Rotator cuff calcific tendinitis: another entity of rotator cuff problems

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Chapter 1

General introduction and outline of the thesis

The incidence of patients who present with shoulder pain in general practice is high. Shoulder pain is the third most common musculoskeletal reason to consult in primary care with a lifetime prevalence of up to 67% and approximately 1% of adults are likely to consult with new shoulder pain annually[1,2]. As shoulder pain often affects patients of working age, it creates a large economic burden for society[3,4]

Rotator cuff calcific tendinitis

Rotator cuff calcific tendinitis (RCCT) is a frequently diagnosed cause of shoulder pain with a reported prevalence of 7% to 54% in patients with shoulder pain[5-8]. RCCT is characterized by the presence of carbonate hydroxyapatite deposits in the rotator cuff tendons. The pathogenesis of this condition is still not fully understood. Several hypotheses have been proposed such as degenerative changes, repetitive trauma, tenocyte necrosis, reactive and endochondral ossification[7, 9-12]. More recent research suggests that calcific tendinitis should be considered as a failed cell-mediated healing process in which tendon stem cells play a principal role. In the presence of altered local conditions, such as excessive mechanical loading and the accumulation of microinjuries, tendon stem cells could differentiate into chondrocytes or osteoblasts instead of tenocytes. The activity of these non-tenocytes results in chondrometaplasia and ossification which leads to the formation of calcific deposits within the tendon structure[13].

RCCT mainly affects patients of working age (30-60 years old), is more common in women (affected 1.5-2 times more often than men) and is bilateral in 10%–25% of patients. It is suggested that RCCT is more common in patients whose occupation requires internal rotation and slight abduction of the arm, such as desk and production line workers. The condition is also found more often in patients with insulin-dependent diabetes and thyroid disorders[13].

The natural course of the disease is self-limiting and can be divided into three subsequent stages: precalcific, calcific, and postcalcific. The calcific stage can be further divided into the formative, resting, and reabsorption phase. Pain is the main clinical feature of symptomatic RCCT. Pain usually increases during the reabsorption phase probably due to an inflammatory response, which ultimately will lead to resorption of the calcific deposit. Other symptoms of RCCT could be restriction of joint mobility and loss of strength[14-16].

Calcific deposits are usually visible on plain radiographs and can, according to Gärtner and Heyer, be classified into three types: 1) well circumscribed and dense, 2) soft counter/dense or sharp/transparent, and 3) translucent and cloudy appearance without clear circumscription (figure 1)[17]. Ultrasound examination of the shoulder can further aid the diagnosis and detect associated conditions such as bursitis, rotator cuff tears and long head of the biceps pathology[18,19].

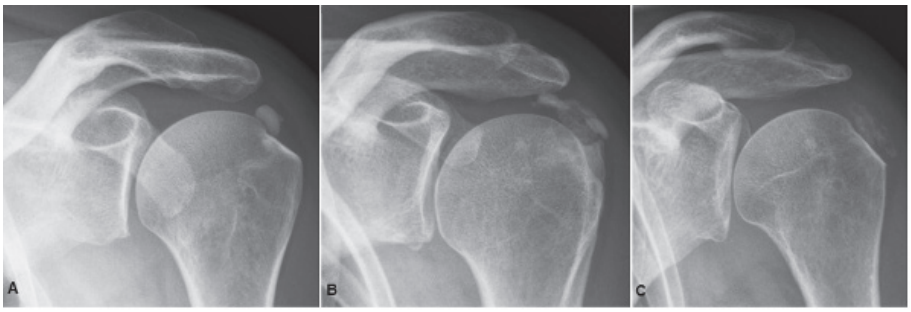

Figure 1: Gärtner and Heyer classification of calcific deposits. (A) type I calcific deposit: dense with a well-defined border; (B) type II calcific deposit: dense with an indistinct border or transparent with a well-defined border; (C) type III calcific deposit: translucent and cloudy appearance without clear circumscription.

Not all calcific deposits in rotator cuff tendons are symptomatic. In asymptomatic populations, calcific deposits were found in 3 to up to 20% of the population. Larger calcific deposits (>1.5 cm in length) seem to have the highest chance of becoming symptomatic while some authors state that larger calcific deposits will always become symptomatic in time[20-23].

Although RCCT is believed to be a self-limiting disease, treatment is warranted for symptomatic patients with a prolonged duration of symptoms, as spontaneous resorption of the calcium deposit may take years. Initial treatment of RCCT includes conservative therapies such as non-steroidal anti-inflammatory drugs (NSAID's), physiotherapy (stimulating shoulder depressors) and subacromial injections with corticosteroids (SAI). Success rates of these conservative measures range from 70–90%[8 ,15, 24-26]. Negative prognostic factors for the outcome of conservative treatment are bilateral calcific deposits, localization of the deposit near the anterior portion of the acromion, medial (subacromial) extension and a high volume of calcific deposits. Gärtner and Heyer type III calcific deposits and lack of sonographic sound

extinction were identified as positive prognostic factors[25]. When conservative measures fail, other treatment modalities such as extracorporeal shockwave therapy (ESWT) and needle aspiration of calcific deposits (NACD) are advocated[27-29]. Comparative studies between these treatment modalities are scarce but NACD seems to be more effective in restoration of function and pain relief in the short term[30,31].

Needle aspiration of calcific deposits (NACD)

NACD was introduced in 1937 using fluoroscopic guidance[32]. Farin et al. were the first to describe the outcome of ultrasound-guided NACD[33]. During this procedure a needle is introduced into the calcific deposit after which a small amount of fluid is injected in the calcific deposit. If necessary, the calcific deposit can be repeatedly perforated after which the calcific remains can removed by aspiration. Some authors advocate the use of a second needle for aspiration[34]. Studies on the efficacy of NACD for RCCT show good mid-term and long-term results but are limited to relatively small sample sizes[33, 35-43]. In a large prospective study, Serafini et al. reported the outcome of NACD in 219 patients and compared it to a control group of 68 patients who refused to undergo NACD for unreported reasons. They found significantly better results in the NACD group at one, three- and 12-months follow-up, but at five- and ten-years follow-up no more significant differences were found between groups[42]. In a large randomized controlled study by De Witte et al., NACD was compared with SAI and patients were reviewed after one and five years. Results of this study showed significantly superior results for NACD at one-year follow-up, but at five-year follow-up differences between groups were absent. However, during the course of these studies 36% (9/25) of the patients in the SAI group underwent additional NACD during the first year of follow-up and over half the patients in the SAI group (13/25) required additional NACD during the five-year follow-up. The authors therefore concluded that NACD is associated with faster improvement and a lower number of patients requiring additional treatment[44,45].

Despite these promising reports, up to 30% of patients experience persisting or recurrent symptoms after NACD[33, 35-43]. At long term follow-up this percentage even increases: 42% of patients with RCCT had a severely impaired shoulder function (i.e. WORC score $<$ 60 points) in a study with a mean follow-up of 14 years[46]. Although it is unclear whether the impaired shoulder function in the long term is

due to persisting or recurrent RCCT, or due to other shoulder pathology, this might indicate that the calcium deposit as such is just one (small) part of a more complex, and perhaps degenerative, shoulder disease.

Regarding prognostic factors for the outcome of NACD, type I calcific deposits, according to the Gärtner and Heyer classification, are believed to affect the outcome of NACD negatively[17]. Female gender, dominant arm involvement, bilateral disease, prolonged duration of symptoms and presence of multiple calcifications are associated with inferior shoulder function in patients with RCCT[46]. No studies aimed at identifying prognostic factors for the outcome of NACD have, however, been conducted. Even more, large studies on the effectiveness of NACD are lacking, as well as studies investigating novel therapies for the treatment of RCCT.

Platelet-rich plasma (PRP)

A possible novel treatment for RCCT could be platelet-rich plasma (PRP). PRP is a small volume of autologous blood plasma that has been enriched with blood-derived platelets. PRP is considered to have beneficial effects on many healing processes as a result of the growth factors contained in the platelet alpha-granules. Several studies show favorable outcomes of PRP in the treatment of tendinopathies such as lateral epicondylitis and patellar tendon tendinitis[47-50]. The role of PRP in the treatment of rotator cuff pathology is more controversial. In the conservative treatment of rotator cuff disease, such as partial rotator cuff tears and tendinopathy, conflicting results have been published on the efficacy of PRP[51-59]. However, in comparison with corticosteroid injections, PRP seems to give better results at short-term in patients with partial rotator cuff tears[58,59]. The use of PRP in the treatment of RCCT has never been investigated.

Aim of this thesis

The aim of this thesis is to evaluate and optimize the outcome of the treatment of rotator cuff calcific tendinitis (RCCT). In order to do so, the clinical outcome of needle aspiration of calcific deposits (NACD) and prognostic factors for the outcome are evaluated in two cohorts: a retrospective and prospective cohort of patients with symptomatic RCCT. Furthermore, the efficacy of platelet-rich plasma (PRP) in RCCT is investigated in a randomized controlled trial.

Outline of the thesis

First, the outcome of NACD in the treatment of RCCT is evaluated and prognostic factors for the effectiveness of NACD are identified. To do so, a cohort study on the outcome of NACD in 431 patients with symptomatic RCCT is conducted (**chapter 2)**. In **chapter 3**, factors associated with successful NACD and factors associated with the need for multiple NACD procedures are evaluated in a retrospective cohort study. This study is followed up by a prospective cohort study to further identify prognostic factors for the effectiveness of NACD (**chapter 4**).

Secondly, the efficacy of the use of PRP in the treatment of RCCT is investigated. In **chapter 5,** the differences in concentrations of blood components between the different available PRP separation systems and techniques are evaluated in a review of literature. Finally, in **chapter 6**, the efficacy of the adjuvant application of platelet-rich plasma for the treatment of RCCT is evaluated in a randomized controlled trial.

A summary of the main results of the studies in this thesis and a general discussion including future perspectives is provided in **chapter 7**.

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