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# Calcific tendinopathy of the shoulder: clinical perspectives into the mechanisms, pathogenesis, and treatment

Valerio Sansone<sup>1,2</sup>  
Emanuele Maiorano<sup>1</sup>  
Alessandro Galluzzo<sup>1</sup>  
Valerio Pascale<sup>1,2</sup>

<sup>1</sup>Department of Orthopaedics, University of Milan, <sup>2</sup>Department of Orthopaedics, I.R.C.C.S. Istituto Ortopedico Galeazzi, Milan, Italy

**Abstract:** Calcific tendinopathy (CT) of the shoulder is a common, painful condition characterized by the presence of calcium deposits in the rotator cuff tendons. Current theories indicate that CT may be the result of a cell-mediated process in which, after a stage of calcium deposition, calcifications are spontaneously resorbed. However, in a minority of cases, this self-healing process is somehow disrupted, resulting in symptoms. Recent literature shows an emerging role of biological and genetic factors underlying CT. This new evidence could supplement the classic mechanical theory of rotator cuff tendinopathy complicated by calcium precipitation, and it may also explain why the majority of the therapies currently in use are only able to provide partially satisfactory outcomes. This review aims to summarize the current knowledge about the pathological processes underlying CT of the shoulder and thereby justify the quest for advanced biological treatments of this condition when it becomes symptomatic.

**Keywords:** rotator cuff tendons, calcific tendinopathy, calcific deposits, shoulder, tendinitis, review

## Introduction

Rotator cuff disease of the shoulder includes a broad spectrum of disorders, among which calcific tendinopathy (CT) plays a prominent role. Although CT is observed mostly in the shoulder, it can be found throughout the body.<sup>1</sup> CT of the shoulder is a common painful disorder characterized by the presence of calcifications in either the mid-substance or insertion of the rotator cuff tendons and in the synovial tissues, including the subacromial bursa. The calcific material comprised clusters of calcium hydroxyapatite in crystalline or amorphous form.<sup>2</sup> Pain related to repetitive activities, tenderness, local edema, and varying degrees of impairment are the usual clinical features. Although the condition resolves spontaneously in many cases, a significant number of patients remains symptomatic, with no radiographic evidence of improvement. In these cases, the natural cycle of calcific deposition within tendons followed by deposits' resorption is somehow halted. Several treatments are currently in use, although the best choice remains controversial. There is, however, a fairly large consensus in starting with a conservative therapeutical approach based on rest, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and, in later stages, corticosteroids' subacromial infiltrations. Surgery is recommended only when conservative treatment is unsuccessful. The aim of this review is to illustrate the recent advances in the understanding of the pathological processes that characterize CT of the shoulder and to provide current evidence for its diagnosis and treatment.

Correspondence: Valerio Sansone  
Department of Orthopaedics, I.R.C.C.S.  
Istituto Ortopedico Galeazzi, Via  
Riccardo Galeazzi 4, 20161 Milan, Italy  
Tel +39 02 6621 4921  
Fax +39 02 6621 4736  
Email [valerio.sansone@unimi.it](mailto:valerio.sansone@unimi.it)

## Epidemiology

The prevalence of CT in adults has been reported to span between 2.7% and 10.3%;<sup>3–6</sup> ~50% of these patients eventually become symptomatic.<sup>7</sup> The condition is more common in women, who are two-fold more affected than men.<sup>8</sup>

It is commonly presented in patients aged 30–60 years and is bilateral in ~10%–25% of subjects.<sup>7–9</sup> Furthermore, CT is known to plague people whose occupation necessitates extended implementation of the arms in internal rotation and slight abduction, such as desk workers, cashiers, tailors, and production line workers. CT patients with these backgrounds demonstrate a different kind of etiopathogenesis when compared with other forms of tendinopathy. When the arm is maintained in internal rotation with a slight abduction, the rotator cuff muscles contract, making the most susceptible zone more vulnerable as a result of its ischemic state. This zone corresponds to the hypovascular area of the supraspinatus tendon just medial to the insertion on the greater tuberosity.<sup>10</sup> This biomechanical explanation of rotator cuff tendinopathy is dissimilar to the biological rationale of tendon degeneration used to explain tendinopathy in other locations in the body (eg, achilles tendinopathy and lateral epicondylitis). A correlation with hip calcifications has also been reported.<sup>11</sup>

However, most of these data are not recent and are primarily based on radiographic observations of asymptomatic populations.<sup>3,12–14</sup> With the recent technological advances in imaging techniques such as ultrasound (US) and magnetic resonance, more accurate and detailed analysis of anatomic structures is now possible. Therefore, it is reasonable to deduce that the prevalence of CT may be higher than previously reported.

The US equipment currently in use has a resolution so high that details as small as 300  $\mu$  can be detected, allowing the visualization of very small deposits. Using this technology, two recent studies on female populations between 18 and 65 years showed a CT prevalence of 24.4% and 17.1%, respectively.<sup>15,16</sup>

Regarding the localization of calcifications, all previous reports concur that the supraspinatus tendon is most commonly involved (with an incidence of 51.5%–90% of cases), with negligible rates for the other tendons.<sup>3,5,17</sup> While one study<sup>16</sup> confirmed the most frequent localization in the supraspinatus tendon, they reported a much higher involvement of infraspinatus (~50%) and subscapularis (33%) than in previous studies.<sup>3,5,17</sup> In addition, the authors found the distribution of multifocal calcific deposits to have a prevalence of 28.2% compared with the 8% previously reported.<sup>18</sup> In line

with the literature,<sup>13</sup> the authors recorded that all the calcifications were insertional, situated in the so-called “critical zone” resulting from its poor vascularization.<sup>16</sup>

## Etiology

The origin of CT is still controversial. Several hypotheses for the pathological process have been suggested: degenerative,<sup>19</sup> repetitive trauma,<sup>3</sup> tenocyte necrosis,<sup>20</sup> reactive,<sup>9</sup> and endochondral ossification;<sup>21,22</sup> however, none of these explanations have shown to be entirely satisfactory. Furthermore, extrinsic factors such as age and BMI have proved to be associated with shoulder pain in CT. The increase in pain with age closely resembles the observations for rotator cuff tears,<sup>23,24</sup> and similarly, an abnormal BMI was also found to be a risk factor for developing a rotator cuff tear or tendinopathy.<sup>25,26</sup>

Recent investigations using tendon stem cells (TSCs) housed in particular spaces called “niches” of humans, rabbits, mice, and rats have revealed new evidence on the mechanisms that could be involved in the disease.<sup>27,28</sup> The niches are a three-dimensional, specialized microenvironment that maintains a balance of self-renewal and cell-fate commitment.<sup>29</sup> Bi et al<sup>27</sup> showed that the TSC niche is composed predominantly of extracellular matrix (ECM) and that biglycan and fibromodulin are critical in the organization of this structure.

In this study, changes in the matrix composition affected TSC pool size and channeled TSCs from the tenogenic to osteogenic lineage, resulting in ectopic ossification in the tendon. According to Wang et al,<sup>30</sup> such nontenocyte differentiation may account for the histopathological changes seen in advanced stages of tendinopathy, such as proteoglycan accumulation, lipid deposition, and calcification. Thus, CT may be considered as a failed cell-mediated healing process in which TSCs play a principal role, undergoing aberrant nontenocyte differentiation under excessive mechanical loading conditions.<sup>31</sup> In normal circumstances and after trauma, TSCs can differentiate into tenocytes and self-renew, thus playing a major role in tendon repair and maintenance. However, in the presence of altered local conditions, such as excessive mechanical loading and the accumulation of microinjuries, TSCs could differentiate into chondrocytes or osteoblasts instead of tenocytes, likely through a prostaglandin E2-mediated mechanism.<sup>32,33</sup> The activity of these nontenocytes results in chondrometaplasia and ossification, thereby creating an aberrant ECM and bringing about the formation of calcific deposits within the tendon structure. This theory appears to support the hypothesis shown by Uthoff,<sup>22</sup> who assumed that the presence of chondrocyte

phenotype cells surrounding the calcific deposits could be one decisive histopathological feature of calcifying tendinopathy, indicating a cell-mediated formation of calcifications rather than a precipitation of inorganic ions.

In addition, an association between CT and diabetes has been observed; >30% of patients with insulin-dependent diabetes were reported to have tendon calcifications.<sup>5,34,35</sup> It has been suggested that exposure to high levels of glucose may precipitate the glycosylation of several matrix proteins, as was also observed in *in vitro* studies.<sup>36</sup> It follows that these ECM changes could impact on the structure and functioning of the TSC niches. Besides diabetes, it has also been reported that patients with associated thyroid disorders exhibit an earlier onset of symptoms, a longer natural history, and more readily undergo surgery with respect to the general population, but the precise mechanism is not clear.<sup>37</sup>

In the last few years, genetic predisposition is gaining momentum.<sup>38–40</sup>

An increased frequency of human leukocyte antigen serotype class A1 has been observed in patients with CT, suggesting a possible genetic predisposition to the disease.<sup>41</sup> However, other authors were not able to confirm this relationship in patients with CT.<sup>42</sup>

A stronger evidence of the influence of genetics has been derived from murine models. Mice with the “ANK” mutation (ANK stands for progressive ankylosis locus) experience a generalized progressive form of arthritis accompanied by mineral deposition, osteophyte formation, and joint degeneration, mimicking human arthritis caused by apatite deposition disease. The ANK gene codes for a transmembrane protein essential for the transport of inorganic pyrophosphate (PPi) out of cells. PPi is a major inhibitor of calcifications. Mutation of the ANK gene causes a marked decrease in extracellular PPi, thus producing an environment favorable to crystal deposition, and the human ANK protein on chromosome 5p is nearly identical to the murine ANK protein.<sup>43</sup>

More on the clinical setting, Peach et al<sup>44</sup> published a study on the relationship among rotator cuff tear arthropathy, ANK, and the tissue nonspecific alkaline phosphatase (TNAP) gene. Rotator cuff tear arthropathy was linked with mutations in ANK and TNAP that alter extracellular PPi concentrations, causing calcium crystal deposition. In the cases of cuff tear arthropathy, significantly more variant genotypes were found than those in controls (ANK, 45% and 20%, respectively; TNAP, 32% and 9%, respectively). These results support the theory that genetic mutations predispose patients to primary crystal deposition that, when combined with a massive rotator cuff tear, induces degenerative joint changes

(rotator cuff tear arthropathy). Several human genomes with joint abnormalities, such as arthritis and chondrocalcinosis, have been mapped to the same locus as the human ANK gene, although the role of the ANK gene in CT of the rotator cuff remains to be ascertained.<sup>45</sup>

In conclusion, even if the exact pathway of calcium crystal deposition remains incompletely understood, in recent years, we gathered cutting-edge information about the mechanisms of apatite deposition in humans. It seems appropriate to hope that knowledge about CT etiology will progress further in the next years, with obvious positive consequences on therapy and prevention of the disease.

## Natural history and clinical presentation

A detailed description of the natural history of the pathology was given by Uthoff and Loehr,<sup>9</sup> who proposed that CT involves multiple phases, including both the deposition of calcium within the tissues and spontaneous calcium resorption.<sup>13</sup> The process is based on cellular mediation, which contributes to both the formation and removal of calcium crystals from the area. According to the authors, calcific deposits develop in the following three subsequent stages: precalcific, calcific, and postcalcific. The first stage consists of a fibrocartilaginous metaplasia and would represent the reaction to changed metabolic and mechanical conditions of the tendon. The calcific stage is further divided into formative, resting, and reabsorption phases. The cycle ends with the postcalcific stage.<sup>13</sup> Other authors have added a fourth stage, which involves healing and tendon repair.<sup>11</sup> It is a natural cycle targeted toward a self-healing tendon condition; however, the cycle may not follow its own pattern and may be blocked at any point by various causes. The relatively poor tendon vascularity may not cause tissue degeneration, but it may be the reason for the self-healing capacity of the human body to fail in these specific tendon sites.<sup>11</sup>

The main clinical feature of CT is shoulder pain, acute or chronic. It may or may not be associated with acute or gradual restriction of joint mobility. Acute symptoms may be ascribed to several causes. According to Uthoff and Loehr,<sup>9</sup> pain is usually associated with the reabsorption phase and is probably sustained by an inflammatory reaction leading to calcium deposits removal. US visible fragmentation of the calcific deposit has been demonstrated to be one morphological characteristic that is correlated with pain and may provide evidence in support of the acute resorption of calcifications leading to the spontaneous resolution of symptoms.<sup>17,46,47</sup>

Thus far, only limited attempts have been made to reveal possible links between the characteristics of calcifications

and symptoms. Bosworth<sup>3</sup> reported that symptoms mostly presented when calcifications were >1.5 cm in diameter, and this finding has been largely confirmed in more recent studies.<sup>17</sup> Other authors did not confirm this evidence. Instead, they demonstrated that small calcifications (with a diameter of <1 cm) do not correlate with shoulder symptoms; however, they propose a relationship between anatomical location (ie, tendon involved) and symptoms. Calcifications in the supraspinatus tendon were found to be significantly related to pain.<sup>16</sup>

Symptoms could also be associated with muscle spasm, inflammation of subacromial bursa (bursitis), long head of the biceps pathology, secondary adhesive capsulitis, or RC tears.<sup>48</sup>

Greater tuberosity osteolysis and ossifying tendinopathy have been described as rare complications of CT.<sup>49</sup>

## Diagnosis

### Imaging

#### Plain radiographs

Radiographs were the first imaging modality used to identify CT and currently represent the first examination performed in the presence of shoulder pain. A standard radiographic workup should include anteroposterior – neutral, internal, and external rotations – axillary, and outlet view. Calcifications typically appear as homogeneous and amorphous densities with smooth or ill-defined margins.<sup>11</sup> Several radiological classifications have been proposed,<sup>50</sup> according to size criteria or morphological features, although none of them guarantee sufficient reliability and reproducibility. Although CT scans provide a better characterization of shoulder anatomy, it is rarely required for the diagnosis of CT.<sup>51</sup> According to Gärtner and Heyer,<sup>52</sup> calcific deposits can be divided into the following three types: 1) well circumscribed and dense, 2) soft counter/dense or sharp/transparent, and 3) translucent and cloudy appearance without clear circumscription.

#### Ultrasonography

US has proved to be an instrumental diagnostic tool for identifying and localizing calcifications within the rotator cuff tendons.<sup>4,53</sup> Its accuracy has been reported to be similar to that of magnetic resonance imaging (MRI).<sup>54</sup> Calcifications are visible as echogenic focus with or without posterior acoustic shadowing. Current developments in high-resolution US technology have enabled the detection of very small calcific deposits, altering the previous knowledge regarding the epidemiology and the distribution of shoulder calcifications.

Chiou et al<sup>47</sup> classified calcific plaques, according to their high-resolution US morphology, into the following five types: arc-shape (echogenic arc with clear shadowing), fragmented (at least two separated echogenic plaques with or without shadowing) or punctuated (tiny calcific spots without shadowing), nodular (echogenic nodule without shadowing), and cystic (bold echogenic wall with echo-free content). They found that fragmented deposits were associated with shoulder pain, along with a positive Doppler signal.<sup>46</sup> These findings have been confirmed by Le Goff et al.<sup>17</sup>

However, as a result of the compound scanning technique, the acoustic extinction deep to a calcific deposit is almost eliminated; it is perceptible only in the relatively rare case of really dense targets,<sup>55</sup> disclosing a markedly different morphology of calcifications. Taking into consideration this technical advance, Sansone et al<sup>16</sup> adopted the following terminology: “granular”, calcifications with partially defined margins and irregular echogenicity (encompassing the previously defined “arc-shaped”, “nodular”, and “fragmented” calcifications); “nodular”, cystic appearance with a sediment-type content (previously “cystic” calcifications); and “linear”, slight thickening following the course of the collagen fascicle.<sup>16</sup>

US could also detect associated conditions such as rotator cuff tears and long head of the biceps pathology and allows us to perform a dynamic evaluation to assess the subacromial impingement.

#### MRI

MRI is now not recommended as an essential tool for the diagnosis of CT. It offers excellent soft tissue contrast and allows for multiplanar imaging with high spatial resolution, but calcific deposits appear hypointense in all MRI sequences and can therefore not be reliably distinguished from artifacts that result from tissue interfaces or hemorrhage,<sup>56</sup> even though the development of new MR sequence such as susceptibility-weighted imaging (SWI) seemed to overcome this problem. MRI remains an expensive diagnostic technique compared to US and is not always well tolerated, so its use should be reserved for complications such as rotator cuff tears and greater tuberosity osteolysis that are suspected.<sup>57–59</sup>

## Treatment

The management of CT includes the use of NSAIDs, often useful to relieve pain in the acute phases of the pathology, appropriate physiotherapy to prevent articular stiffness, local steroid injections, and more recent treatment modalities such as extracorporeal shock wave therapy (ESWT) and

US-guided needling (UGN). Surgical removal of the calcium deposits, open or arthroscopic, is usually considered after the failure of conservative treatment. However, in the light of the latest, even if not conclusive, advances about the origin and the mechanisms of the disease, a more conscious and responsive therapeutic approach might be advisable.

## Conservative treatment

Ogon et al<sup>18</sup> examined the outcome of conservative treatment that included physical therapy (ie, application of cold and heat), manual therapy, electrotherapy, iontophoresis, systemic use of analgesic and NSAIDs, and up to three subacromial injections of corticosteroids. They defined the failure of nonoperative therapy as persistent symptoms for at least 6 months, including 3 months of standardized nonoperative treatments at their institution. The overall failure rate was 27%. They identified bilateral calcific deposits' occurrence, localization near the anterior portion of the acromion, medial (subacromial) extension, and high volume of calcific deposits as negative prognostic factors. Positive prognostic factors were identified as Gartner type III calcific deposits and lack of sonographic sound extinction.<sup>18</sup>

Conservative treatments are rather effective in improving symptoms of rotator cuff CT in most cases, as reported also by Cho et al<sup>60</sup> who had excellent to good results in 72% of their patients.

In the acute phases of the disease, pain reduction is the primary objective. NSAIDs are the most commonly used drugs, although no studies have focused on what medication regimen is optimal. Caution should be used especially in patient with a history of gastrointestinal or cardiac disease since the association of this class of drugs with upper gastrointestinal complication and vascular events.<sup>61–63</sup> A study of Yokoyama et al<sup>64</sup> demonstrated the efficacy of cimetidine to reduce symptoms associated with CT. The mechanism is unclear, but the authors used the rationale of serum calcium reduction in patients with hyperparathyroidism treated with a histamine blocker. However, the sample size was small and this option needs to be further investigated.<sup>64</sup> The conservative management of shoulder pain related to rotator cuff CT usually involves a physiotherapy program, including range of motion exercises to avoid articular stiffness and strength exercises to restore normal scapular mechanics. Scapular dyskinesia can contribute to shoulder pain because of subacromial impingement, and a therapy program finalized to improve this aspect has been shown to reduce shoulder pain.<sup>65,66</sup> A local corticosteroid injection can also be used in the acute phases if the patient has symptoms of bursitis or

impingement, but this treatment is debated because it could have no effect<sup>67</sup> or even a negative effect interrupting calcium deposits' reabsorption.<sup>13,68</sup>

## ESWT

ESWT has been used in musculoskeletal disorders since the 1990s. Several studies demonstrated the efficacy of this modality in CT, but the treatment parameters, eg, dosage, duration, and interval of administration, are still under discussion. The shock wave can be generated through electrohydraulic, electromagnetic, or piezoelectric mechanism. An US or radiographic pointing system is available for some devices. The magnitude of the shock wave at its focal point is commonly expressed by its energy flux energy (EFD), measured in millijoules per millimeter square ( $\text{mJ}/\text{mm}^2$ ). Low-energy ( $<0.08 \text{ mJ}/\text{mm}^2$ ), medium-energy ( $0.08\text{--}0.28 \text{ mJ}/\text{mm}^2$ ), and high-energy ( $0.28\text{--}0.60 \text{ mJ}/\text{mm}^2$ ) shock waves have been defined.<sup>69</sup> Most of the studies reported good clinical results with low-energy and medium-energy treatments.<sup>69–74</sup> Experimental studies in vitro on tendon tissues demonstrated a local neoangiogenesis associated with an increase in anti-inflammatory cytokines and growth factors after shock wave administration, followed by cell proliferation and increased metabolism.<sup>75–81</sup> These events would lead to a cell-mediated reabsorption of calcifications. A meta-analysis published by Ioppolo et al<sup>82</sup> reported a higher rate of total resorption and partial resorption of calcific deposits 6 months after ESWT compared with placebo treatment. Limited data are available on long-term outcomes following ESWT. Daecke et al<sup>74</sup> found that, by 4 years after treatment, 20% of patients required surgery whereas 70% were successfully treated. ESWT was compared with UGN by Kim et al,<sup>83</sup> finding better radiological and clinical results for UGN, though both treatments led to improvement relative to initial findings. Combined treatment (ESWT and UGN) showed greater efficacy compared to ESWT alone.<sup>73</sup> Rebuzzi et al<sup>84</sup> compared ESWT with arthroscopic surgery and found no difference between groups in functional improvement or pain reduction. Fewer complications associated with ESWT have been reported, including pain during treatment and local transitory skin reaction. Although further studies are needed to better understand the mechanism of action and to define treatment protocols, ESWT appears to be an effective, safe, and noninvasive option to manage rotator cuff CT.

## UGN

UGN is a minimally invasive technique increasingly used in the treatment of rotator cuff CT. Farin et al<sup>85</sup> were the first

to describe the outcomes of this technique, reporting 73% of excellent results correlated with the reduction in calcifications' size. The procedure involves the introduction of one<sup>86-88</sup> or two needles<sup>89-93</sup> inside the calcific deposit under US guidance. In the single-needle technique, once inside the calcification, a small amount of fluid is injected and the pressure on the plunger is released to allow the flow of calcium deposit back into the syringe. In the two-needle technique, the second needle aspirates the introduced fluid. Usually, before puncturing the deposit, a small amount of local anesthetic is injected in the subacromial bursa and, at the end of the procedure, a corticosteroid injection is administered to prevent subsequent bursitis. Most investigators reported short-term and mid-term good results after UGN.<sup>94</sup> Serafini et al,<sup>87</sup> using a two-needle technique, found improved clinical outcomes in the treated compared to untreated group 1, 3, and 12 months after procedure, but the effect disappeared at 5- and 10-year follow-ups. Despite the promising results of UGN, more long-term studies with larger population and well-defined protocols are needed. Due to the variation and the low quality of evidence, related to the absence of a control group in many studies, the efficacy of UGN could not be ascertained.<sup>94</sup>

### Platelet-rich plasma (PRP) therapy

In recent years, therapies based on autologous PRP have gained striking attention as a potential mean to enhance musculoskeletal tissue repair and regeneration, including tendinopathies. The rationale behind the use of PRP relies on the delivery of supraphysiological concentrations of growth factors and other bioactive molecules at the targeted area to promote healing.<sup>95-97</sup> These substances are expected to upregulate proliferation, differentiation, and migration of necessary cells in the site of regenerating tissue.<sup>98</sup>

However, results from clinical studies on the effectiveness of PRP applications seem to be conflicting. This may be due to methodological differences of PRP composition. More than 40 different devices for PRP preparation are available on the market, and variations in the concentration of platelets in plasma, the volume of PRP, the presence or absence of leukocytes, and the addition of different substances for activating platelets can substantially alter the efficacy of PRP preparations. Moreover, a study conducted on supraspinatus tendinopathy showed that the effects of PRPs differ depending on the severity of tissue damage.<sup>99</sup>

Nevertheless, the current overall opinion on PRP applications for tendon healing is positive: *in vitro* tenocyte prolifera-

tion has been reported, as well as the upregulation of tendon structure re-arrangement *in vivo*.<sup>100-103</sup>

The use of PRP therapy has thus been advocated for CTs' unresponsiveness to conservative treatments.<sup>11</sup> Unfortunately, in the literature, there is only one case study (level of evidence V) in this regard.<sup>104</sup> The patient was a 44-year-old female with chronic CT of the supraspinatus who received three treatments at 2-week intervals. After 6 weeks, the patient was asymptomatic and follow-up at 1 year confirmed the result and the complete radiographic disappearance of calcifications. Further prospective, randomized controlled studies replicating these findings would be ideal for supporting the efficacy of PRP therapy.

### Surgical treatment

Most authors recommend surgical treatment for patients not responding to conservative treatment for >6 months.<sup>105-108</sup> Currently, arthroscopy is the preferred technique because of its fewer morbidity rates and similar results compared to open surgery.<sup>35</sup>

The debate regarding the amount of calcification to be removed remains open to discussion.<sup>109</sup> Several investigators underline the importance of a complete removal of calcium deposits, and an inverse relation between the functional outcome and the amount of remaining deposit has also been reported.<sup>35,40,108,110,111</sup> In contrast, many authors, even suggesting to remove the largest possible amount of deposits, found that complete eradication is unnecessary because the cell-mediated resorption can be triggered already by the surgical incision of the affected area.<sup>105,106,109</sup> Moreover, a partial removal preserves better the tendon.<sup>106</sup> According to Seil et al,<sup>106</sup> a radiographic control at the end of the procedure is opportune to evaluate the amount of remaining deposit. Postoperative functional results do not seem influenced by the size and the type of calcifications.<sup>106,108</sup>

Most authors agree that the nature of the disease is self-healing, thus suture of the residual tendon lesions after the complete removal of deposits is not requested.<sup>35,109,112</sup> However, some authors recommend a suture repair of the tendon if the postexcision remaining defect is large.<sup>35</sup> Porcellini et al<sup>108</sup> reported their results of arthroscopic removal of calcific deposits of rotator cuff. When the removal of calcific deposits was complete, the tendon interruption was left unsutured; a side-to-side suture or a suture anchor repair was performed in the other cases. No difference of the constant outcome was observed between the two groups and an US examination performed at 5-year follow-up failed to show any residual

cuff tears. The authors commented that suturing the tendon gap allowed the patients to begin early rehabilitation.<sup>108</sup>

There is a substantial agreement among the authors about the opportunity of performing an acromioplasty only when there are signs of subacromial impingement with rough coracoacromial ligament borders or when the undersurface of the acromion is exposed.<sup>106,108,113</sup> Seil et al<sup>106</sup> suggested a subacromial decompression also when the calcific deposit cannot be completely removed without creating major damage to the tendon. In the literature, the results after the removal of calcification with or without acromioplasty are substantially similar. A specific comparative study was performed by Gleyze et al.<sup>114</sup> The authors did not observe any difference between two groups of 30 patients, one treated with arthroscopic calcification removal alone and the other treated with a combined procedure including acromioplasty. However, other studies support subacromial decompression alone. The rationale relies on the hypothesis that the operation alters the equilibrium of the subacromial space and causes deposits to enter the resorption stage.<sup>115,116</sup>

## Conclusion

Recent scientific evidence shows that CT of the shoulder is a cell-mediated disease with the deposition of calcium hydroxyapatite, often followed by deposits' resorption. Thus, many cases may resolve spontaneously and require no special treatment. Cases, which fail to follow this benign course, can be treated by several modalities. However, a gold standard therapy does not exist. The etiology of the disease remains partially unknown, and the results of treatment are not completely satisfactory. Furthermore, regarding the surgical treatment option, which should be considered as the last option, there is debate as to whether the removal of calcium deposits should always be pursued. In summary, there is still a lack of adequate evidence to support the efficacy of the available therapies. Indeed, most publications are case studies, and proper randomized controlled studies are necessary to validate their efficacy. Moreover, in addition to the classic mechanical theory of rotator cuff disease, more evidence supporting the theory of a biological and genetic basis for CT adds new intricacy to the understanding of the course of the disease.

As new information about the cause of the disease emerges, a broader use of biological therapies or of modalities able to stimulate a targeted biological response could be considered. From this perspective, ESWT, UGN, and platelet-rich plasma therapy may be promising treatments, which probably deserve more in-depth attention.

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The authors report no conflicts of interest in this work.

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