CHAPTER 6

General discussion
Practical implications
and Future perspectives
GENERAL DISCUSSION, PRACTICAL IMPLICATIONS AND FUTURE PERSPECTIVES

The scope of this thesis was to optimise management of degenerative rotator cuff tears. When treating these degenerative full-thickness rotator cuff tears, the main question is whether treatment should be surgically or conservative. A randomised controlled trial is conducted comparing functional and radiological outcome following surgical and conservative treatment (Chapters 2 and 3). Chapter 4 compares the radiological changes on MRI pre-treatment and after one year follow-up of the patients treated in our randomised controlled trial. Chapter 5 describes prognostic factors predicting outcome following rotator cuff repair.

SURGICAL VS CONSERVATIVE TREATMENT

First aim of this thesis was to observe if there are differences in functional and radiological outcome between surgery and conservative treatment of degenerative rotator cuff tears. Primary functional outcome measures used in our randomised controlled trial showed no difference. In a subgroup analysis of our data we found that in patients with a successful intact repair the functional outcome was significantly better at final follow-up (one year). A recent meta-analysis found increased strength for patients with an intact repair compared with patients with a retear, but no differences in pain or function. This suggests that when using outcome measures in which strength is an important factor, e.g. the Constant Murley score, differences will be found between both treatment modalities, but when outcome measures are used in which strength is a less dominant factor no differences are to be found.

LONG-TERM FATE OF A CONSERVATIVELY TREATED ROTATOR CUFF

Radiological changes in the rotator cuff of conservatively treated patients were compared with the rotator cuffs of patients treated surgically, including those with a healed rotator cuff and with a retear. An MRI was made pre-treatment and after one year. At one year no increase or decrease in tear size, atrophy or fatty infiltration in and between patients treated conservatively and surgically (with and without an intact repair) was found. When comparing our data with available literature, our follow-up time might be too short to find a difference. In a prospective cohort study of full-thickness rotator cuff tears tear progression was found in 61% of patients at 2.3 years follow-up. This is observed in other series too,
but not all cuff tears have the tendency to increase in tear size.\textsuperscript{56,57} When an increase is seen, it appears to be symptomatic in most cases.\textsuperscript{55,58} An asymptomatic increase in tear size is seen in only 5-22\% of patients.\textsuperscript{20,30,58}

WHO WOULD BENEFIT FROM SURGERY
The second aim of this thesis was to identify factors influencing the outcome of rotator cuff repair. As intact repair results into superior outcome to conservative treatment and retears, anatomical healing should be pursued. Most studies describing prognostic factors for rotator cuff repair do not conduct a multivariate regression analysis, therefore in these series it is unclear how outcome depends on different independent variables. Furthermore, most series describing prognostic factors have a heterogeneous patient population, for example including patients with subscapular tendon tears. The systematic review included prospective studies describing prognostic factors for rotator cuff repair with supraspinatus and infraspinatus tears and with linear or multivariate regression analysis. Considering the available evidence, as presented in the review, rotator cuff repair should be carefully considered in older patients, in patients with multiple tendon involvement or greater tear sizes, and in patients with a WCB (workers compensation board) status, as this may negatively influence the outcome of surgery.

PRECISION MEDICINE
The practical implication of the findings of this thesis is that we can advise commencing with conservative treatment in patients who do not require specific strength for work/hobbies or activities of daily living. In patients who do need specific strength (e.g. heavy labourers like plasterers, masons, etc.), and since the presented prognostic factors are favourable, surgical repair can be considered as first treatment option. This stresses the need for patient-specific medicine.

Some patients may wonder if they are worse-off trying a conservative approach first. Combining our data and those from literature, the window to switch from conservative treatment to surgical repair seems to be one to two years, as an increase in tear size usually does not occur earlier. Some advise regularly checking up conservatively treated patients in case there is an increase in tear size.\textsuperscript{59} The necessity for this is debatable, as only a minority of patients have asymptomatic increases in tear size. As an increase in tear size mostly leads to a surge in complaints, patients who are treated conservatively should be
advised to consult their orthopaedic surgeon if that happens. It seems unethical to perform a rotator cuff repair in patients with no or few symptoms, exposing them to possible risks and complications.

It remains difficult to predict the fate of a rotator cuff tear, or even how a conservatively treated rotator cuff tear progresses to an irreparable large tear and eventually cuff tear arthropathy. Our follow-up was too short to advise for long-term conservative treatment; further rotator cuff degeneration and aggravation of symptoms in longer follow-up cannot be ruled out. This could have consequences for younger patients. The average age of patients included in our randomised controlled trial was over 60 years. There may be an indication to perform surgical treatment to prevent further cuff degeneration in a younger age group, e.g. 40-50 years. Further research should objectify this.

In degenerative rotator cuff tears the tissue quality of the rotator cuff is structurally lower. In traumatically tears this is not the case. We did not examine this in our trial, but it can be assumed that degenerative and acute tears may be treated differently. This also applies to the subscapularis tendon, which is an anterior stabiliser of the shoulder joint. Tears typically occur traumatically. We included some patients with a subscapularis tear in our trial; these patients may need an approach other than that suggested above, which might only be applicable to degenerative supraspinatus and infraspinatus tears.

**PRACTICAL IMPLICATIONS**

Based on the findings in this thesis, the following practical implications can be summarised:

- Conservative care can be advised as primary treatment for patients with a degenerative rotator cuff tear.
- Surgical repair can be considered for patients who need strength in activities of daily living and/or work (e.g. heavy labourers), and maybe also for younger patients (ages 40-50).
- The window to switch from conservative treatment to surgical repair seems to be one to two years.
- When patients are treated conservatively, a surge in complaints can be an indication of increase in tear size. These patients should be advised to consult their orthopaedic surgeon.
- Higher age, larger tear size and multiple tendon involvement negatively influence cuff integrity following cuff repair.
FUTURE PERSPECTIVES

Identification of tears prone to enlarge will help us further refine indication for surgical or conservative treatment. As the follow-up time of our randomised controlled trial was rather short, studies with longer follow-up should be deployed to identify these tears. It is suggested that rotator cable disrupted tears have a higher chance of tear enlargement. The rotator cuff muscles can produce a distributed load along the cable that gets transferred to bone at the cable attachments. In this way a distally torn rotator cuff can still function by load transmission. When the rotator cable is disrupted, the load transmission is disrupted too and a higher chance of muscle degeneration is to be expected. However, a recent study found a similar risk of tear enlargement for cable-disrupted and intact tears. When specific tears prone to enlargement or further degeneration are identified, a more patient-specific advice can be given.

Within orthopaedics there is a continuous search to improve functional outcome and patient satisfaction. The history of rotator cuff repair is full of refinements and improvements in surgical techniques, instrumentation, different sutures and anchor types, and imaging modalities, as well as identification of patient-specific factors. Inferior results are reported in the literature for side-to-side rotator cuff repairs. Tendon-to-bone healing should be strived for. Different repair techniques are described: single-row, double-row, suture bridge and double-layer. Despite all efforts to improve surgical outcome in recent decades no significant improvement in functional outcome has been found. (Figure 1) One might question what the role of rotator cuff repair in the future will be. It is questionable whether specific surgical techniques or anchors can make a significant improvement in this tendon-to-bone healing of degenerated tendons.
Recently, Moor et al. described the ‘critical shoulder angle’. This angle measures the inclination of the glenoid vs. the lateral extension of the acromion (Figure 2). A critical shoulder angle (CSA) above 35° is associated with an increasing chance of degenerative rotator cuff tears, a CSA below 30° with an increasing chance of glenohumeral osteoarthritis. As a larger CSA leads to greater loading of the rotator cuff to counterbalance the force component of the deltoid, this higher workload might influence the weakened rotator cuff, which ultimately can fail.

Gerber et al. recommend correcting the critical shoulder angle (CSA) by performing a lateral acromioplasty. Decreasing medial-lateral distance of the acromion results in a decreased CSA, and it is suggested that this reduces the shear force on the repaired rotator cuff. This should improve healing and reduces retear rate. There are no comparing clinical series at this moment supporting this theory though. Furthermore, using this technique may compromise deltoid functioning. The correlation between a high CSA and rotator cuff deficiency might be due to other causes, for example medialisation or laterisation of the
glenoid with respect to the coracoid, in which case correcting this at the acromion is of no use. This technique does not improve tendon-to-bone healing either.

One way to improve tendon-to-bone healing might be administering antibiotics of the tetracycline group (for example doxycycline) intravenously before surgery. The benefit of use of doxycycline is twofold. First, doxycycline is a matrix metalloproteinases (MMP) inhibitor. MMPs are responsible for the remodelling of the extracellular matrix of connective tissues. Modelling MMP activity to basal levels reduces excessive degradation or remodelling at the repair site of the rotator cuff. It is shown that doxycycline-mediated inhibition of MMP activity after acute rotator cuff repair is associated with significant improvements in biomechanical and histological parameters of healing at the tendon-bone interface in a rat model. Second, doxycycline is effective against propioni acnes, is a known cause of low-grade infection in shoulder surgery. Hence benefits of offering doxycycline might be reduced chances of infection and improved healing rates.

The insertion of the rotator cuff to bone consists of four distinctive tissue regions, made up of different types of collagen, fibrocartilage, proteoglycans and bone. This multi-tissue organisation mediates load transfer between tendon and bone. After rotator cuff repair this normal insertion is not regenerated with current repair techniques. Tendon grafts or augmentation devices based on extracellular matrix (ECM) scaffolds to improve anatomical healing have been explored to repair rotator cuff tears. The problem with these ECM scaffolds, which are based on small intestinal submucosa (SIS), is that they lack the mechanical properties of a normal tendon. An ideal scaffold improves tendon-to-bone healing: it has mechanical properties like a normal tendon, will be replaced by new tissue as it is biodegradable, integrates with the tendon and bone, and promotes native tendon-to-bone healing. Nanofiber-based scaffolds can be engineered with distinctive nanofiber organisation and alignment, thereby recapitulating the inherent structure-function relationship of the rotator cuff as well as tendon-to-bone interface. A pending issue with nanofiber technology is that problems with scaffold fabrication and large-scale production must be overcome before widespread use is possible. Bioactive agents must also be inactive and immobilised in the carrier. How to control their releases after rotator cuff repair should be investigated further.

There are other surgical approaches to degenerative rotator cuff tears. Long-head biceps tendon tenotomy has been recommended as treatment for years. In a series of 307 patients with a rotator cuff tear treated by tenotomy of the long head of the biceps tendon,
published by Walch, an additional acromioplasty was performed in 110 patients, 24 of them below age 55. There seems to be considerable selection bias, therefore the patient categories for which this treatment can be recommended remain unclear. We are currently deploying a randomised controlled trial comparing debridement of the rotator cuff and bursa, with long-head biceps tendon tenotomy and conservative treatment in patients aged over 65 with a degenerative supraspinatus and/or infraspinatus tear (METC number: 15.08131).

‘Prevention is better than cure’ also applies to rotator cuff tears. Key point is to enhance or at least maintain the tendon quality of the rotator cuff. Increasing age may contribute with general health problems, such as hypercholesterolemia or hypertension. These metabolic changes may influence the rotator cuff quality. Hypertension can cause peripheral hypovascularity. This can be a reason why significantly more massive rotator cuff tears are found in patients with hypertension.75 Hypercholesterolemia is also associated with full-thickness rotator cuff tears.76 These factors influence the intrinsic pathway of rotator cuff development. General health improvements, like reducing stress and overweight, will probably influence rotator cuff quality.

Another factor influencing tendon quality is the decrease of the amplitude of the circadian clock. The circadian clock is a 24-hour cycle of being a sleep or awake. It is a well-known effect that this cycle extends with increasing age,77 leading to compromised tissue homeostasis and increased risk of tendon pathology.78 Influencing this circadian clock by BMP signalling may prevent tendon pathology. Is it possible to influence the circadian clock to prevent tendon pathology? Further research in this field is essential.
CONCLUSIONS

The scope of this thesis was to optimise treatment of degenerative full-thickness rotator cuff tears. The first objective was to determine differences in functional and radiological outcome between conservative and surgical treatment of degenerative rotator cuff tears. In a randomised controlled trial no significant differences between the two treatment modalities were found, except for those patients with an intact rotator cuff following surgical repair. After one year no increase in degenerative changes was found in the group of patients treated conservatively compared to the surgically treated patients. The second objective was to identify prognostic factors influencing the intervention results. Increasing age, multiple tendon involvement, greater tear sizes and a WCB status negatively influence the results of rotator cuff repair. The practical implication of these findings is that a conservative approach can be advised as primary treatment. Only in patients who require specific strength, for example at work, and in whom cuff integrity following repair is to be expected (smaller single-tendon tears in younger patients), can rotator cuff repair be considered. When patients are treated conservatively, a surge in complaints can be an indication of increased tear size. These patients are advised to consult their orthopaedic surgeon. Future research should aim at investigating which type of rotator cuff tears are prone to enlargement and which are stable in the long term in order to further develop patient-specific treatment.
REFERENCES


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