. We asked whether patients treated with high-energy ESWT showed a greater increase in Constant-Murley score compared with patients treated with low-energy ESWT at 3 months and at 6 months. We also asked whether there was a greater chance of complete resorption in patients treated with high-energy ESWT compared with patients treated with low-energy ESWT at 3 and at 6 months. This meta-analysis has some limitations; one is that the functional outcome (Constant-Murley score) after 3 and 6 months showed moderate heterogeneity, and we investigated the possible causes for this. One possible explanation could be that energy levels of the different studies were not equivalent and the devices used were not the same (Table 4). Although the comparisons were for high-energy ESWT versus low-energy ESWT, the intensity was always either more than 0.28 mJ/mm2 or less than 0.08 mJ/mm2. Another explanation could be that the included studies had different Constant-Murley scores before treatment, although they did not differ much (range, high-energy ESWT, 39.0-60.0; low-energy, ESWT, 39.4-62.7). Another limitation of the current review is use of the Constant-Murley score. Although it is a simple method to assess function of the shoulder and it has high intraobserver and interobserver reliability, the minimal clinically important difference and minimal detectable difference for patients with calcifying tendinitis has not been set yet. The minimal clinically important difference has been set for patients with a rotator cuff tear. [16] However, an increase of 9.88 points on a scale of 1 to 100 is likely to be clinically important. The reason for choosing a follow-up of 6 months as an end point in the included articles is because at this point the effect of the ESWT is expected but the natural self-limiting course of the disease is not yet expected. [9] High-energy ESWT resulted in a better functional outcome compared with low-energy ESWT in the short-term and mid-term. Constant-Murley scores at 3 months improved to a greater degree in patients treated with high-energy ESWT than in patients treated with low-energy ESWT (Fig. 2). Pooled analysis [1, 9, 17] showed that patients in the high-energy group improved by a mean of 25.82 points, compared with 15.94 points in the low-energy group (Fig. 3). The mean difference was 9.88 (25.82 versus 15.94,

95% CI, 9.04-10.72; p < 0.001). These findings are in line with those of Huisstede et al. [13] and Vavken et al. [24]. Huisstede et al. [13] performed a systematic review on the effectiveness of ESWT on calcific and noncalcific rotator cuff tendinitis and two studies [1,9] were included and presented narratively that compared high-energy ESWT with low-energy ESWT. Vavken et al. [24] performed a meta-analysis in which they chose a new, nonevidence-based, cutoff point (0.20 mJ/mm2). Less than this intensity was labeled low-energy and greater than 0.20 mJ/mm2 was considered high-energy. Because of this new classification of ESWT, their included studies differed substantially from those in our study. They studied only the results 6 months after treatment. Even with these differences, the conclusions by Vavken et al. [24] are similar to those in our study. High-energy ESWT resulted in a greater chance of complete resorption calcium deposits when compared with low-energy ESWT. The chance of complete resorption of the calcifications at 3 months was greater in patients treated with high-energy ESWT than in patients treated with low-energy ESWT (Fig. 5). Pooled analysis [1,17,21] showed patients in the high-energy group had a greater chance of complete resorption compared with patients in the low-energy group (odds ratio = 3.40; 95% CI, 1.35-8.58; p = 0.009) (Fig. 6). These findings are in line with the findings of Ioppolo et al. [15] and Vavken et al. [24]. Ioppolo et al. [15] performed a meta-analysis on the clinical improvement and resorption of calcifications after shock wave therapy compared with sham treatment. Vavken et al. [24] used a different cutoff point of 0.20 mJ/mm2. They also found a greater chance of complete resorption after 6 months.

Based on our meta-analysis we believe that high-energy ESWT is more effective than low-energy ESWT in terms of functional outcome (Constant-Murley score) and radiographic resorption (chance of complete resorption) of the deposits after 3 months. However, there is still a need for high-quality RCTs to discover the exact dose-response relation. In our opinion, this future research should focus on high-energy ESWT because current available evidence indicates that high-energy ESWT is more effective than low-energy ESWT regarding the functional and radiologic outcomes in the short term and midterm. It also would be interesting to compare (high-energy) ESWT with other treatment modalities for conservative treatment-resistant calcifying tendinitis of the shoulder such as surgery or needling/ barbotage of the calcific deposits.

REFERENCES

1. Albert JD, Meadeb J, Guggenbuhl P, Marin F, Benkalfate T, Thomazeau H, Chale`s G (2007) High-energy extracorporeal shockwave therapy for calcifying tendinitis of the rotator cuff: a randomised trial. J Bone Joint Surg Br;89:335–341
2. Conboy VB, Morris RW, Kiss J, Carr AJ (1996) An evaluation of the Constant-Murley shoulder assessment. J Bone Joint Surg Br;78:229–232
3. Constant CR, Gerber C, Emery RJ, Sojbjerg JO, Gohlke F, Boileau P (2008) A review of the Constant score: modifications and guidelines for its use. J Shoulder Elbow Surg;17:355–361
4. Constant CR, Murley AH (1987) A clinical method of functional assessment of the shoulder. Clin Orthop Relat Res;214:160–164
5. Diehl P, Gerdesmeyer L, Gollwitzer H, Sauer W, Tischer T (2011) [Calcific tendinitis of the shoulder] [in German]. Orthopade;40:733–746
6. Durst HB, Blatter G, Kuster MS (2002) Osteonecrosis of the humeral head after extracorporeal shock-wave lithotripsy. J Bone Joint Surg Br;84:744–746
7. Furlan AD, Pennick V, Bombardier C, van Tulder M; Editorial Board, Cochrane Back Review Group (2009) 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine (Phila Pa 1976);34:1929–1941
8. Gartner J, Heyer A (1995) [Calcific tendinitis of the shoulder] [in German]. Orthopade;24:284–302
9. Gerdesmeyer L, Wagenpfeil S, Haake M, Maier M, Loew M, Wortler K, Lampe R, Seil R, Handle G, Gassel S, Rompe JD (2003) Extracorporeal shock wave therapy for the treatment of chronic calcifying tendonitis of the rotator cuff: a randomized controlled trial. JAMA;290:2573–2580
10. Gosens T, Hofstee DJ (2009) Calcifying tendinitis of the shoulder: advances in imaging and management. Curr Rheumatol Rep;11:129–134
11. Higgins JP, Green S, eds (2011) Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration; Available at: http://handbook.cochrane.org. Accessed January 4, 2014
12. Hofstee DJ, Gosens T, Bonnet M, De Waal Malefijt J (2007) Calcifications in the cuff: take it or leave it? Br J Sports Med;41:832–835
13. Huisstede BM, Gebremariam L, van der Sande R, Hay EM, Koes BW (2011) Evidence for effectiveness of Extracorporal ShockWave Therapy (ESWT) to treat calcific and non-calcific rotator cuff tendinosis: a systematic review. Man Ther;16: 419–433
14. Hurt G, Baker CL Jr (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am;34:567–575
15. Ioppolo F, Tattoli M, Di Sante L, Venditto T, Tognolo L, Delicata M, Rizzo G, Di Tanna G, Santilli V (2013) Clinical improvement and resorption of calcifications in calcific tendinitis of the shoulder after shock wave therapy at 6 months' follow-up: a systematic review and meta-analysis. Arch Phys Med Rehabil;94:1699–1706
16. Kukkonen J, Kauko T, Vahlberg T, Joukainen A, Aarimaa V (2013) Investigating minimal clinically important difference for Constant score in patients undergoing rotator cuff surgery. J Shoulder Elbow Surg;22:1650–1655
17. Loew M, Daecke W, Kusnierczak D, Rahmanzadeh M, Ewerbeck V (1999) Shockwave therapy is effective for chronic calcifying tendinitis of the shoulder. J Bone Joint Surg Br;81:863–867

18. Loew M, Jurgowski W, Mau HC, Thomsen M (1995) Treatment of calcifying tendinitis of rotator cuff by extracorporeal shock waves: a preliminary report. J Shoulder Elbow Surg;4:101–106
19. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF (2000) Improving the quality of reports of meta-analyses of randomized controlled trials: the QUOROM statement. QUOROM Group. Br J Surg;87:1448–1454
20. Mouzopoulos G, Stamatakos M, Mouzopoulos D, Tzurbakis M (2007) Extracorporeal shockwave treatment for shoulder calcific tendonitis: a systematic review. Skeletal Radiol;36:803–811
21. Pleiner J, Crevenna R, Langenberger H, Keilani M, Nuhr M, Kainberger F, Wolzt M, Wiesinger G, Quittan M (2004) Extracorporeal shockwave treatment is effective in calcific tendonitis of the shoulder: a randomized controlled trial. Wien Klin Wochenschr;116:536–541
22. Rompe JD, Burger R, Hopf C, Eysel P (1998) Shoulder function after extracorporal shock wave therapy for calcific tendinitis. J Shoulder Elbow Surg;7:505–509
23. Speed CA, Hazleman BL (1999) Calcific tendinitis of the shoulder. N Engl J Med;340:1582–1584
24. Vavken P, Holinka J, Rompe JD, Dorotka R (2009) Focused extracorporeal shock wave therapy in calcifying tendinitis of the shoulder: a meta-analysis. Sports Health;1:137–144

CHAPTER 6

6

CHAPTER 7

ESWT versus NACD for therapy resistant CT of the shoulder: study protocol of a randomized controlled trial

Verstraelen FU
Verhagen S
Giesberts A
Bonneux I
Koot H
Boer WD
van der Steen MC

2022 BMC Musculoskelet Disord; 23:308

ABSTRACT

Background

Calcific tendinitis of the shoulder (CT) is a common disorder with a large disease burden. The initial treatment is with conservative measures. However, when this fails the next step treatment remains unclear. Minimal invasive treatment modalities have emerged. Needle aspiration of the calcific deposits (NACD) and extracorporeal shock wave therapy (ESWT) have both shown good clinical results. Nonetheless, in the current orthopaedic literature there are not any studies available that compare both the effectiveness and cost-effectiveness of those two treatment modalities. Therefore, our primary objective is to compare the effectiveness of NACD to ESWT. A secondary objective is to compare the cost-effectiveness of both treatment modalities and workability.

Method

Following a power calculation using the minimal clinical important difference of our primary outcome (Constant-Murley score, CMS) 140 patients will be included in the study. Enrolment is based upon strict inclusion/ exclusion criteria outlined in the Methods section. Participants will be randomized by computer in two groups (e.g. 70 patients will receive NACD and 70 patients will receive ESWT). The NACD treatment will consist of a sonographically guided removal of the calcific deposits and the ESWT treatment will be a focused ESWT. Both treatments will be conducted according to a standardized protocol, as part of care as usual in our hospital. The primary outcome will be the between group differences in functional outcome (measured with the CMS) between baseline and after 12 months follow-up. Secondary outcomes will be questionnaires regarding the clinical outcome (SST) and quality of life (EQ-5D-5L). Furthermore, NRS pain and cost related questionnaires (iPCQ and ProDisQ) will be collected during follow-up after two months, six months and at final follow-up after 12 months.

Discussion

This study will provide more insight regarding treatment for conservative therapy resistant calcific tendinitis of the shoulder by comparing NACD to focused ESWT, which will aid the physician and patient in determining the appropriate treatment plan.

Trial registration

Dutch trial register

NTR7093 registered on 11 March 2018.

BACKGROUND

Calcifying tendinitis (CT) of the shoulder is a common disease of the rotator cuff in which calcium particles are deposited in one or more tendons of the rotator cuff. This can result in a typical pattern of pain, impairments in daily living and decreased range of motion. This disease mainly affects individuals between 30 and 60 years of age and females are more often affected by this condition. [1,2,3,4,5,6] The aetiology of CT of the shoulder is still a matter of dispute. Several hypothesis have been postulated including a degenerative hypothesis, repetitive microtrauma, tenocyte necrosis, reactive and endochondral ossification. All leading to a postulated same end point in which that a locally decreased oxygen tension or hypoxia initiates the formation of the calcific deposit. [2] Initially, the treatment consists of conservative measures such as anti-inflammatory drugs, ice-therapy, physical therapy and/or corticosteroid injections. [2, 7,8,9,10] However, if this conservative treatment fails additional treatments must be considered. Historically, the next step treatment has been a surgical procedure. [1] However, other –less invasive– treatment modalities such as needle aspiration of the calcific deposits (NACD) and focused extracorporeal shockwave therapy (ESWT) have emerged. Over the past years both minimal invasive treatments have proven to be effective therapeutic options. [9, 11,12,13] NACD showed promising results mainly in non-comparing studies. [14] In addition, ESWT has also been proven to be effective, especially high-energy ESWT. [11] Although in the available orthopaedic literature both treatment methods seem to be viable options, evidence comparing both treatment methods is limited. [15] Two randomized controlled trials (RCTs) have evaluated and compared the effectiveness of NACD compared to ESWT. In 2014, a RCT was published in which radial shock wave therapy was compared to NACD. [16] However, radial shock wave therapy have been shown to be less effective than focused ESWT and therefore this comparison different from the current study. [13] In 2020, the most recent RCT was published. Louwerens et al [15] compared a protocol of ESWT with four sessions of high-energy focused ESWT to ultrasound guided NACD. Both studies showed that both treatment modalities were effective in treating calcifying tendinitis of the shoulder with low complication rates. However, both studies used markedly different treatment protocols compared to the current study. [15, 16] Therefore, the exact place of NACD or ESWT in the treatment paradigm of CT is not clear yet. [10] Besides, there is limited evidence available about the cost-effectiveness of any intervention of CT of the shoulder. As far as we are aware, only Haake et al [7] published results concerning the cost-effectiveness of the treatment of CT. They found that ESWT costs society €1.750 to € 3.500 as a results of being unfit to work compared to €9.710 to €19.440 after surgical treatment for therapy resistant CT of the shoulder. However, there is no data available about the comparison between the minimal invasive techniques (e.g. NACD vs ESWT). [7] Therefore, this randomized controlled trial (RCT) has several objectives. The primary objective is to compare the short and midterm effectiveness of NACD and ESWT as

treatment options for conservative therapy resistant CT to define a preferable minimal invasive treatment. The hypothesis is superiority of either NACD or ESWT regarding functional outcome after 12 months. The secondary objective is to compare the cost-effectiveness of both minimal invasive techniques.

METHODS

Study design

The design of the current study is a single centre open-labelled RCT. Patients will be randomized to receive either NACD or ESWT as treatment for conservative therapy resistant CT of the shoulder (Fig. 1). All patients will be followed for 1 year. The trial was approved by the local medical and ethical commission (METC) on 16th of February in 2018 (NL60762.015.17) and is registered in the Dutch trial register (NL5527/ NTR7093). Amendments were made and approved by the METC.

Objectives

Primary objective

To compare the effectiveness of NACD and ESWT in patients with conservative therapy resistant CT of the shoulder over a period of 12 months. The hypothesis is superiority of either NACD or ESWT in functional recovery based on improvement of the Constant Murley Score (CMS) over a period of 12 months (superiority design).

Secondary objectives

1. To assess group differences in change scores on pain and quality of life between baseline and 12 months follow-up, and differences between groups with respect to adverse events and the use of medications in 12 months follow-up.
2. To assess and compare the cost-effectiveness of both interventions over a period of 12 months.

Setting

The study will be conducted at the outpatient department of orthopaedic surgery and trauma of the Máxima Medical Centre in the Netherlands. This is a large regional hospital equipped with a training-program for residents in orthopaedic surgery. The upper extremity group consists of three experienced orthopaedic surgeons.

Population

Patients with chronic (> 6 months) shoulder complaints, calcifications visible on conventional X-rays and who did not respond to conservative, non-operative therapy for at least three months are eligible for inclusion the study. Further in/exclusion criteria are listed in Table 1.

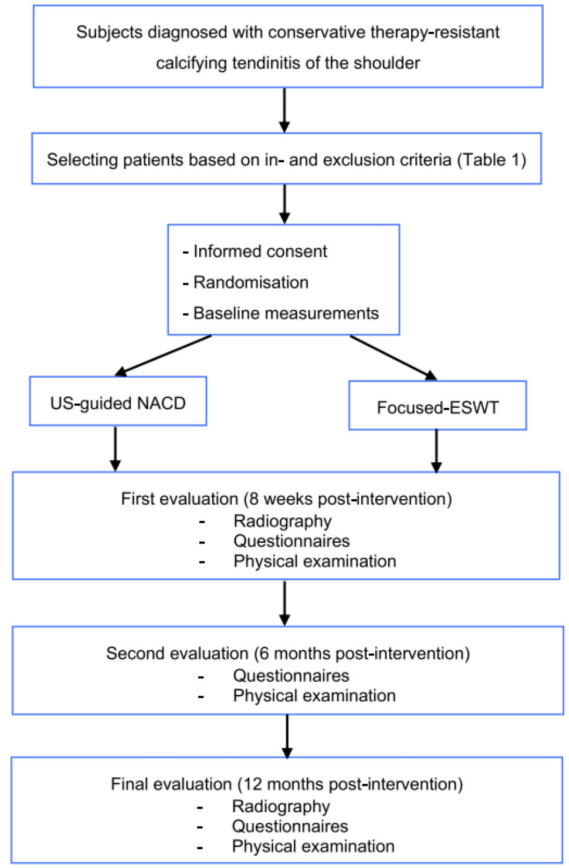

Figure 1. SPIRIT-Flowchart

Table 1. In- and exclusion criteria

Inclusion criteria	Exclusion criteria
Age: > 18 years	ESWT or NACD treatment during the last 6 months
Chronic shoulder complaints (>6 months)	Any contra-indication for the specific treatments (e.g. coagulopathies, malignancies in treated area).
Calcifications visible on conventional radiographs - type I or II calcifications according to the Gärtner classification. minimal diameter of 10mm.	Clinical signs of a frozen shoulder or adhesive capsulitis
Able and willing to comply to study protocol	Operations of the affected shoulder in medical history
	Clinical and radiological signs of acute subacromial bursitis.
	Full-thickness lesion of the rotator cuff tendon(s) on sonography
	Clinical and radiological sign of acromioclavicular osteoarthritis
	Rheumatoid arthritis or fibromyalgia
	Other intra articular pathology: cartilage lesions, biceps pathology

Recruitment
All patients are seen and screened for in/exclusion criteria by an experienced shoulder surgeon. If the patient is eligible for inclusion a patient information form is given to the patient and an appointment is made at the specifically for this study created consultation hour. During this consult the eligibility is verified, further information about the study is giving, and after consent the patient will be included and randomized by a researcher. Furthermore, the baseline measurements are assessed and the subject screening and enrolment log filled in.

Randomization, blinding and treatment allocation
After consent, eligible patients will be randomized and allocated to a treatment group (e.g. either NACD or ESWT) by a computer-generated randomization list using Research Manager (Research Manager, Cloud9 Software, Deventer, The Netherlands). The patients and outcome assessors will not be blinded during the study.

TREATMENT OF SUBJECTS

Group NACD
The NACD treatment aims to remove the calcific deposits in the rotator cuff and will be guided by sonography. The procedure will be performed by an experienced musculoskeletal radiologist. For this procedure, the patient will be placed in a supine position with the affected arm towards the radiologist. The skin will be disinfected. Analgesics to the skin, the subacromial bursa and cuff will be administered (Lidocaine HydroCloride 1%). Under ultrasound guidance a needle (18 gauge) will be placed in the calcific deposits to fragment these under vacuum. In case of clogged needles during treatment, multiple needles can be used. After the completion of the procedure 40 mg Kenacort will be injected in the subacromial bursa as well under ultrasound guidance.

Group ESWT
The ESWT treatment consists of a single session of focused ESWT and aims to fragment the calcific deposits and initiate the resorption phase of calcifying tendinitis. The calcific deposits will be marked sonographically on the patient's skin with the patient in the exact same sitting position as he/she will receive the focused ESWT. After disinfection of the skin, 1000 pulses focused ESWT with an energy flux density (EFD) of 0.15 mJ/mm2 will be applied targeted at the skin marks.

Rehabilitation after intervention
Both treatment group will receive the rehabilitation as they would have received within the care as usual for CT. This means that after the treatment patients will be instructed to perform pain-based movements of the affected arm. The usage of a sling is not standardized. Patients will be instructed to take NSAIDs as needed. Furthermore, if necessary, exercise therapy will be prescribed at the consultation two months after treatment. If other co-interventions (such as repeating the treatment procedure, cross-over to other treatment group or even surgical treatment) are necessary during follow-up it will be initiated by the treating orthopaedic surgeon. Intake of painkillers (e.g. NSAIDs), additionally exercise therapy and co-interventions will be recorded in the case report form during study evaluations.

Baseline characteristics
At baseline several characteristics will be documented, including age, gender, height, weight, body mass index, dominant side, affected side, duration of symptoms, occupations, hobbies. Furthermore, several radiological measurements will be conducted on the conventional X-ray to determine the size of the calcification, Gartner classification [17] and the affected tendon(s).

OUTCOME MEASURES

The primary outcome will be the group differences in recovery of functional outcome measured with the Constant-Murley Score (CMS) between baseline and 12 months follow-up. The Constant-Murley score (CMS) is a 100-points scale composed of a number of individual parameters. These parameters define the level of pain and the ability to conduct the normal daily activities of the patient. [18] The Constant-Murley score was introduced to determine the functionality after the treatment of a shoulder injury. The test is divided into four subscales: pain (15 points), activities of daily living (20 points), strength (25 points) and range of motion: forward elevation, external rotation, abduction and internal rotation of the shoulder (40 points). A higher score indicates higher quality of the function. [18] Secondary outcomes measures will be extensive and include the Numeric Rating Scale (NRS) for pain, EQ-5D-5L and simple shoulder test (SST). The NRS assesses pain intensity using a 0–10 ranking scale in which 0 represents "no pain" and 10 "unbearable pain". [19] EQ-5D is a standardized instrument to measure of health-related quality of life. It consists of the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system explores five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ VAS records the patient's self-rated health on a vertical visual analogue scale, where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. The VAS can be used as a quantitative measure of health outcome that reflect the patient's own judgement. [20] The SST is a patient reported outcome measurement (PROM) in which a score between 0 and 100 can be calculated based on a 12-item long questionnaire. [21] Zero represent the worse

shoulder function and 100 a perfect shoulder function. Besides these outcome measures adverse events, co-interventions and co-medications will be monitored during follow-up. Furthermore, the IMTA Productivity Cost Questionnaire (iPCQ) [22] and PROductivity and DISease Questionnaire (PRODISQ) [23] are included to evaluate the cost-effectiveness. The extensive data collection schedule is outlined in Table 2.

Table 2. Data collection schedule

	Baseline T=0	**8 weeks post-intervention**	**6 months post-intervention**	**12 months post-intervention**
Range		**± 1 week**	**± 2 weeks**	**± 4 weeks**
Demographic Information	√			
Historical records	√			
Sonography	√			
HADS	√			
PCS	√			
CMS	√	√	√	√
NRS	√	√	√	√
EQ-5D	√	√	√	√
SST	√	√	√	√
iPCQ	√	√	√	√
ProDisq	√	√	√	√
X-rays	√	√		√
Used co-medication		√	√	√
Adverse Events		√	√	√

Data management

All data will be handled confidentially and is pseudonymized in compliance with the Dutch Personal Data Protection Act. All patient reported outcome measures are collected digitally and all patient data will be stored coded using data management software (Research Manager, Cloud9 Software, Deventer, The Netherlands). Each patient gets a unique study number which is used in all documents regarding the study. Access to the randomization key is restricted to the study-team. The local METC will be annually informed regarding rates of inclusion, adverse events and study results. The local METC graded the study as a 'low risk' study. A monitoring plan will be conducted by an external party during execution of the study.

Statistical analyses

The primary analyses will be performed according to the 'intention to treat'-principle, indicating that participants will be included in the analysis according to the by randomization allocated group. Secondary analyses will be limited to the compliant participants, independent of which intervention they were randomized (per protocol

analysis). Distribution analysis of all variables will be evaluated by the Shapiro–Wilk test. Primary outcome will be analysed by linear regression analyses with change in CMS between baseline and 12 month follow up as dependent variable. The assumptions of constant variance and linear relationships will be assessed using scatter plots. Should any of these assumptions seriously fail then variable transformations will be used. Analyses will be adjusted for baseline variables that change the effect estimate with more than 10%. Similar analyses will be performed for the secondary continuous outcome parameters. Differences between groups on complications and additional treatment will be analysed by means of Mann–Whitney tests. Furthermore, differences in recovery trajectories between groups will be explored by means of mixed ANOVA. Statistical analyses will be performed using SPSS software (IBM, USA). An alpha level of 0.05 will be accepted as significant.

Sample size calculation

For the sample size calculation, we used the minimal clinically important difference (MCID) for the Constant Murley Score as determined by the study of Kukkonen et al. [24] The reported MCID over a period of 12 months was 10.4 points, with a mean Constant Murray Score of 53.1 (standard deviation of 17.2) at baseline. [24] We aim to find a superiority of one of the two treatment options to treat patients with calcifying tendinitis of the shoulder. Our hypothesis is that superiority of NACD or ESWT above the other treatment in functional recovery over a period of 12 months will be found. Superiority will be expressed by an additional effect size of minimally 0.5. Using a standard deviation of 17.2 of the CMS, we aim to detect a minimally difference of 8.6 points between both groups. Using a power of 80% and an alpha of 0.05 the required sample size is 63 patients per group, resulting in a total of 126 patients. With this number of patients, we will also be able to detect a MCID between both groups of 10.4 points (required number of patients is 43 per group). The final sample size required is 140 patients, to accommodate 10% potential dropout rate over 1 year.

DISCUSSION

This RCT study is the first to compare NACD and a single session of focused ESWT as treatment for conservative therapy resistant calcific tendinitis of the shoulder. The results of this study will aid the physician as it provides valuable information for a shared decision strategy in which treating physician and patient determine the most appropriate treatment. Furthermore, the cost-effectiveness analysis can assist the physician and health care institution to decide whether to provide a certain treatment for conservative therapy resistant calcific tendinitis of the shoulder. The inclusion period was initially supposed to be approximately two years. In 2015 and

2016 a total of 140 patients with conservative therapy resistant calcific tendinitis of the shoulder were treated with either NACD or ESWT in the Máxima Medical Centre. It was the expected that almost all of these patients would have been eligible candidates for the current study. Although it was expected that 10% of these patients would not be willing to be randomized or comply to the study protocol. Therefore, an inclusion period of two years seemed feasible. However, in the first year the recruitment was slower than expected because more patients than anticipated did not fulfil the in- and exclusion criteria. Therefore, an amendment to the original protocol was made to extend the inclusion period. As a result of the global COVID-19 pandemic, the orthopaedic outpatient clinic was temporarily closed and the inclusion ceased for a short period. Several attempts were made to speed up the inclusion rate. The first was to include another hospital as participating centre for the study. However, this turned out not to be possible because other surrounding hospitals did not offer focused ESWT treatment. The second was to request the department of Rheumatology at the Máxima MC as well as all physical therapists in the region to refer their patients with calcifying tendinitis to the orthopaedic outpatient clinic for possible inclusion. Inclusion rate are now according to the adjusted feasibility rate. Besides slowing down recruitment, COVID-19 also influenced the follow-up. Patients were not allowed to visit the orthopaedic outpatient department. As a result, the follow-up of a small number of patients (n = 12) was administrated by phone call or video call. This was especially challenging when determining the items abduction, anteflexion and force of the CMS, which requires specific physical examination and testing. In order to obtain the necessary information as reliable as possible one single outcome assessor gave specific instructions to the patient, mainly by explaining the patient how range of motion is determined. Although, the contribution of these items to the total score of the CMS (45 out of 100 points) is considerable in one patient. One should take into consideration that only a small amount of the measurements was done in this manner and they were equally divided between the two groups (seven in NACD group and five in ESWT group). Therefore, the research team expects that potential bias due to this digital compared to in person assessment of the CMS was negligible. Furthermore, the number of patients in which digital assessment was performed was equally distributed between both groups. Considering the extended inclusion period, additional outcome assessors joined the research team during the execution of the study. The primary investigator trained these assessors to make sure that all measurements were done according to the protocol. In addition, the principal investigator observed the execution of several measurements and give feedback in order to minimize variability in the assessment of the CMS, a measurement which showed good inter-observer reliability in the past. [19] Radiologically assessment will be performed by the principal investigator. In addition, all sessions of focused ESWT treatment will be performed by the same experienced health care professional. Multiple radiologists will perform the NACD treatment, all

having a comparable and extensive experience in sonographically guided interventions. Health care professionals performing the ESWT or NACD treatment will not explicitly be informed that the patient is participating in the current study. As a result, it is expected that all performed treatments will be of a comparable high standard. Despite these precautions, a potential source of bias in the current study might be information bias. Considering the content and logistics of the treatments under investigation, patients and outcome assessors cannot be blinded for treatment allocation. However, since patients at the start of the study are informed that it is not yet known which treatment will lead to the best results and most likely only patients without a pre-existing treatment preference will participate in a RCT, this potential source of bias seems to be small. In addition, outcome assessors will not be the referring shoulder surgeon of the participating patients.

Overall, this study will provide more insight regarding treatment for conservative therapy resistant calcific tendinitis of the shoulder by comparing NACD directly to focused ESWT, which will aid the physician and patient in determining the appropriate treatment plan. At time of manuscript submission 118 participants had joined the trial. Current protocol version is 6. The first patient was included in May 2018; the aim is to fulfil the inclusion in 2022 after which the study will be finalized in 2023.

Availability of data and materials

The datasets generated during and/or analysed during the current study are available from the corresponding author (freekverstraelen@hotmail.com) on reasonable request.

REFERENCES

1. Diehl, P, et al. Calcific tendinitis of the shoulder. Orthopade, 2011.40(8): p. 733-746
2. Gosens T, Hofstee DJ (2009) Calcifying tendinitis of the shoulder: advances in imaging and management. Curr Rheumatol Rep;11(2):129-134
3. Mouzopoulos G, et al (2007) Extracorporeal shock wave treatment for shoulder calcific tendonitis: a systematic review. Skeletal Radiol;36(9):803-811
4. Hofstee DJ, et al (2007) Calcifications in the cuff: take it or leave it? Br J Sports Med;41(11):832-835
5. Balke M, Bielefeld R, Schmidt C, Dedy N, Liem D (2012) Calcifying tendinitis of the shoulder: midterm results after arthroscopic treatment. Am J Sports Med;40(3):657-661
6. Speed CA, Hazleman BL (1999) Calcific tendinitis of the shoulder. N Engl J Med;340(20):1582-1584
7. Haake M, Rautmann M, Wirth T (2001) Assessment of the treatment costs of extracorporeal shock wave therapy versus surgical treatment for shoulder diseases. Int J Technol Assess Health Care;17(4):612-617
8. Ioppolo F, et al (2013) Clinical Improvement and Resorption of Calcifications in Calcific Tendinitis of the Shoulder After Shock Wave Therapy at 6 Months' Follow-Up: A Systematic Review and Meta-Analysis. Arch Phys Med Rehabil; 94(9):1699-1706
9. Huisstede BM, et al (2011) Evidence for effectiveness of Extracorporal ShockWave Therapy (ESWT) to treat calcific and non-calcific rotator cuff tendinosis-a systematic review. Man Ther;16(5):419-433
10. NOV. Diagnostiek en behandeling van het subacromiaal pijnsyndroom- richtlijn. Website: http://www.orthopeden.org/ 2012.
11. Verstraelen FU, id Kleef NJHM, Janssen L, Morrenhof JW (2014) High-energy Versus Low-energy Extracorporeal Shock Wave Therapy for Calcifying Tendinitis of the Shoulder: Which is Superior? A Meta-analysis. Clin Orth Rel Res;472(9):2816-2825
12. Abo Al-Khair MA, El Khouly RM, Khodair SA, Al Sattar Elsergany MA, Hussein MI, Mowafy MEE (2020) Focused, radial and combined shock wave therapy in treatment of calcific shoulder tendinopathy. Phys Sportsmed;6:1-8
13. Huisstede BM, Gebremariam L, van der Sande R, Hay EM, Koes BW (2011) Evidence for effectiveness of Extracorporal Shock-Wave Therapy (ESWT) to treat calcific and non-calcific rotator cuff tendinosis--a systematic review. Man Ther;16(5):419-433
14. Gatt DL, Charalambous CP (2014) Ultrasound-Guided Barbotage for Calcific Tendonitis of the Shoulder: A Systematic Review including 908 Patients. Arthroscopy;30(9):1166-1172
15. Oudelaar BW, Schepers-Bok R, Ooms EM, Huis In 't Veld R, Vochteloo AJ (2016) Needle aspiration of calcific deposits (NACD) for calcific tendinitis is safe and effective: Six months follow-up of clinical results and complications in a series of 431 patients. Eur J Radiol;85(4):689-694
16. Louwerens JKG, Sierevelt IN, Kramer ET, Boonstra R, van den Bekerom MPJ, van Royen BJ, Eygendaal D, van Noort A (2020) Comparing Ultrasound-Guided Needling Combined With a Subacromial Corticosteroid Injection Versus High-Energy Extracorporeal Shockwave Therapy for Calcific Tendinitis of the Rotator Cuff: A Randomized Controlled Trial. Arthroscopy;36(7):1823-1833
17. Kim YS, Lee HJ, Kim YV, Kong CG (2014) Which method is more effective in treatment of calcific tendinitis in the shoulder? Prospective randomized comparison between ultrasound-guided needling and extracorporeal shock wave therapy. J Shoulder Elbow Surg;23(11):1640-1646
18. Gärtner J, Heyer A (1995) Calcific tendinitis of the shoulder. Orthopade;24(3):284-302
19. Conboy VB, Morris RW, Kiss J, Carr AJ (1996) An evaluation of the Constant-Murley shoulder assessment. J Bone Joint Surg Br;78(2):229-232
20. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, et al (2005) Core outcome measures for chronic pain in clinical trials: IMMPACT recommendations. Pain;113:9–19
21. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, Bonsel G, Badia X (2011) Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L) Qual Life Res;20(10):1727-1736
22. Kampen van D, Beers van LWAH, Scholtes VAB, Terwee CB, Willems JW (2012) Validation of the Dutch version of the Simple Shoulder Test. J Shoulder Elbow Surg;21(6):808-814
23. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Hakkaart-van Roijen L (2015) The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. Value Health;18(6):753-758
24. Koopmanschap MA (2005) PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. Expert Rev Pharmacoecon Outcomes Res;5(1):23-28
25. Kukkonen J, Kauko T, Vahlberg T, Joukainen A, Äärimaa V (2013) Investigating minimal clinically important difference for Constant score in patients undergoing rotator cuff surgery. J Shoulder Elbow Surg;22(12):1650-1655

CHAPTER 8

General discussion and future perspectives

Calcifying tendinitis of the shoulder (CT) is a common disease of the shoulder. In this disease one or multiple calcific deposits are present in one or more tendons of the rotator cuff. It has a large disease burden and causes significant impairments in daily living and decreases the workability of the affected patients. [1-3] Initial treatment is with conservative measures for at least six months. The conservative measures in the treatment of CT are in line with those described in the guideline of the subacromial pain syndrome, stated in the guideline of the Dutch orthopaedic society. [4] These measures include education, pain based activities, exercise therapy in combination with stabilisation of the scapula and postural therapy, NSAIDs for a short period and/or a single subacromial injection. [4] However, in approximately 30% of the patients these measures fail and a next step treatment is necessary. Negative prognostic factors for this conservative therapy have been appointed. These negative prognostic factors include bilateral occurrence, a more anterior and medial localisation of the calcific deposit, a size of more than 1.5cm and Gartner type I calcification. [5,6] Historically, the next step treatment for therapy resistant CT is a surgical procedure. More recently, several minimal invasive treatments have emerged. In recent studies promising clinical results are reported. Though, in the treatment algorithm of CT, the exact place of these minimal invasive treatment options have not been established yet. [7-9] The general aim of the current thesis was to outline and further develop the treatment algorithm for patients with conservative therapy resistant CT. To achieve this aim several research questions needed to be addressed. At first, in ***Part 1,*** the historically proposed surgical treatment options were evaluated and clarified whether a preferable surgical procedure could be appointed. ***Part 2*** is considered as a transitional part. In this part of the thesis the transition was made between the surgical treatment to a minimal invasive treatment for CT. For this we evaluated the clinical outcomes of both treatment modalities. In ***Part 3*** of the thesis minimal invasive treatment modalities were evaluated to clarify whether a preferable minimal invasive treatment strategy could be appointed.

PART 1

Do the available surgical procedures lead to different functional outcome in patients with conservative therapy resistant calcifying tendinitis of the shoulder?

Although most patients can be treated with conservative measures a minority of the patients require additional treatment. Historically, the next step treatment is a surgical procedure. However, debate remains what should be the preferable surgical procedure. Several surgical treatment options are available. The first is to perform only a subacromial decompression and leaving the calcific deposits untouched. The second is debriding the calcific deposits without an additional subacromial decompression. The third is a debridement of the calcific deposits in combination with a subacromial

decompression. [10-14] The rationale to consider one or the other treatment is related to whether subacromial impingement is considered as a causative factor in the etiology of CT (**chapter 1)**. [2] Some authors state that the underlying cause of CT could be that subacromial impingement causes repetitive microtrauma and micro tears to the rotator cuff tendons, which could trigger the metaplasia of tenocytes to chondrocytes. Additionally, it is hypothesized that the influx of phagocytes around the calcific deposits leads to subsequent edema and cause a rise of the intratendineous pressure. Consequently, this could lead to secondary subacromial impingement as the thickened and calcified tendon decreases the subacromial space. [15,16] These hypotheses seems to advocate a subacromial decompression. [11-13] Furthermore, some authors state that the subacromial decompression can serve as a stimulus for the tendon to return to the resorption stage. [16,17] This is supported by the fact that multiple growth factors are found in the subacromial space immediately after a subacromial decompression. [18] On the other hand, it is also hypothesized that CT is not related to subacromial impingement and that CT is only a cell-mediated reactive process which is self-limiting and goes through several consecutive stages. [1] To answer the question whether or not to perform a subacromial decompression the currently available literature was reviewed. In **chapter 2** a systematic review was performed with a clear research question: Is there a difference in functional and clinical outcomes after debridement of the calcific deposits with and without an additional subacromial decompression? The currently available literature showed that both surgical procedures result in good clinical and functional outcome with little side effects. However, a preferable surgical procedure is not appointed. Another ongoing dispute in current literature is whether or not to debride the calcific deposits. Some authors state that damage to the rotator cuff can be avoided by leaving the calcific deposits untouched. [11,12]. It is postulated that the calcific deposits are an insignificant transient radiological finding. In line with these findings in **chapter 3** a retrospective study is presented which evaluated the midterm effectiveness of a subacromial decompression without debridement of the calcific deposits in patients with therapy resistant CT. This retrospective cohort study demonstrated good clinical results after a mean follow-up of three years. In 52% of the patients, the calcific deposits resolved during follow-up. This finding also is in line with the findings of the studies of Hofstee et al. [11] and Tillander et al. [12] Interestingly, no correlation could be established between the persisting presence of calcific deposits and the clinical outcome. Therefore, a subacromial decompression without a debridement of the calcific deposits could be a viable surgical procedure for patients with therapy resistant CT and needed further evaluation. Contrastingly, other authors emphasize the need for the debridement of the calcific deposits and even state there that is a correlation between complete removal of the calcium deposits (with or without rotator cuff repair) and persisting symptoms. [13, 19-22] In **chapter 2** a systematic review of the current literature was performed with a clear research question: Is there a difference

in the functional and clinical outcomes after subacromial decompression compared to subacromial decompression in combination with a debridement of the calcific deposits? However, based on the results of the systematic review a preferable treatment could still not be appointed since no significant differences could be detected. In conclusion, all three available surgical treatment options for patients with conservative therapy resistant CT showed good functional and clinical outcome and were safe procedures. Therefore, we performed a randomized clinical trial that compared the above-mentioned surgical treatment procedures for therapy resistant CT (**chapter 4**). All three surgical treatment modalities resulted in significant pain relief and improvement of shoulder function six months after surgery. However, patients who had a subacromial decompression without debridement showed inferior improvement in VAS for pain and DASH score after six weeks. Furthermore, these patients required more postoperative side treatments. No significant differences were observed between patients who had a debridement with and without an additional subacromial decompression. Therefore, an arthroscopic debridement without an additional subacromial decompression seems to be the preferred surgical treatment option for conservative treatment resistant CT.

Key Points Part 1

- All the investigated surgical procedures result in significant pain relief on the short term.
- When a surgical treatment is chosen for therapy resistant CT of the shoulder, arthroscopic debridement without subacromial decompression is advisable.

PART 2

Can minimal invasive techniques result in comparable functional outcome compared to surgical treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder?

The exact place of minimal invasive treatment techniques in the current treatment algorithm of CT has not been established yet. The literature on the mid and long-term clinical outcomes is limited and a comparative study between the minimal invasive techniques and a surgical treatment is not available. Therefore, we performed a comparative cohort study which compared the midterm clinical outcome of a surgical treatment (arthroscopic debridement) to the NACD treatment for patients with therapy resistant CT of the shoulder (**chapter 5**). We showed that both treatment options result in good clinical outcomes after a mean follow-up of 5.5 years. More additional treatments and a substantial number of cross-over (31.7%) was observed in

patients who received the NACD treatment. This should be considered and discussed with the patient when choosing a next step treatment option for CT. Especially, if negative prognostic factors are apparent. These negative prognostic factors include a size of more than 1.5cm, absence of a good initial response after NACD treatment, a prolonged course of symptoms prior to treatment (>12 months). [23-25] Furthermore, Oudelaar et al. [23] demonstrated that Gartner and Heyer type I calcifications are more likely to fail to a single session of NACD and would require multiple NACD sessions. In the study presented in **chapter 5** the majority of the patients had a Gartner and Heyer type I calcification. This might explain the high number of cross-over to the surgical treatment. In our opinion this highlights the need for further investigation on the relationship between calcification morphology and other negative prognostic factors on the outcome of minimal invasive treatment for therapy resistant CT. Since this high number of cross-over to the surgical treatment was observed we were particularly interested in the outcome of this group. Would an initial NACD treatment be a negative prognostic factor for the surgical treatment? Therefore, in **chapter 5**, the clinical outcome in patients of this cross-over group was evaluated. The clinical outcome was good and comparable to the initial surgical treatment group. Thus, the initial NACD treatment was not a negative prognostic factor for the clinical outcome of the surgical treatment. In addition to cross-over between groups, significantly more additional treatments were observed in the NACD group. This could be explained by a subacromial bursitis, which is caused by the erupting calcific particles in the subacromial bursa. [26,27] It can be hypothesized that these additional treatments (e.g., mainly cortisone injections) were needed to alleviate symptoms caused by these calcific particles. Once this resorption phase is completed the tendon will return to normal tendinous tissue and the patients symptoms will resolve. [1] In conclusion, NACD treatment is a valid next step treatment option for conservative therapy resistant CT. Since, in the majority a surgical treatment can be avoided. However, negative prognostic factors such as prolonged course of symptoms prior to treatment and absence of initial clinical and radiological response within the first three months should be taken into consideration. [24]

Key Points Part 2

- NACD is a valid next step treatment option for conservative therapy resistant calcifying tendinitis of the shoulder.
- The high percentage of cross-over to surgical treatment should be discussed with the patient.
- In presence of negative prognostic factors for NACD, surgical treatment can be considered if symptoms are unchanged and no significant resorption is achieved within three months after a single session of NACD.

PART 3

Is there a preferable minimal invasive treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder?

a. What is the preferred intensity for extracorporeal shockwave therapy (ESWT)?

The effectiveness of ESWT has been studied extensively and has been proven to be an effective treatment option for conservative therapy resistant CT. Besides, it is a safe treatment option. [7,28] It has few adverse events and minor side effects such as bruising and hematoma which are often short-lived. [7,28,29] As mentioned in the general introduction there are numerous ESWT treatment protocols available. However, an optimal treatment protocol has not been established. For example, there are radial and focused ESWT options and ESWT can be subdivided into high- and low-energy options. However, the optimal treatment intensity has not been set yet. [30-32] High-energy ESWT is more painful and more expensive, and usually is done in an inpatient setting, whereas low-energy ESWT can be performed in an outpatient setting by a physical therapist. [32] In **chapter 6,** a meta-analysis was performed to appoint a preferable intensity of the focused ESWT. Based on this meta-analysis it can be stated that high-energy ESWT is more effective than low-energy ESWT in terms of functional outcome (Constant-Murley score) and radiographic resorption of the calcific deposits (chance of complete resorption). However, more research is needed to further optimize the protocol used in high-energy ESWT. For example, it remains unknown how many sessions are necessary and if an interval is needed between the different sessions.

b. Is there a difference in effectiveness between needle aspiration of calcific deposits (NACD) compared to extracorporeal shockwave therapy (ESWT) regarding functional outcome?

The optimal minimal invasive treatment has not been appointed yet. As described above high-energy focused ESWT is recommended when ESWT is chosen as a treatment. However, the evidence comparing the functional outcome of different minimal invasive techniques for CT is limited. [9] As mentioned in the general introduction currently only two randomized studies are available. In 2014, a randomized trial was published in which radial ESWT was compared to NACD. [33] Kim et al. [33] reported that both treatment modalities showed an improvement in functional outcome and elimination of the calcific deposits after a follow-up of 23 months. NACD was superior to radial ESWT regarding pain relief and improvement of shoulder function. It should be noted that the used ESWT was radial ESWT with a low intensity level and it was not adequately aimed at the calcific deposit. Therefore, the results should be carefully interpreted. Furthermore, in

2020 the most recent randomized trial was published in which a treatment with multiple sessions of focused high-energy ESWT was compared to NACD. [9] The used protocol of ESWT was four sessions with focused high-energy ESWT with a 1-week interval. Louwerens et al [9] showed no significant differences between the two treatment groups. Although, more additional interventions and less elimination of the calcific deposits were observed in patients after the ESWT treatment. As mentioned above, both studies used markedly different treatment protocols and therefore a preferable treatment protocol cannot be appointed yet and more research is needed. [9, 33-34] Besides, both studies only focused on the clinical and radiological outcomes of NACD and ESWT. Though, in current health care several other perspectives are needed to be evaluated to come to a preferential treatment. For example, what treatment is more cost-effective and do the return-to-work rates differ between the two treatments? In **chapter 7**, a study protocol is presented of a randomized trial that compares NACD and a single session of high-energy focused ESWT as treatment for conservative therapy resistant CT. This study will provide more insight regarding treatment for conservative therapy resistant CT by comparing NACD to high-energy focused ESWT. The study consists of 140 patients randomly allocated to the two treatment groups. The hypothesis is superiority of either NACD or ESWT regarding functional outcome after 12 months. The first patient was included in May 2018. The final patient was included in August 2022. Follow-up will be completed in September 2023. Next to the clinical and radiological outcome other secondary outcomes will be evaluated such as the cost-effectiveness of both treatments and the influence of psychological disorders (such as depression, anxiety and pain catastrophizing) on the clinical outcomes and treatment effect.

Key Points Part 3

- High-energy focused ESWT is more effective compared to low-energy or radial ESWT regarding clinical outcome and the likelihood of resorption after three months.
- An optimal treatment protocol of ESWT has yet to be established.
- High-energy focused ESWT as well as NACD show promising clinical outcomes and can both be a next step treatment option for therapy resistant CT of the shoulder.

Treatment algorithm for conservative therapy resistant calcifying tendinitis of the shoulder

The general aim of the current thesis was to outline and further develop the treatment algorithm for patients with conservative therapy resistant CT. To this end several research questions were answered. Below the final version of this treatment algorithm is presented (Figure 1). This step-by-step algorithm is based on findings of the individual studies within this thesis as well as it is the result of a concise review of literature presented in this discussion. In this way it will help the orthopaedic surgeon treating patients with conservative therapy resistant CT. Besides, this also can be of aid for a general physician or physical therapist in deciding whether to refer a patient with CT to an orthopaedic surgeon.

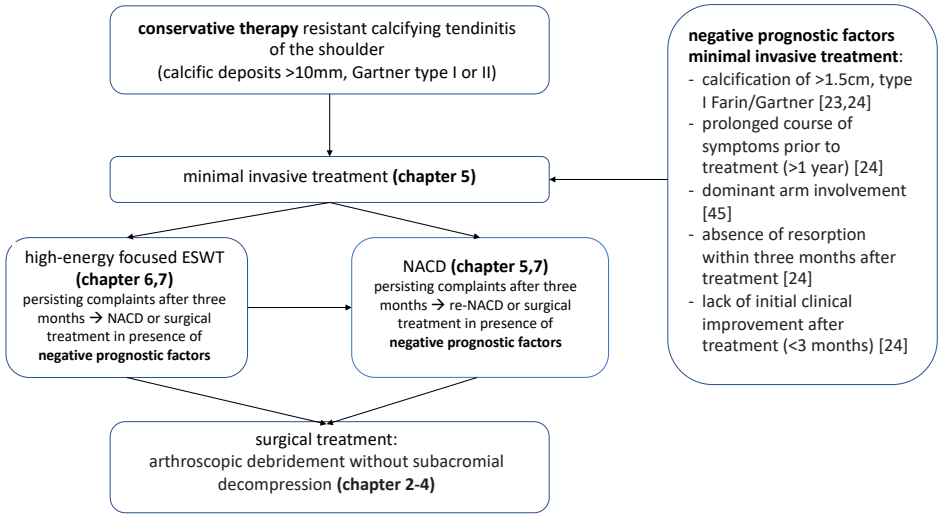

Figure 1. Treatment algorithm for patients with conservative therapy resistant calcifying tendinitis of the shoulder.

FUTURE PERSPECTIVES

This thesis has filled in several knowledge gaps in the management of conservative therapy resistant CT. However, several other knowledge gaps remain. These topics can give direction for the ongoing research on optimizing treatment for CT of the shoulder. In the current society costs of health care and value-based health care is becoming more important. [35, 36] From this perspective, it would be valuable to assess the cost-effectiveness of the available minimal invasive and surgical treatments. On this topic only one study has been published by Haake et al [36]. This is a cohort study published in 2002 which reviewed 60 patients with chronic non traumatic shoulder complaints (with and without calcifying tendinitis) 12 weeks after treatment (either ESWT or surgical treatment). They found that the short-term functional outcomes were comparable and the costs of operative treatment were 5-7 times higher than a ESWT treatment. The authors concluded that ESWT is more cost-effective compared to surgical treatment. However, several issues can be appointed. Firstly, it is not clear how many patients actually were suffering from CT. Secondly, the follow-up of 12 weeks after the procedure can be considered as too short. In 2020 Louwerens et al. [3] reported a study on the return to work and workability after minimal invasive treatment for CT. The authors concluded that CT has a significant impact on the workability and treatment of CT resulted in an increase in the workability as well as a decline in sick leave. In particular in patients with medium and high physically demanding work treatment of CT would be beneficial. However, a comparison in cost-effectiveness between different treatment modalities was not performed in this study. Therefore, there is a need for further evaluation of the cost-effectiveness of the minimal invasive treatments and make a comparison with the cost-effectiveness of the surgical treatment for CT. With the results of the RCT, of which the study protocol is presented in **chapter 7**, we can further fill this gap in knowledge and further improve the treatment algorithm. Another interesting topic for further evaluation could be the influence of patient specific, but not shoulder specific, prognostic factors such as psychological factors on the outcome of the treatment of patients with CT. In patients with shoulder complaints about 26% also have depressive symptoms. [37, 38] Depressive symptoms are known to be related to functional complaints and greater disability in patients with chronic shoulder complaints. [39] Besides, pain catastrophic behaviour is known to show inferior overall treatment effects in patients with chronic shoulder complaints. [38] In analogy with patients with chronic low back pain it would be interesting to evaluate whether a more multidisciplinary treatment (focused on these psychological disorders) would improve the overall treatment efficacy of patients with chronic atraumatic shoulder complaints (including conservative therapy resistant CT). [40] The effect on the outcome of these psychological factors was also one of the research aims of the study presented in **chapter 7**. A final direction for future research worth mentioning is the use of additives in the NACD

treatment. The calcific deposits consist of calcium hydroxyapatite. [1,2] Some additives could be considered, for example, the addition of acetic acid in the NACD treatment could be promising. [41] Acetic acid, which is also the main ingredient of Antikal®, is an inorganic anion and can serve as a catalysator for the resorption of the calcific deposit as it does in the kitchen and bathroom. [42] In early 2000s a small sample size randomized trial was performed which showed good short-term results and showed no significant side effects. However, this study had a very heterogeneous population which included patients with and without calcifying tendinitis. [43] Therefore, further investigation seems advisable. Another additive that can be considered is sodium thiosulfate. This has shown its efficacy in several calcific deposition disorders. In a small cohort study it showed no significant side effects although the addition of a sodium thiosulfate solution did not show favourable results over the conventionally used serum saline solution. [44]

Key Points future perspectives

- Evaluating cost-effectiveness and return to work time of different treatment strategies is advisable to determine an optimal next step treatment for CT.
- The influence of psychological factors and other patient specific prognostic factors on the outcome of CT can be evaluated.
- Additives in the NACD treatment (such as acetic acid) should be considered and evaluated to optimize the minimal invasive treatment strategy.

REFERENCES

1. Uhthoff HK, Sarkar K, Maynard JA (1976) Calcifying tendinitis: a new concept of its pathogenesis. Clin Orthop Relat Res, 118 (1):164-168.
2. Diehl P, Gerdesmeyer L, Gollwitzer H, Sauer W, Tischer T (2011) Die Kalkschulter - Tendinosis calcarea [Calcific tendinitis of the shoulder]. Orthopade, 40(8):733-746.
3. Louwerens JKG, Kuijer PPFM, Sierevelt IN, van den Bekerom MPJ, van Royen BJ, Eygendaal D, van Noort A (2020) The Impact of Minimally Invasive Treatment for Rotator Cuff Calcific Tendinitis on Self-Reported Work Ability and Sick Leave. Arthrosc Sports Med Rehabil, 2(6):e821-e827.
4. Startpagina - Subacromiaal Pijnsyndroom van de Schouder (SAPS) - Richtlijn - Richtlijnendatabase. (z.d.). Geraadpleegd op 17 januari 2023, van https://richtlijnendatabase.nl/richtlijn/saps/saps_-_korte_beschrijving.html
5. Drummond Jr M, Ayinon C, Rodosky M, Vyas D, Lesniak B, Lin A (2021) Predictive factors for failure of conservative management in the treatment of calcific tendinitis of the shoulder. JSES Int, 26(3):469-473.
6. Ogon P, Suedkamp NP, Jaeger M, Izadpanah K, Koestler W, Maier D (2009) Prognostic factors in nonoperative therapy for chronic symptomatic calcific tendinitis of the shoulder. Arthritis Rheum, 60(10):2978-2984.
7. Gatt DL, Charalambous CP (2014) Ultrasound-guided barbotage for calcific tendonitis of the shoulder: a systematic review including 908 patients. Arthroscopy, 30(9):1166-1172.
8. Castillo-González, FD, Ramos-Álvarez, JJ, Rodríguez-Fabián, G, González-Pérez, J, Calderón-Montero, J (2014) Treatment of the calcific tendinopathy of the rotator cuff by ultrasound-guided percutaneous needle lavage. Two years prospective study. Muscles, ligaments and tendons journal, 14(2):220-225.
9. Louwerens JKG, Sierevelt IN, Kramer ET, Boonstra R, van den Bekerom MPJ, van Royen BJ, et al (2020) Comparing Ultrasound-Guided Needling Combined With a Subacromial Corticosteroid Injection Versus High-Energy Extracorporeal Shockwave Therapy for Calcific Tendinitis of the Rotator Cuff: A Randomized Controlled Trial. Arthroscopy, 36(7):1823-1833.
10. Seil R, Litzenburger H, Kohn D, Rupp S (2006) Arthroscopic treatment of chronically painful calcifying tendinitis of the supraspinatus tendon. Arthroscopy: J Arthrosc Rel Surg, 22(5):521–527.
11. Hofstee DJ, Gosens T, Bonnet M, De Waal Malefijt J (2007) Calcifications in the cuff: take it or leave it? Br J Sports Med, 41(11):832-835.
12. Tillander BM, Norlin RO (1998) Change of calcifications after arthroscopic subacromial decompression. J Shoulder Elbow Surg, 7(3):213-217.
13. Ark JW, Flock TJ, Flatow EL, Bigliani LU (1992) Arthroscopic treatment of calcific tendinitis of the shoulder. Arthroscopy, 8(1):183-188.
14. Clement ND, Watts AC, Phillips C, McBirnie JM (2015) Short-Term Outcome After Arthroscopic Bursectomy Debridement of Rotator Cuff Calcific Tendonopathy With and Without Subacromial Decompression: A Prospective Randomized Controlled Trial. Arthroscopy, 31(9):1680-1687.
15. Bosworth BM (1941) Calcium deposits in the shoulder and subacromial bursitis. A survey of 12,122 shoulders. JAMA, 116(1):2477-2482.
16. Hurt G, Baker CL (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am, 34: 567-575.
17. Speed CA, Hazleman BL (1999) Calcific tendinitis of the shoulder. N Engl J Med, 340:1582-1584.

18. Randelli P, Margheritini F, Cabitza P, Dogliotti G, Corsi MM (2009) Release of growth factors after arthroscopic acromioplasty. Knee Surg Sports Traumatol Arthrosc, 17(1):98-101.
19. Porcellini G, Paladini P, Campi F, Paganelli M (2004) Arthroscopic treatment of calcifying tendinitis of the shoulder: clinical and ultrasonographic follow-up findings at two to five years. J Shoulder Elbow Surg, 13(5):503-508.
20. Lorbach O, Haupert A, Berger C, Brockmeyer M (2021) Clinical and Structural Results of Rotator Cuff Repair Compared With Rotator Cuff Debridement in Arthroscopic Treatment of Calcifying Tendinitis of the Shoulder. Am J Sports Med, 49(12):3196-3201.
21. Cho CH, Bae KC, Kim BS, Kim HJ, Kim DH (2020) Recovery pattern after arthroscopic treatment for calcific tendinitis of the shoulder. Orthop Traumatol Surg Res, 106(4):687-691.
22. Pang L, Li T, Li Y, Cao Y, Li J, Zhu J, Tang X (2022) Combined arthroscopic rotator cuff repair leads to better clinical outcomes than isolated removal of calcific deposits for shoulder calcific tendinitis: A 2- to 5-year follow-up study. Front Surg, 9:912779.
23. Oudelaar BW, Ooms EM, Huis In 't Veld R, Schepers-Bok R, Vochteloo AJ (2015) Smoking and morphology of calcific deposits affect the outcome of needle aspiration of calcific deposits (NACD) for calcific tendinitis of the rotator cuff. Eur J Radiol, 84:2255-2260.
24. Oudelaar BW, Huis In 't Veld R, Schepers-Bok R, Ooms EM, Nelissen RGHH, Vochteloo AJH (2020) Prognostic factors for the outcome of needle aspiration of calcific deposits for rotator cuff calcific tendinitis. Eur Radiol, 30(7):4082-4090
25. Chou WY, Wang CJ, Wu KT, Yang YJ, Ko JY, Siu KK (2017) Prognostic factors for the outcome of extracorporeal shockwave therapy for calcific tendinitis of the shoulder. Bone Joint J, 99-B(12):1643-1650.
26. Beyth S, Safran O (2021) Acute Calcific Tendonitis of the Shoulder Mimicking Septic Arthritis. Isr Med Assoc J, 23(8):531-533.
27. Oudelaar BW, Van Liebergen MR, Van Arkel ERA (2021) Een vrouw met acuut ontstane schouderklachten [A woman with acute-onset shoulder pain]. Ned Tijdschr Geneeskd, 18;165.
28. Mouzopoulos G, Stamatakos M, Mouzopoulos D, Tzurbakis M (2007) Extracorporeal shock wave treatment for shoulder calcific tendonitis: a systematic review. Skeletal Radiol, 36:803–811.
29. Rompe JD, Burger R, Hopf C, Eysel P (1998) Shoulder function after extracorporal shock wave therapy for calcific tendinitis. J Shoulder Elbow Surg, 7:505–509.
30. Gerdesmeyer L, Wagenpfeil S, Haake M, Maier M, Loew M, Wortler K, et al (2003) Extracorporeal shock wave therapy for the treatment of chronic calcifying tendonitis of the rotator cuff: a randomized controlled trial. JAMA, 290:2573–2580.
31. Vavken P, Holinka J, Rompe JD, Dorotka R (2009) Focused extracorporeal shock wave therapy in calcifying tendinitis of the shoulder: a meta-analysis. Sports Health, 1:137–144.
32. Pleiner J, Crevenna R, Langenberger H, Keilani M, Nuhr M, Kainberger F, et al (2004) Extracorporeal shockwave treatment is effective in calcific tendonitis of the shoulder: a randomized controlled trial. Wien Klin Wochenschr, 116:536–541.
33. Kim YS, Lee HJ, Kim YV, Kong CG (2014) Which method is more effective in treatment of calcific tendinitis in the shoulder? Prospective randomized comparison between ultrasound-guided needling and extracorporeal shock wave therapy. J Shoulder Elbow Surg, 23(11):1640–1646.

34. Ioppolo F, Tattoli M, Di Sante L, Venditto T, Tognolo L, Delicata M, Rizzo RS, Di Tanna G, Santilli V (2013) Clinical improvement and resorption of calcifications in calcific tendinitis of the shoulder after shock wave therapy at 6 months' follow-up: a systematic review and meta-analysis. Arch Phys Med Rehabil, 94(9):1699-1706.
35. Yu H, Côté P, Wong JJ, Shearer HM, Mior S, Cancelliere C, et al (2021) Noninvasive management of soft tissue disorders of the shoulder: A clinical practice guideline from the Ontario Protocol for Traffic Injury Management (OPTIMa) collaboration. Eur J Pain, 25(8):1644-1667.
36. Haake M, Rautmann M, Wirth T (2001) Assessment of the treatment costs of extracorporeal shock wave therapy versus surgical treatment for shoulder diseases. Int J Technol Assess Health Care, 17(4):612–617.
37. Koorevaar RC, Terluin B, van 't Riet E, Madden K, Bulstra SK (2016) Validation of the four-dimensional symptom questionnaire (4DSQ) and prevalence of psychological symptoms in orthopedic shoulder patients. J Orthop Res, 34(4):683-691.
38. Koorevaar RC, van 't Riet E, Gerritsen MJ, Madden K, Bulstra SK (2016) The Influence of Preoperative and Postoperative Psychological Symptoms on Clinical Outcome after Shoulder Surgery: A Prospective Longitudinal Cohort Study. PLoS One, 15;11(11):e0166555.
39. Koorevaar RCT, Van't Riet E, Ipskamp M, Bulstra SK (2017) Incidence and prognostic factors for postoperative frozen shoulder after shoulder surgery: a prospective cohort study. Arch Orthop Trauma Surg, 137(3):293-301.
40. Hochheim M, Ramm P, Amelung V (2022) The effectiveness of low-dosed outpatient biopsychosocial interventions compared to active physical interventions on pain and disability in adults with nonspecific chronic low back pain: A systematic review with meta-analysis. Pain Pract. Epub ahead of print.
41. Hashmi Y, Zhou AK, Jawaid A, Zhou AY, Shah V, Thahir A, Krkovic M (2022) The role of acetic acid in orthopaedic surgery. J Perioper Pract, 32(6):162-166.
42. Acetic Acid. (2022, 14 oktober). Chemical Safety Facts. Geraadpleegd op 17 januari 2023, van https://www.chemicalsafetyfacts.org/chemicals/acetic-acid/
43. Leduc BE, Caya J, Tremblay S, Bureau NJ, Dumont M (2003) Treatment of calcifying tendinitis of the shoulder by acetic acid iontophoresis: a double-blind randomized controlled trial. Arch Phys Med Rehabil, 84(10):1523-1527
44. Darrieurtort-Laffite C, Bertrand-Vasseur A, Garraud T, Planche L, Le Goff B (2020) Tolerance and effect of sodium thiosulfate in calcific tendinitis of the rotator cuff. Clin Rheumatol. 39(2):561-569.
45. Kim SC, Lee SM, Park GT, Jang MC, Yoo JC (2021) Ultrasound-guided needle decompression and steroid injection for calcific tendinitis of the shoulder: risk factors for repeat procedures and outcome analysis. Clin Shoulder Elb, 24(2):55-65.

CHAPTER 9

Impact paragraph

Calcifying tendinitis of the shoulder is a disease in which one or multiple calcific deposits are located within one or more tendons of the rotator cuff. This results in a clinical presentation very similar to the subacromial pain syndrome with pain of the shoulder most often in combination with a limitation in the range of motion. [1] In the working population a lifetime prevalence of 34% is estimated. [2] In the Netherlands, the incidence of shoulder disorders in primary care is 19 per 1.000 persons-year. [2,3] Of the patients referred to the orthopaedic surgeon with atraumatic shoulder complaints in about 42.5% subacromial calcifications are observed. [2] Calcifying tendinitis of the shoulder has a large disease burden and causes impairments in daily living and decreases the workability of the affected patients. [4-6] Successful treatment of these patients will decrease their sick leave and improve the workability, particularly in patients with physically demanding jobs. [6] At first, the treatment is with conservative measures including physical therapy, anti-inflammatory drugs and/ or subacromial injection therapy. [5] When this conservative therapy fails the next step treatment still is not fully determined yet. Historically, a surgical treatment is proposed. However, in recent decades several minimal invasive treatment option have emerged and showed promising results. [5]

MAIN OBJECTIVE AND RESULTS

The main objective of the thesis was to outline a treatment algorithm for patients with conservative therapy resistant calcifying tendinitis of the shoulder. Several research questions needed to be addressed to propose such a treatment algorithm. In **chapter 2, 3 and 4** surgical treatment options of therapy resistant calcifying tendinitis were evaluated, because in current literature debate remains whether the calcifications need to be debrided and if an additional subacromial decompression is beneficial. Based on the performed studies included in the current thesis a preferable treatment procedure could be appointed. If a surgical treatment is chosen as a treatment for therapy resistant calcifying tendinitis an arthroscopic debridement of the calcification without a subacromial decompression is recommended. After this in **chapter 5**, the transition was made to a more minimal invasive approach and an evaluation was performed between surgical treatment and a minimal invasive treatment. This resulted in the recommendation that needle aspiration of calcific deposits (NACD), as a minimal invasive treatment option, is a valid alternative next step treatment option after a failed conservative treatment. Besides, chapter 5 showed that when a surgical treatment was performed after a failed NACD the clinical results were equal. Finally, in **chapter 6 and 7**, different minimal invasive treatment options were evaluated to clarify whether a preferable minimal invasive treatment strategy could be appointed. This showed that high energy focussed ESWT and NACD showed the most promising results and can be both be considered as a next step treatment option. In **chapter 7** a study protocol is presented which compares the two aforementioned minimal invasive therapies in a randomized fashion which evaluates the clinical outcome as well as cost effectiveness of both treatments.

RELEVANCE

In current orthopaedic literature debate remains what the next step treatment should be after a failed conservative treatment of calcifying tendinitis of the shoulder. [2] Surgical treatment show good and predictable clinical outcomes, but are invasive and desire a prolonged rehabilitation. [7] On the other hand, minimal invasive techniques, such as extracorporeal shockwave therapy (ESWT) or needle aspiration of the calcific deposit (NACD), show promising short-term clinical outcomes. Though, long term results were sparse in current literature. [8,9] Some authors even stated that these minimal invasive techniques may show comparable clinical outcomes to the surgical treatment. [10,11] However, trials that compare both minimal invasive treatment modalities were not available in current orthopaedic science. Therefore in orthopaedic literature, the exact place of these newer treatment modalities in the treatment algorithm for calcifying tendinitis was not established yet. [9,11] As such in the current guideline of subacromial pain syndrome (richtlijn subacromiaal pijnsyndroom) of the Dutch orthopaedic society (Nederlandse Orthopedische Vereniging, NOV), in which calcifying tendinitis is incorporated, the treatment of conservative therapy resistant calcifying tendinitis of the shoulder was marked as one of the knowledge gaps. Considering the acquired findings in this thesis, the current available treatment algorithm for calcifying tendinitis can be revisited. This algorithm will support the orthopaedic surgeon to make evidence-based decisions for the treatment of these patients (Figure 1).

TARGET GROUP AND COMMUNICATION TOWARDS TARGET GROUP

With the completion of this thesis knowledge gaps appointed in the current guideline of the subacromial pain syndrome were filled in. Communication towards other health care professionals was done by presenting the results of the individual studies at several congresses of the Dutch orthopaedic society and also at international congresses. Furthermore, the results of this thesis were published in several scientific articles. Besides, the presented algorithm could be incorporated within the guideline of the NOV regarding the subacromial pain syndrome. In this way it will help the

orthopaedic surgeon treating patients with calcifying tendinitis of the shoulder. The individual studies included in the current thesis all came from a clinical perspective to improve the quality of the treatment of conservative therapy resistant calcifying tendinitis of the shoulder. Therefore, for patients suffering from this disease the results and presented algorithm serves as a guide for treatment and provides more clarity on the next steps after conservative treatment of calcifying tendinitis of the shoulder has failed.

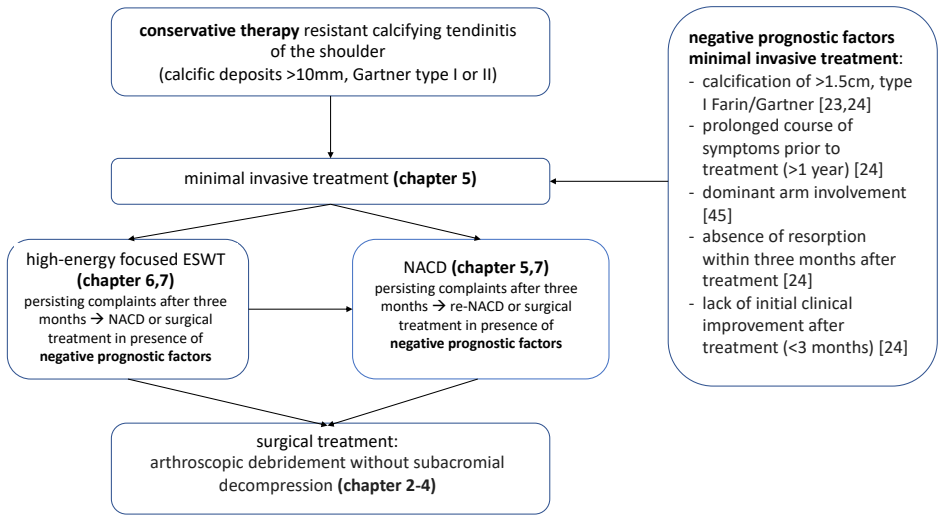

Figure 1. Treatment algorithm for patients with conservative therapy resistant calcifying tendinitis of the shoulder.

REFERENCES

1. Hurt G, Baker CL Jr (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am;34(4):567-575
2. Diercks R, Bron C, Dorrestijn O, Meskers C, Naber R, de Ruiter T, Willems J, Winters J, van der Woude HJ; Dutch Orthopaedic Association (2014) Guideline for diagnosis and treatment of subacromial pain syndrome: a multidisciplinary review by the Dutch Orthopaedic Association. Acta Orthop;85(3):314-322
3. Reilingh ML, Kuijpers T, Tanja-Harfterkamp AM, van der Windt DA (2008) Course and prognosis of shoulder symptoms in general practice. Rheumatology (Oxford);47(5):724-730
4. Uhthoff HK, Sarkar K, Maynard JA. (1976) Calcifying tendinitis: a new concept of its pathogenesis. Clin Orthop Relat Res;118:164-168
5. Diehl P, Gerdesmeyer L, Gollwitzer H, Sauer W, Tischer T (2011) Die Kalkschulter - Tendinosis calcarea [Calcific tendinitis of the shoulder]. Orthopade;40(8):733-746
6. Louwerens JKG, Kuijer PPFM, Sierevelt IN, van den Bekerom MPJ, van Royen BJ, Eygendaal D, van Noort A (2020) The Impact of Minimally Invasive Treatment for Rotator Cuff Calcific Tendinitis on Self-Reported Work Ability and Sick Leave. Arthrosc Sports Med Rehabil;2(6):821-827
7. Clement ND, Watts AC, Phillips C, McBirnie JM (2015) Short-Term Outcome After Arthroscopic Bursectomy Debridement of Rotator Cuff Calcific Tendonopathy With and Without Subacromial Decompression: A Prospective Randomized Controlled Trial. Arthroscopy;31(9):1680-1687
8. Bazzocchi A, Pelotti P, Serraino S, Battaglia M, Bettelli G, Fusaro I, Guglielmi G, Rotini R, Albisinni U (2015) Ultrasound imaging-guided percutaneous treatment of rotator cuff calcific tendinitis: success in short-term outcome. Br J Radiol;89(1057):20150407
9. Gatt DL, Charalambous CP (2014) Ultrasound-guided barbotage for calcific tendonitis of the shoulder: a systematic review including 908 patients. Arthroscopy;30(9):1166-1172
10. Castillo-González, FD, Ramos-Álvarez, JJ, Rodríguez-Fabián, G, González-Pérez, J, Calderón-Montero, J (2014) Treatment of the calcific tendinopathy of the rotator cuff by ultrasound-guided percutaneous needle lavage. Two years prospective study. Muscles, ligaments and tendons journal;4(2), 220–225
11. Randelli P, Margheritini F, Cabitza P, Dogliotti G, Corsi MM (2009) Release of growth factors after arthroscopic acromioplasty. Knee Surg Sports Traumatol Arthrosc;17(1):98-101

CHAPTER 10

Summary
Nederlandse samenvatting

SUMMARY

Shoulder disorders are common in the general population with an estimated lifetime prevalence of 34% in the Netherlands. [1] In patients with shoulder complaints, calcifying tendinitis is one the most commonly diagnosed diseases. [2] Conservative treatment is the first-choice treatment option. Conservative measures should include exercise therapy, anti-inflammatory drugs, ice therapy and/ or subacromial corticosteroid injections. However, in about 27% these treatment options are not successful and additional treatment is necessary. [3] The next step in the treatment of conservative therapy resistant calcifying tendinitis of the shoulder is however a matter of debate. In the general introduction several of these gaps in knowledge are pointed out. Also the following research questions are presented.

- *Part 1* Do the available surgical procedures lead to different functional outcomes in patients with conservative therapy resistant calcifying tendinitis of the shoulder?

- *Part 2* Do minimal invasive techniques result in comparable functional outcome compared to surgical treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder?

- *Part 3* What is the preferred minimal invasive treatment option for patients with conservative therapy resistant calcifying tendinitis of the shoulder?

The thesis is built up based on these knowledge gaps and is divided into three parts. In the general discussion a treatment algorithm is proposed for the treatment of calcifying tendinitis of the shoulder: In *part 1* the surgical treatment options are evaluated. Historically the surgical treatment is seen as the next step treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder. In **chapter 2** a systematic review of the literature is performed concerning three surgical treatment options. The first is only a subacromial decompression and leaving the calcifications untouched. The second is debriding the subacromial calcific deposits without an additional subacromial decompression. The third is a combination of debridement of the calcific deposits in combination with a subacromial decompression. Based on the available orthopaedic literature the clinical and functional outcomes after all these aforementioned surgical procedures are good to excellent. However, a randomized controlled trial comparing all three surgical procedures was not performed yet. Therefore, a preferential procedure cannot be appointed. In **chapter 3** we present retrospective study that evaluated the mid-term clinical outcomes of patients who underwent a subacromial decompression while leaving the calcific deposits untouched. The primary outcome (Constant-Murley Score, CMS) was good to excellent (mean CMS 84.9) after a mean follow-up of 2.9 years. In 52% the calcific deposits vanished during follow-up. However, a correlation between the presence of any residual calcific deposits could not be established: The CMS did not differ significantly between patients with and without residual subacromial calcific deposits. In **chapter 4** a randomized controlled trial (RCT) was executed. The short-term clinical outcomes of the three aforementioned surgical treatment options were evaluated. All three surgical treatment options provided good clinical outcomes six months after treatment, while at six months follow-up the VAS for pain did not differ between the three groups. Noteworthy however, significant differences were observed in the VAS for pain and Disability of Arm, Shoulder and Hand (DASH) scores six weeks after treatment. The group of patients that only had a subacromial decompression showed less clinical improvement compared to the group of patient in which the calcifications were debrided. Furthermore, they needed more additional treatment in the postoperative period. We therefore advise to debride the calcification without an additional subacromial decompression when operating on a patient with conservative therapy resistant calcifying tendinitis of the shoulder.

In *part 2* a transition from a surgical approach to a more minimal invasive approach is explored. Needle aspiration of the calcific deposits (NACD) is proposed as a next step treatment for conservative therapy resistant calcifying tendinitis of the shoulder. In current literature, no comparative studies are available in which the clinical outcome of a surgical treatment is compared to the NACD treatment. In **chapter 5** a comparative cohort study was performed and the midterm clinical outcomes were evaluated. The primary outcome was improvement of VAS for pain during follow-up. This improvement did not differ between the two groups after a mean follow-up of 5.5 years: improvement in VAS for pain of 60.6 mm versus 53.4 mm, for the NACD and surgery group, respectively. 31% of the patients switched over from the NACD treatment to the surgical treatment because of unsatisfactory clinical improvement and insufficient decrease in size of the calcific deposit. Patients who had a surgical treatment after a failed NACD also showed good clinical outcomes. Furthermore, partly as a result of the aforementioned substantial number of cross over significantly more additional treatments and adverse events were administered in the NACD group. However, due to the good clinical outcome on the midterm it seems that NACD treatment is a valid alternative treatment option for conservative therapy resistant calcifying tendinitis, although more research in a randomized fashion is desirable.

In *part 3* the optimal minimal invasive treatment strategy is explored. As stated in the general introduction minimal invasive treatment, especially NACD and ESWT, show promising short term clinical results. However, the optimal treatment strategy is still a

matter of debate. Many different treatment protocols of ESWT available. In **chapter 6** a meta-analyses of five RCTs comparing low-energy to high-energy ESWT were performed. The primary outcome was comparing the short-term improvement of the CMS. Furthermore, a secondary outcome was the likelihood of significant resorption of the calcific deposit after low-energy ESWT versus high-energy ESWT. All five RCTs showed greater improvement in CMS in patients treated with high-energy ESWT compared to low-energy ESWT at 3- and 6-months post-treatment. The mean difference was after three 3-months. Besides, high-energy ESWT more often resulted in complete resorption of the deposits at 3 months. Therefore, if ESWT is chosen as a next step treatment for calcifying tendinitis of the shoulder high-energy ESWT should be chosen. Furthermore, in current literature the evidence evaluating the effectiveness of NACD compared to ESWT is limited. Only two RCTs are currently available that both use markedly different ESWT treatment protocols compared to our preferred ESWT protocol. [5,6] In **chapter 7** a study protocol was presented for a RCT comparing NACD and ESWT. In this study patients are randomly allocated to either NACD or ESWT. The primary outcome is difference in improvement of CMS after 12 months. This is final step in answering the relevant research questions to establish a novel treatment algorithm for the treatment of conservative therapy resistant calcifying tendinitis of the shoulder.

In conclusion, this thesis provides the orthopaedic surgeon guidance in choosing the appropriate next step treatment for patients with conservative therapy resistant calcifying tendinitis of the shoulder. Although still some research question remain, in **chapter 8** a treatment algorithm is proposed. Furthermore, in this general discussion several new research aims are appointed.

NEDERLANDSE SAMENVATTING

Schouderklachten zijn veelvoorkomende klachten binnen de Nederlandse maatschappij met een levensprevalentie van 34%. [1] Tendinitis calcarea is een van de meest gestelde diagnosen bij patiënten met schouderklachten gezien door de orthopedisch chirurg. [2] De behandeling van eerste keuze is conservatief. Conservatieve behandelmogelijkheden zijn onder andere oefentherapie onder leiding van een gespecialiseerde schouder-fysiotherapeut, anti-inflammatoire medicijnen (NSAIDs) en/ of subacromiale infiltraties. Echter, in ongeveer 27% van de gevallen zijn deze maatregelen niet succesvol en is een aanvullende therapie noodzakelijk. [3] In de huidige orthopedische literatuur zijn er juist bij deze aanvullende behandelingsmogelijkheden nog veel vragen onbeantwoord en bestaan er enige hiaten in kennis. In de algemene introductie worden deze hiaten onderkent en worden de hieronder genoemde onderzoeksvragen geformuleerd.

- *Part 1* Leiden de beschikbare chirurgische behandelopties tot verschillende functionele uitkomst voor conservatieve therapieresistente tendinitis calcarea van de schouder

- *Part 2* Kunnen minimaal invasieve technieken leiden tot vergelijkbare functionele uitkomsten vergeleken met een operatieve behandeling voor patiënten met conservatieve therapieresistente tendinitis calcarea van de schouder?

- *Part 3* Is er een te prefereren minimaal invasieve techniek voor patiënten met conservatieve therapieresistente tendinitis calcarea van de schouder?

Deze thesis is opgebouwd aan de hand van deze hiaten in kennis en is onderverdeeld in verschillende *'parts'*. In de algemene discussie van het proefschrift wordt een behandelalgoritme gepresenteerd voor de behandeling van conservatieve therapieresistente tendinitis calcarea van de schouder: In '*part 1'* worden de chirurgische behandelopties geëvalueerd. Historisch gezien wordt de chirurgische behandeling gezien als de behandeling van keuze voor conservatieve therapieresistente tendinitis calcarea van de schouder. In **hoofdstuk 2** is een systematische review uitgevoerd. Drie verschillende chirurgische behandelopties zijn bekeken. De eerste is het enkel uitvoeren van een subacromiale decompressie en de verkalkingen ongemoeid laten. De tweede is enkel het verwijderen van de verkalkingen zonder een aanvullende subacromiale decompressie te verrichten. De derde optie is een combinatie van bovenstaande procedure, namelijk het verwijderen van verkalkingen tezamen met een subacromiale decompressie. Op basis van de beschikbare literatuur kan gezegd worden dat elke

van de drie bovengenoemde procedures leidt tot goede tot excellente klinische uitkomsten. Echter, gerandomiseerde studies die de klinische uitkomsten van alle drie de behandelopties vergelijken zijn niet beschikbaar. Daarom kan op basis van de huidige literatuur nog geen te prefereren chirurgische procedure worden gekozen. In **hoofdstuk 3** is een retrospectieve studie gepresenteerd. In deze studie zijn de klinische uitkomsten op middellange termijn gepresenteerd van patiënten die enkel een subacromiale decompressie hebben ondergaan waarbij de verkalkingen ongemoeid zijn gelaten. Na een follow-up van gemiddeld 2.9 jaar liet dit goede tot excellente klinische uitkomsten zien. In 52% van de patiënten werden er bij follow-up geen subacromiale verkalkingen meer waargenomen. Er kon geen correlatie worden vastgesteld tussen de aanwezigheid van restverkalkingen en de goede klinische uitkomst. De CMS verschilde niet significant tussen patiënten waarbij de kalk nog aanwezig vergeleken met patiënt waarbij de kalk verdwenen ten tijde van follow-up. In **hoofdstuk 4** is een gerandomiseerde studie gepresenteerd. De korte termijnsresultaten van de bovengenoemde chirurgische behandelopties vergeleken. Alle drie de opties laten goede klinische uitkomsten zien zes maanden na operatief ingrijpen. De primaire uitkomst (Visual Analog Scale, VAS voor pijn zes maanden na behandeling) was niet significant verschillend tussen de drie groepen. Er werd wel een significant verschil waargenomen tussen de klinische uitkomsten na zes weken. De verbetering in VAS voor pijn en beperkingen (gemeten met de disability of arm, shoulder and hand score, DASH score) was significant minder bij patiënten die enkel een subacromiale decompressie hadden ondergaan. Daarnaast waren er meer bijbehandelingen in deze patiëntengroep. De hypothese hierbij is dat het operatief ingrijpen leidt tot een activatie van de natuurlijke resorptiefase van tendinitis calcarea. Van deze resorptiefase is gekend dat dit leidt tot een hernieuwde tendinitis en kan eveneens een chemische bursitis veroorzaken. [4] Daarom kan geconcludeerd worden dat indien gekozen wordt voor operatief ingrijpen het te adviseren is om de verkalkingen te verwijderen.

In '*part 2*' wordt de transitie van de chirurgische benadering naar een meer minimaal invasieve benadering geëvalueerd en aan NACD-behandeling wordt voorgesteld als behandeling van conservatieve therapieresistente tendinitis calcarea van de schouder. In de huidige orthopedische literatuur zijn er geen vergelijkende studies beschikbaar welke de klinische uitkomsten vergelijken van chirurgische behandeling met de barbotage behandeling. In **hoofdstuk 5** is een vergelijkend cohortstudie uitgevoerd welke klinische uitkomsten evalueert van deze twee behandelingen op de middellange termijn. De primaire uitkomst was de verbetering van VAS voor pijn gedurende follow-up. Deze verbetering verschilde niet significant tussen de twee groepen. Een substantieel deel van de patiënten (31%) die initieel een barbotage behandeling hebben ondergaan zijn overgestapt en hebben een chirurgische behandeling ondergaan. Er werd gekozen voor een chirurgische behandeling vanwege onvoldoende klinische verbetering en daarnaast

onvoldoende afname van de verkalking op de controlefoto. Patiënten die deze overstap gemaakt hebben lieten na een gemiddelde follow-up van 5.5 jaar echter eenzelfde goede klinische uitkomst zien ten opzichte van de patiënten uit de initieel chirurgische groep. Daarnaast werden er significant meer bijbehandelingen en complicaties geregistreerd binnen de barbotage groep. Dit is echter grotendeels toe te schrijven aan het grote aantal patiënten dat is overgestapt tussen de twee groepen. Gezien dat ook deze patiënten een goede klinische uitkomst lieten zien bij follow-up kan een barbotage behandeling toch een geschikte alternatieve behandeling zijn voor patiënten met conservatieve therapieresistente tendinitis calcarea van schouder. Echter, meer onderzoek met name een gerandomiseerde studie is wenselijk.

In *'part 3'* wordt de optimale minimaal invasieve behandeling geëvalueerd. Zoals al benoemd in de algemene introductie laten minimaal invasieve technieken, in het bijzonder NACD en ESWT, veelbelovende resultaten zien. Echter, de optimale behandelstrategie is nog een punt van discussie. ESWT wordt op veel verschillende manieren gebruikt en worden veel verschillende behandelprotocollen gebruikt. Bijvoorbeeld, het is nog niet gekend of hoog-intensiteit of laag-intensiteit ESWT betere korte termijn klinische resultaten geeft. In **hoofdstuk 6** is een meta-analyse uitgevoerd van vijf gerandomiseerde studies die laag-intensiteit ESWT hebben vergeleken met hoog-intensiteit ESWT. De primaire uitkomst was de vergelijking van de CMS en de kans op significante afname (resorptie) van de verkalking na hoog-intensiteit versus laag-intensiteit ESWT. Alle vijf de gerandomiseerde studies lieten na drie en zes maanden een grotere verbetering in CMS zien in patiënten die zijn behandeld met hoog-intensiteit ESWT vergeleken met laag-intensiteit ESWT. Daarnaast was de kans op complete resorptie na drie maanden significant groter na hoog-intensiteit ESWT. Geconcludeerd kan worden dat wanneer er gekozen wordt voor een behandeling middels ESWT, hoog-intensiteit ESWT de te prefereren behandeling is. De huidige literatuur aangaande de vergelijking tussen de verschillende minimaal invasieve behandeling is erg beperkt. Slechts twee gerandomiseerde zijn beschikbaar. Deze beide studies gebruiken beide een significant verschillend ESWT-protocol vergeleken met het door ons geprefereerde protocol. [5,6] Om tot een te prefereren minimaal invasieve therapie te komen wordt momenteel een gerandomiseerde studie uitgevoerd. In deze studie zijn patiënten gerandomiseerd tussen een NACD-behandeling en een ESWT-behandeling. De primaire uitkomst was verbetering in CMS na twaalf maanden. Het studieprotocol hiervan werd gepresenteerd in **hoofdstuk 7.** Dit was de laatste stap om alle benodigde onderzoeksvragen te beantwoorden om tot een nieuw behandelalgoritme te komen voor patiënten met conservatieve therapieresistente tendinitis calcarea van de schouder.

Concluderend geeft deze thesis de orthopedisch chirurg meer sturing bij het kiezen van de adequate behandeling voor patiënten met conservatieve therapieresistente

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tendinitis calcarea van de schouder. In **hoofdstuk 8** wordt het nieuwe behandelalgoritme gepresenteerd en daarnaast worden er nog nieuwe onderzoeksvragen geformuleerd en onderzoeksdoelen gepresenteerd.

REFERENCES

1. Diercks R, Bron C, Dorrestijn O, Meskers C, Naber R, de Ruiter T, Willems J, Winters J, van der Woude HJ; Dutch Orthopaedic Association (2014) Guideline for diagnosis and treatment of subacromial pain syndrome: a multidisciplinary review by the Dutch Orthopaedic Association. Acta Orthop;85(3):314-322
2. Hurt G, Baker CL Jr (2003) Calcific tendinitis of the shoulder. Orthop Clin North Am;34(4):567-575
3. Ogon P, Suedkamp NP, Jaeger M, Izadpanah K, Koestler W, Maier D (2009) Prognostic factors in nonoperative therapy for chronic symptomatic calcific tendinitis of the shoulder. Arthritis Rheum;60(10):2978-2984
4. Oudelaar BW, Van Liebergen MR, Van Arkel ERA (2021) Een vrouw met acuut ontstane schouderklachten [A woman with acute-onset shoulder pain]. Ned Tijdschr Geneeskd;18;165
5. Kim YS, Lee HJ, Kim YV, Kong CG (2014) Which method is more effective in treatment of calcific tendinitis in the shoulder? Prospective randomized comparison between ultrasound-guided needling and extracorporeal shock wave therapy. J Shoulder Elbow Surg;23(11):1640-1646
6. Louwerens JKG, Sierevelt IN, Kramer ET, Boonstra R, van den Bekerom MPJ, van Royen BJ, Eygendaal D, van Noort A (2020) Comparing Ultrasound-Guided Needling Combined With a Subacromial Corticosteroid Injection Versus High-Energy Extracorporeal Shockwave Therapy for Calcific Tendinitis of the Rotator Cuff: A Randomized Controlled Trial. Arthroscopy;36(7):1823-1833

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APPENDICES

&

Dankwoord
Curriculum Vitae
List of publications

DANKWOORD

Dit is een proefschrift met onderzoeken allen gebaseerd op klinische vraagstukken met als doel om bestaande behandelingen voor patiënten met conservatieve therapie resistente tendinitis calcarea van de schouder te optimaliseren. Daarom wil ik als eerste in dit dankwoord alle patiënten bedanken die hebben deelgenomen aan de verschillende studies.

Beste prof. dr. van Rhijn, Beste Lodewijk. Achteraf denk ik dat ik te laat in mijn promotietraject bij u heb aangeklopt, uiteindelijk heb ik dit pas in 2017 gedaan. Toen waren de studies in dit proefschrift veelal al lopende. Uw brede blik hebben me laten inzien dat je klinische vraagstukken op meerdere manieren kunt beantwoorden en daarmee is u bijdrage aan dit proefschrift zeer waardevol gebleken. Daarnaast liet u me zien dat er een licht aan einde van de tunnel was. Waarop ik dan antwoorde dat ik het leven in die tunnel ook wel een beu was. Ook na uw transfer naar Utrecht bent u altijd zeer betrokken geweest bij de voortgang van dit proefschrift. Dank voor deze begeleiding en de vele interessante gesprekken.

Beste dr. Jansen, Beste Ed. Nadat ik was aangenomen als ANIOS in het Orbis MC hadden wij direct een klik. Nadat ik via jullie in opleiding was gekomen ging onze kalk-studie van start. Na zeer veel bijsturing en zeer veel energie die we daar beide ingestoken hebben, hebben we de studie tot een goed einde kunnen brengen. Ik heb je begeleiding altijd als zeer prettig ervaren en enorm gewaardeerd, door jou geloof in mij gedurende mijn ANIOS ben ik nu orthopeed kunnen worden. Ook waardeer ik elke keer weer als een manuscript van je terug kreeg dat je het weer van A tot Z had doorplozen en had becommentarieert. Al mochten de verbeteringen en daarmee het roodgehalte in de tekst wel iets minder.

Beste dr. van der Steen, Beste Marieke. Meermaals vroeg ik (tegen beter weten in) ‘zullen we toch geen interim-analyse doen van de NECST-studie’. Waarop ik steevast het antwoordt kreeg: ‘Nee Freek, dat is niet zo afgesproken in het studie protocol en daar moeten we ons aan houden. ’ Dit kenmerkt jou. Ik kon je altijd alle vragen stellen over de verschillende studies. Het antwoord was altijd correct, alleen niet altijd wat ik wilde horen. Deze eerlijkheid en oprechtheid heb ik altijd enorm gewaardeerd en daarmee ben je voor dit proefschrift zeer belangrijk geweest.

Beste dr. Morrenhof en dr. Loes Janssen. Bij jullie heb ik gedurende de laatste fase van mijn geneeskunde opleiding de eerste stappen gezet op wetenschappelijk gebied. Achteraf bleek dit de basis van dit proefschrift. Wat ik nog goed weet is de maandelijkse besprekingen waar we de voortgang van het onderzoek bespraken maar ook mijn verrichtingen op het voetbalveld die dr. Morrenhof via de krant op de voet volgde. De enthousiasmerende begeleiding van jullie beiden in deze beginfase gaf mij de motivatie om op basis van het daar uitgevoerde onderzoeken nog vervolgonderzoeken op te zetten wat tot dit proefschrift heeft geleidt.

Beste dr. ir. Schotanus, Beste Martijn. Als beginnend ANIOS in het Orbis MC had ik een duidelijk doel voor ogen, namelijk in opleiding komen. Ik wist dat wetenschappelijk onderzoek doen hiervoor noodzakelijk zou zijn. Hierbij heb je me vanaf moment één de juiste begeleiding gegeven met het opzetten van verschillende onderzoeken. Vaak met serieuze tips maar even zo vaak met de meest onzinnige appjes en GIF-jes. Deze onorthodoxe begeleiding zorgde ervoor dat ik altijd met veel plezier aan de verschillende onderzoeken heb gewerkt en daar ben ik je erg dankbaar voor! Jij weet als geen ander iemand te motiveren en kent de waarde van een goed werkend team!

Dank ook aan alle **co-auteurs**. Onderzoek doen is een teamsport. Jullie aanvullingen, kritische blik op de verschillende manuscripten en hulp bij de verschillende studies heb ik altijd zeer gewaardeerd.

Luuk. We zijn eigenlijk al na het einde van de middelbare school aan elkaar verbonden. We zijn beide in Maastricht gestart met de studie gezondheidswetenschappen, later hebben we geneeskunde gedaan en zijn we tegelijkertijd in opleiding gekomen tot orthopedisch chirurg. Daarnaast zijn we ook buiten het ziekenhuis veel met elkaar verbonden door tennis. Daar en ook op de werkvloer waardeer ik je ontzettend. Je ongekende kennis en ongecompliceerde mentaliteit is iets wat ik graag van je zou willen overnemen. Nu is de afstand weliswaar een bemoeilijkende factor maar we hebben nog vaak contact en dat zou ik graag zo blijven zien. Leuk dat jij paranimf bij mij wil zijn.

Anouk. wat vind ik het leuk dat je mijn paranimf wil zijn. Jij bent mijn oudere zus en we verschillen wellicht nog wel meer van elkaar dan dag en nacht. In onze jeugd zijn we beiden niets tekort gekomen en zijn we beide op onze eigen manier op de juiste manier gestimuleerd door onze ouders. Waar we in onze jeugd nog wel eens ruzie hadden, is er nu vooral veel waardering wederzijds. Waardering heb ik voor je doorzettingsvermogen, daadkracht en hoe je een drukke baan kan combineren met een druk gezinsleven in Utrecht.

Orthopeden en opleiders, arts-assistenten, collega’s van de operatiekamers, polikliniek, verpleegkundigen van de verschillende afdelingen van de ROGO-Zuid dank voor de prettige samenwerking de afgelopen jaren. Al heb ik de regio nu verlaten kijk ik met veel plezier terug op mijn opleiding in ROGO-Zuid.

Vakgroep Orthopedie Zorgsaam Zeeuws-Vlaanderen. Cis, Maarten-Paul, Frank, Frank en Bas. Sinds één jaar ben ik bij jullie werkzaam. Hoewel de overgang buiten het

ziekenhuis best wel groot is, hebben jullie ervoor gezorgd dat de overgang van Limburg naar Zeeland binnen het ziekenhuis zeer prettig is verlopen. We zijn een goed team en ik kijk ernaar uit om de komende tijd met jullie te mogen samenwerken. Daarnaast, **dr. Karelse, Anne,** je was vanaf het begin zeer geïnteresseerd naar de voortgang van de eindfase van mijn promotietraject. Nu is het af en zie ik ernaar uit om gezamenlijk ons schouderteam sterk uit te dragen en uit te bouwen.

Beste vriendenclub 'pep/ ut kaartclubje'. Wat hebben we al mooie feesten en vakanties mogen meemaken in de afgelopen 20 jaar. Hoewel ik er ook de nodige gemist heb. Ook ons jaarlijks weekend weg is voor mij altijd iets om naar uit te kijken. Laten we dit de komende 20 jaar ook maar gewoon blijven doen.

Lieve Pap en Mam. Dank voor de ongekende support die jullie mij hebben gegeven eigenlijk al sinds de basisschool. Het geloof dat jullie altijd in mij hebben gehad. Bijvoorbeeld door mij niet naar het VMBO te laten gaan, maar naar een VMBO/HAVO overgangsklas. Wat ben ik dan ook blij dat ik jullie gelijk heb kunnen laten zien! Jullie zijn mijn stabiele basis en zijn in mijn hele studietijd van onschatbare waarde geweest. In het begin om me te motiveren om het beste uit mezelf te halen en later om ook de balans tussen werk/privé te laten inzien. Weet dat ik dat voor altijd zal waarderen! *En zoals pap zeat: 'ut kump allemaol good, wach maar ens aaf'.*

Tonnie en Ellis. Sinds jaar en dag ben ik één van jullie gezin en sinds een paar jaar jullie onderdeel van ons gezin. Dank dat jullie altijd voor ons klaar staan, voor de grenzeloze liefde die jullie geven aan ons en onze jongens, Mats en Siem. Ik bof maar dat ik jullie als schoonfamilie mag hebben.

Mats en Siem. Wat zijn jullie een stel fantastische kinderen. Wat geniet ik ervan om urenlang met jullie te spelen en wat kijk ik ernaar uit om jullie op te zien groeien en te zien hoe jullie zich gaan ontwikkelen. Voor nu geniet van elk moment dat ik met jullie mag doorbrengen, jullie laten me zien wat er echt belangrijk is in het leven.

Lieve Britt. De laatste woorden van dit dankwoord zijn natuurlijk voor jou. Al sinds 2003 ben jij mijn stabiele basis. Ook binnen deze promotie ben je een hele belangrijke factor. Van me de ruimte geven om weer eens een middagje vragenlijsten in Excel of SPSS te tikken, tot het klaarmaken van de enveloppen met vragenlijsten voor de verschillende studies. Ik zeg dit onvoldoende tegen je maar je bent een fantastische vrouw en geweldige moeder voor onze kinderen. We gaan er samen een mooie tijd van maken in Zeeland en hoop samen met je oud te worden.

CURRICULUM VITAE

Freek Verstraelen was born in Venlo, the Netherlands on the 9th of December in 1987. He grew up in the loving family of Leo and Marjet Verstraelen as the younger brother of Anouk Verstraelen. He graduated from the VWO at the Blariacum College in Venlo in 2005. He started studying medicine in the next year. During this study he developed a special interest in the musculoskeletal system and did several internships at the orthopedic and traumatology department in the Viecuri Medical Center in Venlo. In his final internship he performed the research which was the foundation for the current thesis.

After his graduation as Master in Medicine in 2013 he started working as a resident at the Orbis Medical Centre. During this period Freek continued to perform research in the field of calcifying tendinitis of the shoulder. In 2015 he started his residency in orthopedic surgery with the department of general surgery of the Viecuri MC (dr. H. Janzing). His orthopedic residency continued with the orthopedic training in the Màxima MC (dr. R. Janssen), Viecuri MC (dr. O. Lambers Heerspink), Maastricht University Medical Centre (dr. H. Staal). During his residency he continued to work on the several clinical studies within this thesis.

After becoming an orthopedic surgeon in 2020. He started working at the Zuyderland MC and did a shoulder and elbow fellowship at the Zuyderland MC. In 2023 he started working in the Zorgsaam Ziekenhuis Zeeuws-Vlaanderen as an orthopedic surgeon specialized in upper extremity pathology and traumatology.

In 2017 he married Britt Derks and currently they live together with their two sons (Mats, 2019 and Siem, 2021) in Terneuzen, Zeeuws-Vlaanderen, the Netherlands.

LIST OF PUBLICATIONS

WITHIN THIS THESIS

Verstraelen FU, Fievez E, Janssen L, Morrenhof W (2017) Surgery for calcifying tendinitis of the shoulder: A systematic review. World J Orthop;8(5):424-430

Verstraelen FU, Glimmerveen ND, Janssen L, Morrenhof W (2015) Isolated acromioplasty for calcific tendinitis produces good results at 3-year follow-up: clinical outcome is not correlated to presence of residual calcifications. Curr Orthop Practice;26: 363-366

Verstraelen FU, Schotanus MGM, Klemann-Harings SEJM, Lambers Heerspink FO, Jansen EJP (2022) Comparison of clinical and radiological outcomes after three different surgical treatments for resistant calcifying tendinitis of the shoulder: a short-term randomized controlled trial. J Orthop Surg Res;17(1):480

Verstraelen FU, Bemelmans Y, Lambers Heerspink O, van der Steen M, Jong B, Jansen E, Schotanus M. Comparing midterm clinical outcome of surgical versus ultrasound guided needle aspiration of the calcific deposits for therapy resistant calcifying tendinitis of the shoulder. A comparative cohort study. J Orthop Sci. 2023 18:S0949-2658

Verstraelen FU, In den Kleef NJHM, Jansen L, Morrenhof JW (2014) High-energy versus low-energy extracorporeal shock wave therapy for calcifying tendinitis of the shoulder: which is superior? A meta-analysis. Clin Orthop Relat Res;472(9):2816-25

Verstraelen FU, Verhagen S, Giesberts A, Bonneux I, Koot H, Boer WD, van der Steen M. Needle aspiration of calcific deposits versus shock wave therapy for conservative therapy resistant calcifying tendinitis of the shoulder: protocol of a randomized, controlled trial. BMC Musculoskelet Disord. Mar 31;23(1):308

OTHER PUBLICATIONS

Vesseur MA, van Haasteren JC, **Verstraelen FU**, Boonen B. Osteochondral impression fracture of the patella after sports collision injury. BMJ Case Rep;16(2):e253825

Verstraelen FU, Horta LA, Schotanus MGM, Kort NP, Samijo SK, Jansen EJP. (2018) Clinical and radiological results 7 years after Copeland Shoulder resurfacing arthroplasty in patients with primary glenohumeral osteoarthritis: an independent multicentre retrospective study. Eur J Orthop Surg Traumatol; 28:15–22

Verstraelen FU, Arts SJ, Schotanus MGM, Kort NP, Jansen EJP. (2016) Osseous tuberculosis located in the ilium: a case report and review of the literature. Int J Adv Case Rep;3(7):373-377

SCIENTIFIC PRESENTATIONS

Verstraelen FU, Schotanus MGM, Klemann-Haring S, Lambers Heerspink FO, Jansen EJP. All surgical treatment options for therapy resistant calcifying tendinitis of the shoulder are effective, but is there a difference in effectiveness? A three-arm randomized clinical trial. EFORT Congress, July 2021. *Awarded: Best free paper award*

Verstraelen FU, In den Kleef NJ, Jansen L, Morrenhof JW. High- energy Versus Low-energy Extracorporeal Shock Wave Therapy for Calcifying Tendinitis of the Shoulder: Which is Superior? A Meta-analysis. NOF Congress, May 2014

Verstraelen FU, Glimmerveen N, Morrenhof JW, Janssen L. Is the presence of rotator cuff calcifications related with the long term functional outcome in patients with calcifying tendinitis of the shoulder treated by acromioplasty alone? NOV Congress, October 2013