Meniscal problems: to repair and to replace

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Robert J.P. van der Wal

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Dedication

In memory of my father, Henk van der Wal (1948 – 2018)

CONTENTS

1

General introduction

GENERAL INTRODUCTION

In 2018 approximately 49.500 patients in the Netherlands were diagnosed with osteoarthritis (OA) of the knee by their general practitioner.[1] The risk of developing knee OA is increased compared to the general population in people after any knee injury,[2] where meniscal tears are the most common type of knee injury.[3] Meniscal tears are also common among asymptomatic uninjured knees and its prevalence increases with age.[4] These tears can often be painful causing a locking or giving way sensation of the joint, therefore require surgery, which usually involves either meniscal repair or meniscectomy.

Arthroscopic surgery of the knee is one of most common types of knee surgery with an estimated 27.500 procedures per year in the Netherlands. In the majority of cases, an arthroscopic partial meniscectomy is performed.[5] The unfortunate effects of this surgery, in addition of the damage of the meniscal tear itself, are loss of meniscal function, with subsequent higher stresses between the cartilage of femur and tibia during loading.[2,6] For that matter, successful arthroscopic meniscal repair surgery has compared to partial meniscectomy not only better patient outcomes, but also has fewer complications at long-term follow-up.[7] The latter is most notable by a reduced incidence of osteoarthritis of the knee.[8] Although an arthroscopic partial meniscectomy adds to the risk for the development of knee osteoarthritis, one must realize that the meniscal tear itself is a potent structural risk factor for the development of radiographic OA.[9] This highlights the need for better understanding, prevention, and treatment of meniscal tears.

MENISCAL FUNCTION

The meniscal function include loadbearing, shock absorption, joint stability, joint lubrication, and proprioception. It is has been known for decades that both medial and lateral menisci have important biomechanical functions within the knee joint, and that these functions are to be maintained. The latter was one of the reasons to start partial meniscectomies after the introduction of knee arthroscopies in the early 70s. Meniscal function, lack of function of torn menisci and deteriorated function after (partial) meniscectomy, as well the historical treatment options are discussed in **Chapter 2**.

MENISCAL REPAIR

The goal of meniscal tear treatment is to preserve as much meniscal tissue as possible. This means, repair the meniscus whenever possible. Most meniscal repairs were traditionally performed in the so-called red-red or the red-white zone because of the vascular supply, where “red” is depicted as the area at the capsular side of the meniscus were blood vessels enter.[9] These “red” zones were found to be associated with a high likelihood of meniscal healing after repair or injury.[11,12] Other factors determining the success of meniscal repair are shape and length of the meniscal tear, quality of the remaining meniscal tissue and presence of concomitant anterior cruciate ligament injuries.[13,14]

Medium and long-term results of meniscal repair have shown to be successful, with an overall rate of failure (i.e. meniscectomy) of 20% to 24% at 5 years and at 10 years up to 27 to 30% of failures.[15-17] The use of newer meniscus repair techniques (e.g. biomaterials, all inside devices) as well as better patient selection and rehabilitation protocols improved this success rate even further.[18] Survival of meniscal repair depends on knee stability, which is determined by integrity of the “repaired” meniscus as well as ligamentous stability.[19] In unstable knees there is a decrease in the success rate of the meniscal repair with a variety of outcome of 30-70%. If the injured anterior cruciate ligament is reconstructed in conjunction with meniscal repair, the success rate of the meniscal repair is above 90%.[20] Lateral meniscal repairs are expected to heal better compared to medial meniscus repairs.[21]

The optimal time window between the occurrence of a meniscal tear and the meniscal repair as well as until which age this can be done are still controversial. Data on the time interval between the moment of injury and the actual meniscal repair and survival after the meniscal repair are scarce.[22-25] With advancing age, meniscal tissue becomes degenerative (e.g. less elastic, decreasing vascularity) which will have an effect on the healing response after repair. For that matter, chronic tears (existing more than 12 weeks) have a longer period of decreased vascularity and may lead to a lack of tissue vitality over time.[26] In **Chapter 4** a retrospective study was performed to evaluate the failure rates (e.g. revision surgery), patient reported outcome measurements and complications of arthroscopic meniscal repair in relation to the chronicity of the meniscal injury.

Not all meniscal injuries require surgery. When surgery is likely to benefit the patient, certain factors should be assessed to determine whether meniscal repair rather than (partial) resection is the most optimal option for that specific patient. Preoperative knowledge about the reparability of a meniscal tear is one the important steps in the management of meniscal tears. The latter is important in the shared decision making with the patient on his or hers most optimal treatment. Furthermore, it is also important, in case of a surgical repair, what the postoperative management should be, finally it helps surgeons in scheduling the most optimal time for this surgery.

If surgery is decided, intraoperative criteria for the success of the meniscal repair are based on factors like tear length, tear instability and tear type.[27] Magnetic Resonance Imaging (MRI) is the routine modality to evaluate the extend of injuries of the meniscus with a 84-93% sensitivity for medial meniscal injuries and a 70-79% sensitivity for lateral meniscal injuries, and a specificity of 88-94% and 94-96%, for medial and lateral meniscal injury respectively.[28,29] But, using MRI to predict reparability of the torn meniscus is far less established. The tear length of longitudinal or bucket handle tears, the distance from tear to meniscosynovial junction and minimal damage are considered important parameters for meniscal repair.[27,30] However, these three established criteria on reparability were never externally validated in different large studies, nor was intraobserver and interobserver agreement tested. In **Chapter 3**, we performed an observational study to determine intra- and interobserver agreement on meniscal reparability for longitudinal, peripheral meniscal tears based on MRI findings by both orthopaedic surgeons and musculoskeletal radiologists.

As discussed earlier, the aim of meniscus repair is to prevent OA of the knee at the long-run[7] and since patients with a traumatic meniscus injury are often young (mean age < 35 years), they are likely to develop OA after 15-20 years, especially when not having their meniscal tears repaired.[31] To prevent the increase of contract pressure on articular cartilage after a meniscal tear, meniscal repair can be performed to restore its anatomy and function. Once a repairable tear is left untouched or partial meniscectomy is performed the development of OA can be prevented or delayed by decreasing the load on the articular cartilage by a modality such the interposition of an meniscal allograft. All to prevent these patients from a symptomatic meniscus deficient knee or, even worse, knee arthroplasty at a young age.

MENISCAL ALLOGRAFT TRANSPLANTATION

When meniscal repair is not possible or failed, partial resection of the meniscus is an option. However, partial meniscectomy can lead to further meniscal deficiency, which implies a decrease of surface contact area with subsequent increase of contact pressure, leading to wear and gradual disappearance of cartilage within a decade.[32-36] As mentioned earlier up to 30% meniscal repairs fail and still some patients require subtotal or even total meniscectomy. Joint degeneration after partial or (sub)total meniscectomy has been described very well.[37] Before signs of degeneration start, patients with a history of (sub)total meniscectomy, can suffer from pain localised to the meniscus deficient compartment. In these cases, meniscal allograft transplantation (MAT) is a viable option for these patients and can result in pain relief and improvement of function. The basic principle underlying MAT is to restore joint anatomy and thus biomechanics by relocating an allograft implant that will serve and perform in a similar fashion as the original one. Limitations to musculoskeletal donor tissue as well as donor age contribute to the shortage of available allograft meniscal tissue, but also to adequate anthropological parameters which fit the acceptor. The latter as well the strict criteria for meniscal transplant indications as such in selected patients, leads to very few meniscal allograft transplantations each year. This is the reason, that in the Netherlands only two to three orthopaedic surgeons perform this.

MAT can be performed by an open and by an arthroscopically assisted procedure. Since the first open MAT[38] in 1984 many papers have been published regarding different aspects of it, including: indications and contraindications,[39] preoperative graft sizing,[40] graft preservation methods,[41] surgical techniques,[42] allograft fixation,[43] associated chondral and ligamentous damage relevance,[44] concomitant procedures,[45,46] histologic evaluation,[47] clinical and radiographic outcomes,[48-50] and rehabilitation.

Ideally, MAT should delay, or even better prevent, development of severe, symptomatic OA of the knee. The only randomised trial in this field comparing MAT versus personalised physiotherapy for patients with a symptomatic meniscal deficient knee compartment showed clinical superiority at very early, 12 months, follow-up. Even more, that study did not evaluate radiological changes throughout follow-up, or any other effects on the cartilage as such.[51] Despite these studies and the claimed chondroprotective effect, which was shown in a small sheep study (n=45),[52] the chondroprotective effect in humans remain unclear.[49,53]

Concerning the development of OA changes in subchondral bone play a key role in the pathogenesis and progression of OA.[54-58] Subchondral bone changes can be considered both a result and a cause of cartilage damage and cartilage loss.[57,59]

Interestingly, no study evaluates the impact of the history of knee problems and interventions in the years prior to a MAT on patient 's life. The sequel of this not only on the patient's clinical burden, but more over on his or hers daily life activities should be of interest to any clinician These factors will influence the perceived outcome after MAT

OUTLINE OF THE THESIS

This thesis is divided into two parts. The first part of this thesis focuses on meniscal tears and repair. Additionally, this part is focussed on meniscal reparability based on MRI findings and evaluates clinical survival of meniscal repair. The second part of this thesis is focuses on meniscal allograft transplantation. Clinical results of both open and arthroscopically assisted MAT are presented. A Dutch meniscal patient reported outcome measure (PROM) is translated and culturally adapted.

The aims of this thesis were:

1. To provide an overview of meniscal function, effects of meniscal deficiency and (historical) treatment options.
2. To evaluate of meniscal tears
    - Clinically: meniscal repair survival in relation to chronicity of injury
    - Radiologically: meniscal reparability for longitudinal, peripheral meniscal tears

3. To evaluate the clinical outcome of a long-term retrospective cohort of patients having an open MAT
4. To evaluate a novel instrument (Dual-energy X-ray Absorptiometry (DXA)) to gain more insight in the potential chondroprotective effect of MAT.
5. To evaluate patient reported outcomes (PRO), survival of meniscal allograft and the history of MAT patients with respect to knee complaints, interventions and social impact prior to meniscal allograft transplantation is evaluated.
6. To translate and culturally adapt a meniscal specific patient reported outcomes measures (PROM) to evaluate meniscal pathology and its treatment

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2

The approach to meniscal lesions in The Netherlands - a paradigm shift.

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THE HISTORY OF MENISCAL REPAIR

The first repair attempts

The concept of repairing meniscal tissue is not new. By 1883, Scottish surgeon Thomas Annandale had described a case of meniscal repair. He called the procedure “an option for a displaced semilunar cartilage”. Through an arthrotomy of the knee the displaced meniscus was reduced and stitched into position. The excellent result of the repair encouraged Annandale to proclaim that this proceeding may now become an established means of treatment.[1] In 1908, Katzenstein reported on a series of seven meniscal repairs with a follow-up of up to seven years. He used vertical silk sutures for the meniscal repair. Katzenstein believed that only in a minority of cases resection of the meniscus results in a permanently good function. He further stated that it did not make any sense to try to suture a severely degenerated or malformed meniscus. In all the other cases though, he advised strongly in favor of repairing the meniscus. Interestingly he also believed that a traumatic lesion without dislocation of the meniscus might heal spontaneously.[2]

Meniscal vascularization – from repair to complete resection

Following King’s classic paper in 1936 on the healing of semilunar cartilages in the dog many authors have postulated the importance of vascularity to meniscal healing.[3] King demonstrated that meniscal lesions had the potential to heal, provided that the lesions were located in the peripheral vascular zone. Arnoczky and Warren are generally credited as being the first to expose the blood supply for each meniscus. In 1982 they illustrated a microvascular perimeniscal plexus supplied by the vascularized synovial tissue on the periphery of the menisci.[4] However, by 1946 Smillie reported in his book “Injuries of the knee joint” on the study by Poth, which was originally published in 1932 in which an arterial injection with an opaque medium showed that the blood supply of the meniscus was limited to the convex border. In this peripheral area a network of vessels were seen entering the meniscus from the capsule. The central and concave zones had no blood supply.[5] Curiously, these fundamental findings did not steer Smillie to link the importance of vascularization of the meniscus with the possibility of repairing a torn meniscus. On the contrary, the peripheral vascularization of the meniscus was the basis of Smillie’s philosophy in which he stated that when the entire meniscus is excised a new meniscus would grow out of the parietal synovial membrane. This new meniscus would have basically the same form and general appearance of the original meniscal structure, although histological examination revealed fibrous tissue only. This altered meniscal structure was not considered problematic, since the only important function of the meniscus was supposed to be lubrication of articular cartilage. Because of the alleged regenerative potential of the meniscus Smillie advocated for total excision of the torn meniscus and was opposed to partial meniscectomy. To help surgeons in performing these total meniscectomies, he developed the Smillie knife, a knife which has been used until deep in the 1980's at which point arthroscopy was introduced and partial meniscectomy became the standard treatment for meniscal lesions.[5]

Meniscal function – from resection back to repair

The loadbearing function of the menisci in the knee, as well as the consequences of removal of meniscal tissue for the longevity of articular cartilage, started to become clear. In 1948 Fairbank examined post meniscectomy knees and noted that over time these knees developed joint-space narrowing and femoral condylar flattening. He was the first to describe the loadbearing function of the meniscus.[6] Tapper and Hoover confirmed that the late effect of meniscectomy was osteoarthritis; and that the worst results could be expected in those patients who were less than twenty years old at the time of surgery.[7] In the nineteen-seventies it became generally accepted that the meniscectomy could lead to degenerative changes in the knee, and that partial meniscectomy would have less effect on articular cartilage than total meniscectomy.[8-10] In the same period a shift occurred from the traditional open (partial) meniscectomy to arthroscopic partial meniscectomy with better clinical results.[11,12] Gradually became evident how variables such as total meniscectomy, removal of the peripheral rim, lateral meniscectomy, joint instability, degenerative meniscal tears, presence of chondral damage, presence of hand osteoarthritis suggestive of genetic predisposition, and an increased body mass all have negative influence on the outcome of (partial) meniscectomy.[13] Because of the growing understanding of the relationship between loss of meniscal function and degeneration of the knee, combined with the concurrent development of arthroscopic techniques, the technique of meniscal repair was developed to reserve meniscal integrity with encouraging results.[14-19] In 1990 the first paper on meniscal repair was published in The Netherlands.[20] In 2010 the Dutch consensus for meniscal treatment was published in the guideline "Knee arthroscopy; indications and treatment (Table 1).[21] These recommendations are consistent with the French guidelines published in 1999.[22] The implementation of this nationwide guideline may have contributed to a decrease in incidences of meniscus surgeries. However, it is unknown if the amount of meniscal repair procedures increased.[23]

Rationale for maintaining meniscal function

It is now generally accepted that both menisci have important biomechanical functions within the knee joint, and that these functions are to be maintained as much as possible. Meniscal functions include loadbearing, shock absorption, joint stability, joint lubrication, and proprioception.

Table 1: Guideline for Meniscal Treatment. Dutch Orthopaedic Association (Nederlandse Orthopedische Vereniging) guideline "Knee Arthroscopy; indications and treatment".[22]

1.	A meniscal lesion does not necessarily mean meniscectomy. Wait and see or meniscal repair should be given systematic considerations.
2.	If (partial) meniscectomy is performed the peripheral rim should be left intact.
3.	Conservative treatment is preferred in degenerative tears without mechanical obstructions.
4.	In peripheral meniscal tears in the vascular zone, especially in young patients meniscal repair is recommended. A stable knee is indispensable when considering meniscal repair.
5.	A meniscal repair in combination with an anterior cruciate ligament reconstruction (ACL) is preferred over meniscectomy.

Maintaining meniscal loadbearing

During compression the menisci distribute the joint load and protect the articular cartilage by creating a more congruent articulation between tibia and femur, increasing the contact area and subsequently decreasing peak contact pressure on cartilage. The menisci are able to move during knee flexion because they are connected to the tibia through mobile insertion ligaments. The meniscal movement ensures maximal congruency with articular surfaces during flexion, hereby facilitating load transmission, stability, and lubrication.[24,25] Knee motion during rotations demonstrated greater rotations in the lateral compartment compared to the medial compartment. The marked mobility of the lateral meniscus and the limited motion in the posteromedial corner might explain the decreased risk of lateral to medial meniscal injuries.[26] This is fortunate since removal of the lateral meniscus has been shown to be more detrimental to cartilage survival than medial meniscectomy. Pena et al. showed in a finite element study that the maximum shear stresses after total and partial lateral meniscectomies were 288 and 323% higher than the equivalent stresses in the medial counterparts.[27] Studies measuring contact stresses on the tibia plateau have shown that the menisci transmit is at least 50% of the load during the first 90° of flexion.[28] When loaded in vitro 70% and 50% of the loads on the lateral and the medial compartment were transmitted through the corresponding menisci, respectively.[29] After meniscectomy the contact area between menisci and articular cartilage is reduced which leads to increased peek stress and stress concentration on articular cartilage of the femur and tibia, and decreased shock absorption.[29] Partial meniscectomy has less detrimental effect on articular cartilage than total meniscectomy, where degenerative changes are directly proportionally related to the amount of meniscal tissue removed.[9,30] However, even partial meniscectomy significantly alters the loading situation of the meniscus and its attachments. Specifically, the attachment forces decreases with increasing the amount of meniscal tissue loss, which reflects the impaired ability of the meniscus to transform axial load into meniscal hoop stress.[31] In fact it has been shown that simply cutting the peripheral rim of the meniscus causes a complete functional meniscal deficiency equivalent to performing a total meniscectomy.[31] This highlights how only a minor change of meniscal anatomy could have major effect in joint biomechanics, and that any effort to repair meniscal integrity is imperative. For example, LaPrade et al. showed that an anatomic repair of the posterior horn of the medial meniscus could produce near intact contact area and resulted in relatively minimal increases in mean and peak contact pressures compared with intact knees.[32]

Maintaining joint stability

The effect of joint instability on outcome of meniscectomy has been elucidated by Burks et al. They found that patients with anterior cruciate ligament (ACL) deficient knees had significantly higher radiographic osteoarthritis grade changes with more medial joint space narrowing after meniscectomy, compared with patients with ACL-intact knees after meniscectomy. Lateral joint space narrowing was not significantly different between both groups.[33] It is postulated that the menisci are not the primary stabilizers of the knee joint, but that in ligament insufficient knees they assist in joint stability. Levy et al. found that isolated excision of the medial meniscus has little effect on the forced anterior-posterior displacement of the tibia on the femur.[34] However, when medial meniscectomy followed resection of the ACL, the displacement was increased significantly at all flexion angles. The greatest increase was at 90° of flexion.[35] The medial meniscus has not only been shown to enhance anteroposterior stability, but also to provide resistance to varus-valgus and internal-external rotational loads in ACL-deficient knees.[36,37] On the other hand, resection of the lateral meniscus in ACL-deficient knees did not change tibiofemoral kinematics compared to those in ACL intact knees.[37] Briefly, in ACL deficient knees, the medial meniscus is of greater importance to knee stability than the lateral meniscus. In contrast, the lateral meniscus is of greater importance to load transmission than the medial meniscus. Hence, for both medial and lateral meniscal injuries, restoring meniscal function is critical.

Clinical results of meniscal repair

Medium and long-term results of meniscal repair have been shown to be successful. The clinical success rates for all meniscal repair techniques combined in stable knees has ranged from 70 to 90%. In unstable knees there is a decrease in meniscal repair success rate to 30-70%.[38] However, when performing an ACL reconstruction (ACLR) in conjunction with meniscal repair, several studies have demonstrated meniscal repair success greater than 90%. Lateral meniscal repairs are expected to heal better compared to medial repairs.[38] Interestingly, the time interval between trauma and meniscal repair had no influence on meniscal healing. Instead the quality of the meniscal tissue as assessed during arthroscopy was the predicting factor for meniscal repair survival.[39] Despite these encouraging results, data from the French Arthroscopy Society showed that meniscal repair was only considered in a minority of meniscal surgeries, not exceeding the 3-5% limit.[40] Unfortunately, it is not stretching to conjecture that the balance of meniscectomy to meniscal repair in the Netherlands might be very similar to that in France.

DECISION MAKING IN MENISCAL INJURY TREATMENT

Conservative treatment

Not all meniscal injuries require surgery. For example, in patients with meniscal tears and osteoarthritis of the knee no differences in knee function were found after one year between patients treated with surgery compared to patients treated with an exercise program alone.[41] In fact, knee function outcomes in patients with degenerative meniscal tears without locking complaints were no better after partial meniscectomy than after sham surgery.[42] Nevertheless, surgical treatment could be discussed when a patient presents with evident mechanical signs like locking and catching due to a degenerative meniscal lesion. That meniscal debridement should be performed here rather than attempting to repair the degenerative tissue, is self-explanatory, as degenerative tears are associated with chronic damage and could be considered one of the first signs of knee osteoarthritis.[43] Another setting where conservative treatment of meniscal injury might be considered is the setting of a combined non-displaced lateral meniscal tear and ACL injury. It has been shown that the healing response for lateral meniscal tears left in situ during ACLR could be as high as 74%. For the medial meniscus, however, repair is always indicated in concomitant ACLR to decrease the risk of postoperative pain or subsequent meniscectomy.[44]

Meniscal repair

When surgery is likely to benefit the patient, certain factors should be assessed to determine whether meniscal repair rather than resection might be successful. The vascular supply is the most important factor in meniscal healing. Therefore, most meniscal repairs are traditionally performed in the red-red or the red-white zone. However, repair is also recommended for simple or complex meniscal tears that extend into the avascular zone when the conditions are such that a stable repair of a potentially functional meniscus can be obtained. This recommendation is particularly appropriate in young active patients in whom removal of meniscal tissue would result in major loss of function and risk for future knee osteoarthritis.[45] The shape and length of the meniscal tear are other determining factors when contemplating meniscal repair. The length of the tear affects its stability. Tears that are less than 1 cm are considered stable tears and do not require repair.[44] There are vertical longitudinal, horizontal, radial, horizontal flap tears, vertical flap tear and degenerative or complex tears. The root tear, which will be discussed separately, is a special traumatic radial tear of the posterior horn ligamentous fixation. Longitudinal tears, with a length of more than 1 cm, located in the red-red or red-white zone are most amendable for repair (Table 2). Horizontal tears, on the other hand, are often not repaired and are instead partially resected up to the capsule not sparing the peripheral rim. Theoretically though, it might be considered that only the under layer or only the upper layer should be removed depending on the quality and thickness of the tissue.[46] Pujol et al. showed that open repair of horizontal tears extending to the avascular zone was effective in midterm results in young patients.[47] Radial tears are often located in the avascular zone. There is debate whether these tears should be left alone of treated with partial meniscectomy. Especially in younger patients, though a more substantial radial tear, extending in the red-red zone or to the peripheral rim is amendable for repair.[18] Partial meniscectomy of such radial tear extending to the capsule would have the same functional effect as total meniscectomy.[32] As mentioned above, the time interval between trauma and meniscal repair has no influence on meniscal healing. Instead the quality of the meniscal tissue as

Table 2: Indications for Meniscal Repair.

Longitudinal tear <10 mm
Tears in red-red zone
Vertical tears
Radial tears extending to the capsule in younger patients
Posterior horn root tears
Horizontal tears extending in the avascular zone in younger patients
Concurrent ACL reconstruction in ACL deficient knee

assessed during arthroscopy is the predicting factor for meniscal repair survival.[39]

Meniscal repair techniques

Menisci could be repaired using an open technique.[15,48] Nowadays, arthroscopic repair has become the standard, consisting of inside-out, outside-in, or all inside techniques. The inside-out suturing technique was the first one used for arthroscopic meniscal repair, and is still being considered the gold standard for meniscal repair.[49] After a complete arthroscopic assessment of the knee and evaluation of the tear, both margins of the tear are debrided using a rasp. Next, the surgeon has to decide which repair technique is most suited for the meniscal tear; inside-out, outside-in, all-inside, or a combination of those. In the inside-out technique, needles with sutures are passed from inside the joint through the meniscus on either side of the tear through an arthroscopic cannula. Vertically placed sutures have shown to provide stronger fixation than horizontally placed sutures.[50] On the outside of the knee, a small skin incision is then made through which the needles are passed and the sutures are tied down to the capsule. The inside-out technique is difficult to use for posterior horn tears.[51] Care has to been taken to protect the neurovascular structures posterior in the knee. Nonetheless, the inside-out technique remains commonly used and has been proved very effective. In the outside-in technique, sutures are passed through the meniscus from the outside. These repairs are limited mostly to the anterior horns.[52] All-inside devices were developed to reduce surgical time. They were made of absorbable polymers and consisted of screws, arrows and darts, with unfortunate complications such as breakage and articular cartilage damage.[53-55] The newest all-inside repair devices allow placement of sutures in the meniscus without an external incision. The meniscal repair device is loaded with two small anchors bond together with a suture and a sliding knot. First, one anchor is pressed through one side of the tear, after which the device is repositioned and the second anchor is put into place. Finally, the suture with the sliding knot is tensioned. Biomechanical properties of these newer meniscal repair devices were as strong as outside-in sutures and significantly stronger than previous generation all-inside fixation devices.[56] Our preferred technique consists of debridement of both sides of the meniscal rupture. For posterior horn fixation we use an all-inside device, for the midportion of the meniscus we use the inside-out technique, and for the anterior horn we use the outside-in technique. In case of an isolated meniscal repair we perform micro-fracturing in the notch to provide cellular elements and biochemical mediators that are essential for the repair responses. In case of a meniscal repair during a concomitant ACL reconstruction there will be sufficient bone marrow derived cells postoperatively in the knee joint and therefore micro-fracturing of the notch is not performed.[56]

Root tears

Meniscal root tears are specific tears with a profound effect on meniscal biomechanics and kinematics. Injuries of the posterior meniscus root attachments include root avulsions and full-length degenerative tears, and radial tears adjacent to the root, and have been linked to clinically significant meniscal extrusion, defined as displacement of the meniscus with respect to the margin of the tibial plateau. Meniscal extrusion may dramatically impair hoop stress force transmission, leading to accelerated degenerative changes within the knee joint.[57,58] The torn meniscal root is fixed to the tibia plateau with sutures attached to a suture anchor or with trans osseous tibial fixation using an ACL like aiming device. Both techniques have shown good results when the root tear is fixed in anatomical position.[32] In recent years, great insight in the biomechanics of meniscal root tears and subsequent reconstruction has been gained by the research group under the direction of LaPrade. Meniscus root avulsion and all radial tear conditions resulted in significantly decreased contact area and increased mean contact pressure compared with the intact knees. Anatomic repair of the posterior root of either medial or lateral meniscus significantly reduced the increased compartment joint contact pressures seen after posterior horn root avulsions.[32,59] Anterior root tears have been described as well. Anterior root tears can be seen, for example, after intramedullary nailing of a tibial fracture.[60,61] The clinical consequences of anterior root tears remain unknown.

Complications

Arthroscopic meniscal repair surgery is considered to be minimal invasive, and is conducted relatively safely with low complication rates. Nevertheless, the surgeon needs to be aware of the rare but serious risk of damaging the neurovascular structures during surgery. The most severe complication recorded has been sectioning of the popliteal artery, leading to amputation at the level of the knee joint.[62] Less dreaded but serious complications such as hematoma, aneurysm, and pseudoaneurysms of the popliteal artery have been described not only after meniscal repair but also after meniscectomy.[63] Salzler reported 2.8% and 7.6% complication rates for meniscectomy and meniscal repair, respectively, with surgical complications being more common than medical or anesthetic complications.[64] The difference in the complication rate between repair and meniscectomy has been related to the use of older generation rigid all-inside meniscal repair devices. These devices could break, cause articular cartilage damage and aseptic reactive synovitis.[52,54] The third and fourth generation all-inside repair devices are more self-adjusting with anchor placement behind the capsule and with a sliding knot tensioning the suture on the meniscus. In lateral meniscal repair, complications involving the peroneal nerve have been reported using an inside-out technique.[65] If peroneal nerve injury is suspected postoperatively, immediate re-operation should follow, starting with an arthroscopy for cutting of the intra-articular portion of the suture, followed by a posterolateral exploration of the peroneal nerve and removal of the suture. At the medial site, the saphenous nerve is at risk and medial meniscal repair can lead to complications such as transient paresthesia or complete neuropathy.[66] Symptomatic thromboembolism and septic arthritis are more general complications after arthroscopic knee surgery, not specifically related to meniscal repair. The risk of severe complications has to be acknowledged.[67]

Rehabilitation

Rehabilitation guidelines differ among surgeons and with the lack of an evidence based rehabilitation protocol after meniscal repair it remains controversial. It is undisputable though that rehabilitation after meniscal repair has more postoperative restrictions than the rehabilitation after partial meniscectomy.[68] In our postoperative rehabilitation protocol, we distinguish between the types of meniscal tears which are repaired. All patients will have a pressure bandage two to three days after meniscal repair. For repaired longitudinal or dislocated bucket handle tears, the rehabilitation protocol entails six weeks of walking on churches and partial weight bearing up to 50% as tolerated by pain. One could debate, whether or not weight bearing is allowed after meniscal repair. Based on several studies using an all-inside repair only, it appears that there is no notable difference between an accelerated rehabilitation regime with full weight bearing allowed as soon as tolerated and a standard postoperative rehabilitation program with partial weight bearing.[69] The compressive loads applied during weight bearing in full extension in case of a vertical, longitudinal repair or bucket-handle repair can reduce the meniscus and stabilize the tear and may favour meniscal healing.[70] Flexion is limited to 90-100° during the first six weeks. Morgan et al. demonstrated that extension appears to reduce the meniscus to the capsule, whereas flexion causes tears in the posterior horn to displace from the capsule.[71] Becker et al. have reported that weight bearing flexion from full extension to 90° increases the pressure on the posterior horn.[72] Thus, consideration is given to limiting flexion to 90°-100° during the early period of healing. Closed chain exercises including cycling on a stationary bike for 10 minutes are allowed daily when 90° of knee flexion is reached easily during this period. After six weeks postoperatively, open chain exercises and running on a cross trainer or treadmill is advised. Until three months postoperatively, patients are not allowed to perform deep squats (more than 120°). For radial and root tear repair, we prescribe six weeks of walking on crutches of which the first 3 weeks are non-weight bearing and the second three weeks weight bearing to 25% bodyweight. Weight bearing should be delayed because the hoop stresses would distracts the tear margins and compromise healing. Flexion is allowed to between 0-90° during the first six weeks and closed chain exercises are commenced. After six weeks, range of movement is increased to 120°. Nine weeks after surgery, the patient is allowed full weight bearing, open chain exercises, and running on a cross trainer or treadmill. Until three months postoperatively, patients are not allowed to perform deep squats (more than 120°). Tibial rotation causes large excursions of the meniscus within the first 30° of flexion and, as already mentioned, with increasing flexion pressure on the posterior horn.[73] For that reason, deep squats and movements involving pivoting should be avoided in the first phase of rehabilitation. Programs can or even should be individualized to the type of surgical procedure performed and the type of meniscal tear repaired.

CONCLUSION

Based on our current knowledge of the function of the meniscus, and the deleterious biomechanical and long-term clinical effect of removing part of the meniscus, we argue that the meniscus should be preserved whenever possible. Especially in the younger patient, we believe that the risk of failure of a meniscal repair outweighs the predictable immediate outcome, but long-term deleterious results of partial meniscectomy. Therefore we believe that paradigm shift is needed. If a meniscal lesion is diagnosed always consider: can I leave the meniscus alone? If not, is meniscal repair possible? If repair is not possible or fails after all, a partial meniscectomy can still be performed, as a last resort. In complex tears in young patients where fully repair is not possible, consider partial meniscectomy in association with meniscal repair.

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3

Time interval between trauma and arthroscopic meniscal repair has no influence on clinical survival.

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ABSTRACT

Introduction: Arthroscopic meniscal repair is the gold standard for longitudinal peripheral meniscal tears. The time interval between trauma and meniscal repair remains controversial. The aim of this study was to evaluate failure rates and clinical outcome of arthroscopic meniscal repair in relation to chronicity of injury.

Methods: Two hundred and thirty eight meniscal repairs were performed in 234 patients. Anterior cruciate ligament (ACL) was reconstructed in almost all ACL deficient knees (130 of 133). Time interval between injury and repair was divided into acute (<2 weeks), subacute (>2 weeks- <12 weeks) and chronic (>12 weeks). Patients completed postal questionnaires to evaluate clinical outcome and failure rates. Study instruments included Lysholm, Knee injury and Osteoarthritis Outcome Score (KOOS) and Tegner scoring systems.

Results: At a median follow-up of 41 months (interquartile range (IQR) 34 – 53 months) 55 medial and 10 lateral meniscal repairs failed (overall failure rate 27%). There was a significant higher failure rate for medial meniscal repair ($p < 0.05$) and ACL deficient knees without ACL reconstruction. Functional outcome scores showed only significant differences on the KOOS subscale 'Function in daily living' (95% CI 1.05 – 15.27, $p < 0.05$). No significant difference was found for any interval between trauma and repair.

Conclusion: The interval between trauma and arthroscopic meniscal repair has no influence on failure rate. Differences in survival rate of meniscal repair are more dependent on location of the lesion and ACL status, rather than chronicity of injury.

INTRODUCTION

Several determinants contribute to a successful meniscal repair. Firstly suture technique, of which inside-out suturing is still seen as the gold standard for meniscal repair, while all-inside suturing devices are gaining popularity since its introduction by Morgan.[1] Many studies reported their results on survival using different suturing techniques.[2,3,4] Traumatic anterior cruciate ligament (ACL) rupture is commonly found with meniscal tears. Meniscal repair in combination with a concomitant anterior cruciate ligament reconstruction (ACLR) in ACL injured knees show lower failure rates than isolated meniscal repair in a stable knee,[5] also at long-term follow-up.[6] Survival of meniscal repair further depends on type of meniscal lesion, patient's age and knee stability.[3]

Data describing the influence of time interval between the moment of injury and the moment of meniscal repair on meniscal repair survival is scarce.[7,8] The time interval in which it is still possible to perform a meniscal repair is controversial. With advancing age, meniscal tissue becomes degenerative which may lead to a decreased healing response. Chronic tears (existing more than 12 weeks) have a longer period of decreased vascularity and may lead to a lack of tissue viability over time.[9]

We performed a retrospective study to evaluate the reoperation and failure rates, patient-reported outcomes and complications of arthroscopic meniscal repair in relation to the chronicity of injury. We hypothesized that arthroscopic meniscal repair of chronic meniscal tears have higher failure rates (primary outcome) and lower functional outcome scores (secondary outcome).

MATERIALS AND METHODS

Patients

Between July 2006 and March 2013, 311 patients underwent an arthroscopic meniscal repair after a traumatic knee injury. All patients who had an arthroscopic meniscal repair in this period with or without ALCR were included. Only those patients with an arthroscopic meniscal repair in combination with a posterior cruciate ligament reconstruction or a multiligament reconstruction were excluded for evaluation. Operative treatment was performed by three different orthopedic surgeons according a standard procedure. All orthopedic surgeons have at least five years of experience in arthroscopic meniscal repair and ACLR. After getting an approval from the local Institutional Review Board multiple attempts were made, to contact all 311 patients by telephone during summer 2014. All medical records were checked for reoperations, postoperative radiology reports and images and complications. If patients could be reached, they were asked to complete multiple questionnaires after they had given their informed consent. The questionnaires were sent by post or email.

Study instruments included the Knee injury and Osteoarthritis Outcome Score (KOOS),[10] Lysholm score,[11] which is categorized in four groups: excellent (94-100 points), good (84-94 points), fair (65-83 points) and poor (less than 65 points), Tegner score [12] and additional questions about patients' medical history, especially about any possible reoperation or radiological examinations elsewhere.

Lacking any consensus in literature on the definition of an acute or chronic meniscal tear, we divided our patients into three groups according to the interval between trauma and meniscal repair: ≤ 2 weeks (acute), >2 weeks – 12 weeks (subacute) and > 12 weeks (chronic). The definition of a chronic meniscal lesion varies in literature. A problem we see in defining the terms 'acute' and 'chronic' in other orthopaedic sports injuries as well.[13] Time intervals from 2 till 6 months post trauma are used defining a chronic meniscal tear.[7,14] In this study the threshold for chronic meniscal lesions was set at 12 weeks (3 months) and the threshold for acute lesions was set at two weeks. Making this distinction, a group with meniscal injury older than 2 weeks and younger than 12 weeks remains: subacute.

The criteria for failure were partial or (sub)total meniscectomy of the previous sutured meniscus or failure proven by radiological examination using magnetic resonance imaging (MRI) or Computed Tomography (CT) arthrography showing a tear or partial healing of a previous sutured meniscus.

Surgical technique and rehabilitation

All patients were evaluated preoperatively with MRI. Reparability of meniscal tears was first based on preoperative MRI findings described by Thoreux.[15] The definitive decision for meniscal repair was based on the intraoperative findings. Patients with a meniscal tear in the white-white zone, degenerative meniscal tissue at the site of the tear, a meniscal tear smaller than 1 centimeter or any other tear than a vertical meniscal tear, were excluded for meniscal repair. Time interval between injury and meniscal repair was not used as exclusion criterion. The standard procedure for isolated meniscal repair included rasping of the peripheral rim and meniscus, suturing the posterior horn with all-inside sutures and the middle section with inside-out sutures, and drilling holes in the intercondylar notch to provide blood and growth factors. For the inside-out technique we used 2.0 FiberWire sutures (Arthrex, Naples, Florida). The Meniscal Cinch (Arthrex, Naples, Florida) was used for the all-inside technique also with 2.0 FiberWire sutures. If an ACL insufficient knee was reconstructed, autologous semitendinosus and gracilis grafts were used for a single-bundle, transtibial reconstruction using the TransFix ACL reconstruction system (Arthrex, Naples, Florida) for all patients. ACLR was postponed in patients with a locked knee due to a displaced bucket handle tear, allowing range of knee motion to be recovered prior to undergoing ACLR six weeks later.

After meniscal repair, only partial weight bearing was permitted for all patients and all patients were instructed to restrict flexion of the knee to 90 degrees for six weeks. Patients treated with isolated meniscal repair, were allowed to practise sports, including sports involving pivoting, at three months based on clinical progress and similarity in the single leg hop test. In contrast, patients after a concomitant ACL reconstruction were allowed to run at three months postoperatively as tolerated, but sports involving pivoting were permitted at six months postoperatively also based on clinical progress and similarity in the single leg hop test. Compliance regarding rehabilitation was controlled by physiotherapists.

Statistics

Data were tested for normality. If data were not normally distributed median and interquartile range (IQR) was reported, in case of normality mean and standard deviation was presented. Students T-test, Chi-square test and one way analysis of variance (ANOVA) were used to calculate statistical significance. When possible, a post-hoc test (Bonferroni correction) was performed. Logistic regression analysis was used for predicting the outcome of categorical dependent variables. Two-sided 95% confidence intervals were reported, and a P value less than 0.05 was considered significant. Survival rates were calculated using the Kaplan-Meier survival function. Statistical analysis was performed using SPSS statistical software (version 20, SPSS Inc, Chicago, IL)

RESULTS

Median follow-up was 41 months (IQR, 34 – 53 months). Of 311 patients, data of 234 was available for evaluation (75%). Up to date personal data of 34 patients were not available, so they could not be reached by phone or mail, not even after contacting their general practitioner. Eight patients refused to participate. Four patients were excluded because they did not speak Dutch or English so they were unable to answer the Dutch or English questionnaires. Twenty-seven patients did not return their questionnaires after their informed consent. For four patients the exact trauma interval was not available. Altogether 77 patients (25%) were lost to follow-up, so 234 patients were evaluated subjectively. See Table 1 for demographic data.

In the remaining 234 patients 238 meniscal repairs were performed. The three groups divided according to the trauma interval (acute, subacute and chronic) consisted of 36, 91 and 107 patients respectively. The three groups showed no statistical differences for age, sex, and lesion location. Significant more bucket handle tears were sutured and significant more postponed ACLR were performed in the acute group (p = 0.046 and p = 0.001 respectively). The medial meniscus was sutured in more than two third (68%)

Table 1. Demographic data of included patients and patients lost to follow-up.

	Acute	Subacute	Chronic	Total
Included patients				
Number of patients	36	91	107	234
Median age (IQR)	29 (20 – 36)	24 (18 – 34)	23 (18 – 31)	24 (18 – 33)
Sex M/F	24/12	63/28	66/41	153/81
Patients lost to follow-up*				
Number of patients	11	30	30	73*
Median age (IQR)	25 (19 – 29)	26 (22 – 34)	24 (19 – 32)	25 (19 – 32)
Sex M/F	7/4	23/7	23/7	53/18

IQR = interquartile range; M = male; F = female; Age in years. * in 4 of the 77 patients lost to follow-up time interval between trauma and surgery was not known.

of the patients. In 106 of the 133 ACL (80%) deficient knees a concomitant ACLR was performed, in 24 patients an ACLR was performed six weeks after the meniscal repair. In three patients with a ruptured ACL, no reconstruction took place because they refused further ACL treatment. In four patients both medial and lateral meniscus tear was sutured. Almost half of the patients had a bucket handle tear (unstable, displaced, longitudinal tear extending more than 2 cm; 49%). A larger group of the patients had a peripheral vertical tear (a full-thickness, vertical tear extending less than 2 cm, but more than 1 cm; 41%). A small group of patients had a capsular tear (meniscocapsular separation; 10%). See Table 2 for patients' characteristics.

Primary outcome

Results of failure are described in Table 3. In a total of 238 meniscal repairs 65 meniscal repairs in 65 patients failed (27%). Fifty-six patients were known to have a failed meniscal repair according to our own data system, nine patients reported a reoperation by answering the questionnaires. None of the patients reported a failure based on radiological findings elsewhere. Twenty nine of 65 patients (45%) have had an evident new trauma causing a re-rupture of the previous sutured meniscus.

Table 2. Patients' characteristics. ACL = anterior cruciate ligament.

	Acute (n = 36)	**Subacute** (n = 91)	**Chronic** (n = 107)	**Total** (n = 234)
Isolated meniscal repair	21	45	38	104
ACL deficiency	15	46	69	130
Concomitant reconstruction	6	36	61	103
Postponed reconstruction	9	9	6	24
No reconstruction	0	1	2	3
	Acute (n = 36)	**Subacute** (n = 87)	**Chronic** (n = 107)	**Total** (n = 230)*
Medial meniscus	21	60	80	161
Peripheral vertical tear	1	28	38	67
Bucket handle tear	20	26	32	78
Capsular tear	0	6	10	16
Lateral meniscus	15	27	27	69
Peripheral vertical tear	2	10	15	27
Bucket handle tear	11	14	9	34
Capsular tear	2	3	3	8

* Data excluding four patients with bicompartmental meniscal repair.

Table 3. Failure rate of meniscal repairs. ACLR = anterior cruciate ligament reconstruction

	Failure (n = 65)		p-value
Acute	9/36	25.0%	0.923
Subacute	25/91	27.5%	
Chronic	31/107	28.9%	
Medial*	55/161	34.2%	0.001
Lateral	10/69	14.5%	
Capsular tear	8/24	33.3%	0.674
Bucket handle tear	33/112	29.5%	
Peripheral tear	24/94	25.5%	
Stable knee with intact ACL	33/104	31.7%	0.154 †
Stable knee after ACLR	29/127	22.8%	
Unstable knee without ACLR §	3/3	100%	
Concomitant ACLR	21/103	20.4%	0.167 ‡
Postponed ACLR	8/24	33.3%	
No ACLR §	3/3	100%	

* excluding 4 patients with bicompartmental meniscal repair (n = 230). † p-value of stable knee with intact ACL versus stable knee after intact ACL. ‡ p-value of concomitant ACLR versus postponed ACLR. § too small group for statistical analysis.

In the acute group nine meniscal repairs failed (25.0%), in the subacute group twenty-five (27.5%), in the chronic group 31 (28.4%) (Figure 1). These differences were not statistically significant. The medial meniscus failed significantly more than the lateral meniscus, 55 of 161 (34.1%) versus ten of 69 (14.5%) (p = 0.001). After logistic regression analysis, the odds ratio for the compartment coefficient is 2.99 with a 95% confidence interval of [1.42

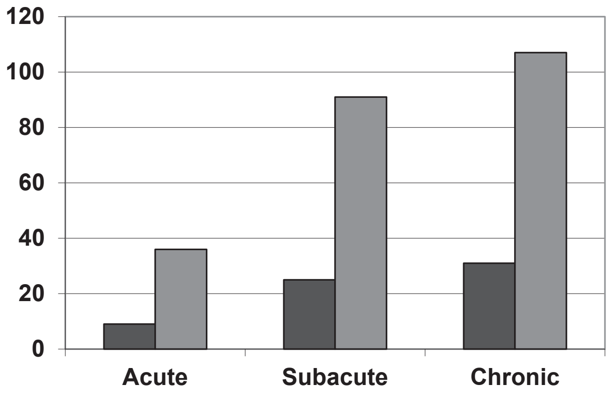

Figure 1. Bar chart showing number of failures and survivors in each group. Black = failure, grey = survivor.

- 6.31]. This suggests that those who have a meniscal repair in the medial compartment are three times more likely to fail than those with a lateral meniscal repair. The success rate of suturing capsular tears (66.7% survival), bucket handle tears (70.5% survival), and peripheral vertical tears (74.5% survival) did not significantly differ. No failure was seen in the four patients with a bicompartmental meniscal repair.

Of 234 patients, 130 patients (55.6%) had an insufficient ACL. All three patients having a meniscal repair in an ACL deficient refusing further ACL treatment failed. In the remaining 127 patients, 103 had a meniscal repair and an ACLR at once. Twenty-four patients had a postponed ACLR. A concomitant ACLR gave fewer failures than a postponed ACLR, but no significant differences in failure rate were found between these two groups. Twenty-one of 103 (20.4%) meniscal repairs with a concomitant ACLR failed, which not significantly differed from the meniscal repairs with a postponed ACLR, where eight out of 24 (33.3%) failed.

Secondary outcomes

Results of functional outcomes are described in Table 4. Functional outcome scores are shown for all 169 survivors. Functional outcome scores of patients with a failed meniscal repair were not evaluated, where we were only interested in the patient reported outcome measurements of patients with a successful meniscal repair to evaluate any differences between the different time intervals. Good Lysholm scores were seen for all subgroups. No significant differences in Lysholm score were found between the three groups. Tegner activity scale showed a higher activity level in the acute group, but the group differences were not significant. For KOOS score no significant difference was seen for all subscales, except for 'Function, daily living' (Activities in daily living; ADL). ADL scores were significantly higher for patients treated in the subacute and chronic group compared to the patients treated in the acute group (95% CI 1.05 – 15.27, p = 0.017). A survival point of

Table 4. Functional outcome scores of meniscal repair survivors (n = 169). All scores are the mean of each group (median, interquartile range).

	Acute (n = 27)	Subacute (n = 66)	Chronic (n = 76)	p-value (95%CI)
KOOS				
Symptoms	90 (96, 86 – 100)	91 (93, 87 – 100)	90 (96, 89 – 100)	0.846 (-8.07 – 5.63)
Pain	88 (97, 91 – 100)	91 (97, 89 – 100)	93 (97, 92 – 100)	0.228 (-12.66 – 2,47)
Function in daily living (ADL)	88 (100, 92 – 100)	95 (100, 97 – 100)	96 (100, 97 – 100)	0.017 (1.05 – 15.27) *

73% was found after 48 months (4 years) of follow-up (Figure 2). Mean time to failure was 13.6 months (median 9, IQR 5 – 19 months). Adverse events were found in only two cases. One patient had a suture granuloma after an all-inside repair. The second adverse event was observed in a patient after an inside-out meniscal repair where a septic arthritis of the knee developed. This was treated by arthroscopic lavage and antibiotics and the meniscal repair could be saved.

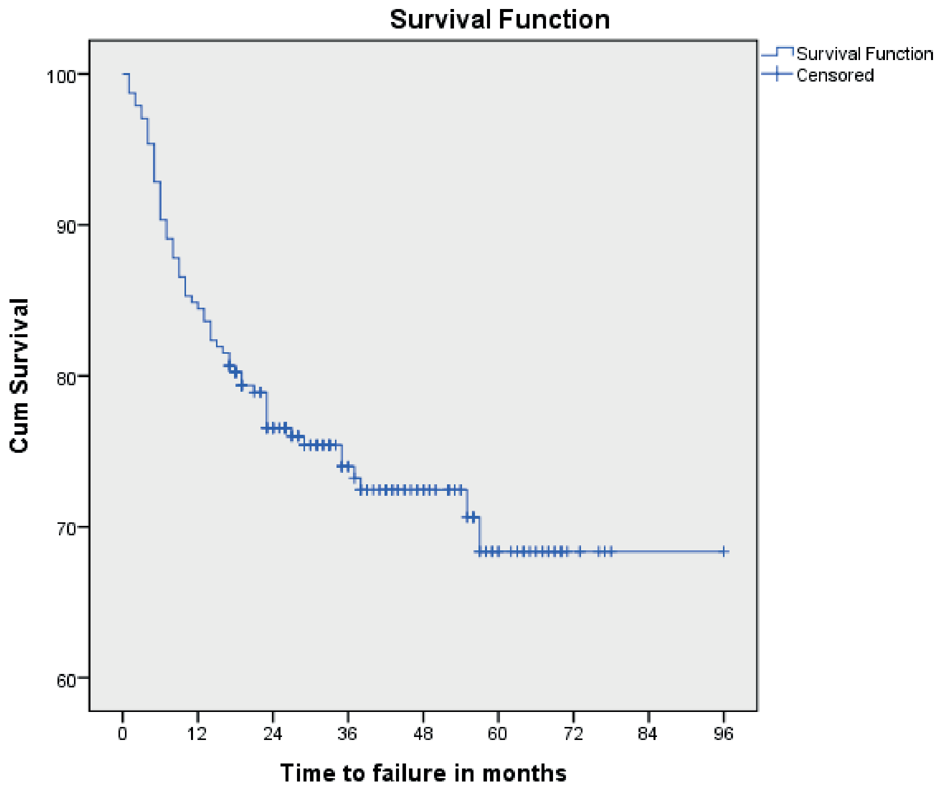

Figure 2. Survival curve of arthroscopic meniscal repair.

DISCUSSION

The goal of this retrospective study was to evaluate the reoperation and failure rates, subjective outcome score and complications of arthroscopic meniscal repair in relation to the time interval between injury and meniscal repair. We hypothesized that arthroscopic meniscal repair of chronic meniscal tears have higher failure rates and lower functional outcome scores. This study shows no significant difference in failure rate regarding the time interval between trauma and arthroscopic meniscal repair. This study also shows a similar clinical and radiological failure rate compared to the literature with a failure rate of 27%.[16]

We focused on chronicity of meniscal injury taking into account that defining acute and chronic meniscal tears is still controversial. In this study the threshold for chronic meniscal lesions was set at 12 weeks (3 months). We think that an acute tear may differ from other tears within the meaning of presence of mechanical problems (locked knee). We think more locked knees are seen in acute meniscal injury caused by displaced bucket handle tears. Making this distinction, a group with meniscal injury older than 2 weeks and younger than 12 weeks remains: subacute.

There is a well-known difficulty in assessing meniscal healing at follow-up. We believe that in an asymptomatic knee after meniscal repair the meniscus is healed, or at least partially healed. Second look arthroscopy is rarely possible because of costs and ethical considerations. Standard radiological follow-up using MRI also has a high additional cost and we did not use it to confirm meniscal healing. We did use it to confirm or exclude meniscal failure in the symptomatic patient. Because we did not perform a second-look arthroscopy, MRI arthrography or CT arthrography to confirm survival[17] at our minimum follow-up of one and a half year, we could have missed asymptomatic failures. So, we acknowledge that our functional outcome scores are an indirect evaluation of meniscal healing, also seen in the majority of similar studies.[18]

In our study, we have four patients with a bicompartmental meniscal repair. Because of the small number we used their data for survival analysis only. Repair of the lateral meniscus has a lower reoperation rate than repair of the medial meniscus in our study, a result also found in other studies.[16,18,19] The lower survival in medial meniscal repair is probably because of movement of the medial meniscus. The medial meniscus is anchored more tightly and has less flexibility and movement compared to the lateral meniscus.[20] Besides, the medial meniscus functions as a secondary stabilizer in the knee where it suffers from greater stress.[21]

Biomechanical laboratory testing has estimated that the lateral meniscus accounts for up to 70% of the load-bearing capacity of the lateral compartment, while the medial meniscus assumes up to 50% of the loads in its respective compartment.[22] After lateral meniscectomy compressive and shear stresses on the cartilage in the lateral compartment are higher than after medial meniscectomy[23] contributing to cartilage degeneration[24] and joint space narrowing.[25] Taken together, the higher success rate of lateral meniscal repair and the bigger deteriorating effect on the cartilage after partial lateral meniscectomy, an attempt to lateral meniscal repair must always be considered facing a lateral meniscal tear.

We found a higher reoperation rate in meniscal repairs after postponed ACLR compared to meniscal repairs with concomitant ACLR. The advantage of a concomitant ACLR during meniscal repair is well described.[4,5,12] In our series, a postponed ACLR shows almost 70% more failure than a concomitant ACLR. Probably, cellular elements and biochemical mediators that are essential for the repair response provided by local bleeding have better influence on meniscal healing during concomitant ACLR than during postponed ACLR. Micro-fracturing may create lower levels of blood and growth factors than tunnel drilling. However, we did not find a significant difference in failure rate between postponed and concomitant ACLR or between isolated meniscal repairs in a stable knee compared to meniscal repair during a concomitant ACLR or postponed ACLR. Micro-fracturing in the notch during isolated meniscal repair, which provides blood and growth factors and can accomplish the same environment as during ACLR can be a possible explanation for that.

Despite our strict preoperative indications some patients may have had a clinically silent lesion of the meniscus which was identified and repaired during the concomitant ACLR where instability was their main indication to operate. We know some stable meniscal tears can heal without suturing,[26,27] giving false positive results for meniscal survival during concomitant ACLR. Meniscal repairs in all patients with an ACL deficient knee failed. This group was too small to yield a significant conclusion. It may be clear that an intact ACL is an important factor for success in meniscal repair. An ACLR must always be performed in an ACL deficient knee together with a meniscal repair.[18,28]

Significant more bucket handle tears were sutured and significant more postponed ACLR were performed in the acute group ($p = 0.046$ and $p = 0.001$ respectively). The majority of these patients had an acute trauma with a locked knee because of a displaced bucket handle lesion. Despite different tear patterns, requiring all inside suture, inside-out sutures or a combination of both, we did not find any significant differences in survival rate between different types of meniscal sutures. Rosso et al,[4] showed in a controlled laboratory study that FiberWire suture repair is significantly stronger in load-to-failure testing compared to Meniscal Cinch (both used is our study). Where other studies showed that some meniscal repair devices have similar biomechanical properties to suture repairs.[29] Both suture repairs and devices have a place in meniscal restoration and for that reason we did not consider suture type as a contributing variable for further evaluation here.

As mentioned before, we believe that in an asymptomatic knee after meniscal repair the meniscus is healed, or at least partially healed. Unfortunately, preoperative function scores are lacking, which is a limitation in this study. Unfortunately, we could not compare functional outcomes between patients with a meniscal repair and patients with a partial meniscectomy after meniscal repair. Clinical survival of meniscal repair should show good patient reported outcome measurements. A good Lysholm score was seen in all groups.

Tegner activity scale showed a higher activity level in the acute group, but differences were not significant. Higher demands in sports and occupation in the acute group might compromise the outcome. As mentioned earlier, preoperative Tegner scores are lacking. An increase in Tegner activity scale in this young active population could tell us if patients had to modify their activity to reduce symptoms. ADL scores were significantly higher for patients treated in the subacute and chronic group compared to the patients treated in the acute group. Lower functional outcome in ADL, in a group with higher demands according to their Tegner score, can be the explanation for the lower 'Function, daily living' scores in the acute group.

The 75th percentile of the survival rate was 19 months which could suggest that the minimum follow-up period of 18 months in this study is too short to give a final conclusion about survival rates. A lengthening of the follow-up period is necessary.

There are several limitations for this study. First, this study is a retrospective case series, lacking a control group. A second limitation is the high rate of patients lost to follow-up. Seventy three patients (25%) were lost to follow-up. Nonetheless, because of the same patient characteristics in this group compared to the group with patients available at follow-up, we think the study population is suitable for evaluation and to draw conclusions. The lack of second look surgery or regular radiological evaluation at follow-up, mentioned earlier, is also a limitation. However, follow-up was performed by chart review and by asking patients if they were re-operated on their affected knee. Patients with recurrent symptoms (low questionnaire scores) without re-operation or radiographic evaluation could be failures, but this was not further evaluated. The difference in after treatment, especially the restriction in pivoting activities, could have had influence on the risk for re-injury. Final limitation of this retrospective cohort study is the heterogeneity of the study population. For that reason, we have chosen not to discuss the different types of repair techniques. Though, we analysed this and we found no significant differences in failure rate in number of sutures and repair technique. Some groups (patients with bicompartmental meniscal repair or an ACL deficient knee without ACLR) were too small to yield a significant conclusion.

In conclusion, there is no significant difference in failure rate regarding the time interval between trauma and arthroscopic meniscal repair. The consideration for meniscal repair should be based on preoperative MRI results and intraoperative findings, not on chronicity of injury. Survival of meniscal repair is more dependent on location of the lesion (medial versus lateral) and ACL status. When an ACLR is indicated together with a meniscal repair in an ACL deficient knee, a concomitant procedure is recommended above a postponed ACLR.

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4

Intraobserver and interobserver agreement of MRI for reparability of peripheral meniscal tears. What criteria do really matter?

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ABSTRACT

Background: Prediction of meniscus reparability is useful for surgeons to optimise surgical scheduling and to inform patients about postoperative management.

Purpose: Determination of the intra- and interobserver agreement of three magnetic resonance imaging (MRI) criteria for reparability: a peripheral rim smaller than 4 mm, a tear longer than 10 mm and homogenous aspect of meniscal tissue.

Study design: Cohort study (diagnosis)

Methods: In two rounds with an interval of at least 6 weeks, 3 orthopaedic surgeons and 3 musculoskeletal radiologists studied the preoperative MRI scans of 63 patients with a longitudinal full-thickness medial or lateral meniscal tear. All patients had an arthroscopic meniscal repair. The blinded images were evaluated measuring the tear length and rim width and meniscal aspect was classified. Agreement was calculated using the linear weighted Kappa coefficient (κ) and the intraclass correlation coefficient (ICC). Examiner agreement strength was defined according to the guidelines of Landis and Koch.

Results: Intraobserver agreement was poor to good (κ 0.12 – 0.72) for the classification of the meniscal aspect and decreased in lateral meniscal tears. The interobserver agreement for meniscal aspect was mainly poor to fair (κ 0.09 – 0.53). The intraobserver reliability for measurement of the length of the meniscal tear was moderate to excellent (ICC 0.51 – 0.80) for all observers in both rounds and moderate to good (ICC 0.59 – 0.73) for measurement of the peripheral rim width. The interobserver agreement on tear length and rim width was moderate in both rounds (ICC 0.58 and 0.50 in round 1 and 0.50 and 0.50 in round 2, respectively).

Conclusions: Tear length and rim width are the only two measurements with moderate to good agreement. However, these measurements do not predict reparability of a longitudinal meniscal tear on MRI images.

INTRODUCTION

Preserving meniscal tissue and thereby saving meniscal function decreases the risk of premature osteoarthritis after meniscectomy.[13,19] For that reason, meniscal repair is preferable above partial meniscectomy in the treatment of meniscal tears whenever possible. Preoperative knowledge about the reparability of a meniscal tear can be an important step in the management of meniscal tears, where it can help to inform patients about their treatment, postoperative management and it helps surgeons to optimise surgical scheduling. Intraoperative criteria for meniscal repair are based on factors like tear length, tear instability and tear type.[10] The International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS) classification of meniscal tears was developed to classify tear depth, rim width, location, tear pattern, and quality of the tissue based on intraoperative findings and provides sufficient interobserver reliability to evaluate the outcome after meniscal treatment.[1] Magnetic Resonance Imaging (MRI) is currently used on a routine base to diagnose ligament injury or meniscal tears of the knee with high sensitivity and specificity.[12] Using MRI to predict reparability is far less established. Criteria for meniscal repair based on MRI were first stated by Matava in 1999. The tear length of longitudinal or bucket handle tears, the distance from tear to meniscosynovial junction, tear location and minimal damage were considered important parameters for meniscal repair.[10] Criteria for prediction of meniscal reparability based on MRI for only medial bucket handle meniscal tears were further prescribed by Thoreux based on anatomical knowledge and surgical experience. They enlarged the criteria based on distance from tear to meniscosynovial junction (rim width) and defined the minimal damage of the inner and peripheral meniscal fragments.[20] Finally, criteria for reparability of both medial and lateral longitudinal full-thickness meniscal tears were defined. A tear was considered reparable when it met all of the following criteria: (1) a bucket handle rim segment less than 4 mm wide; (2) tear length of $\geq$ 1 cm, regardless of the total tear length; and (3) minimal damage to the inner and peripheral meniscal fragments (described as generated low signals or isosignals compared with the normal contralateral meniscus of the same knee, thereby demonstrating the absence of degenerative tears).[11] These three criteria on reparability are used for both medial and lateral longitudinal full-thickness meniscal tears, but were never validated. Useful criteria on reparability should have good intraobserver and interobserver agreement. Therefore, we performed an observational study to determine intra- and interobserver agreement on meniscal reparability for longitudinal, peripheral meniscal tears based on MRI among both orthopaedic surgeons and musculoskeletal radiologists.

According to our knowledge the ISAKOS classification system was never used to describe tear morphology based on MRI images. We evaluated the usefulness of the ISAKOS classification in classifying meniscal tears on MRI. We hypothesized that the three above mentioned MRI criteria and the ISAKOS classification have good to excellent (weighted Kappa (κ) ≥ 0.61) intra- and interobserver agreement.

MATERIALS AND METHODS

Patients

We retrospectively reviewed the preoperative MRI images of 63 consecutive patients, who underwent an arthroscopic meniscal repair of a longitudinal, peripheral meniscal tear between June 2008 till August 2011. The study included 45 (71%) men and 18 women with a median age of 24 years (Inter Quartile Range (IQR), 18 – 31 years). No revision cases were included in our study. Thirty-eight out of 63 (60%) patients had a medial meniscal tear, of which 22 were displaced. Twelve of the 25 patients with a lateral meniscal tear, had a displaced meniscal tear. The Medical Ethical Review Board decided that approval for this study was not necessary.

Patient evaluation

Multiple attempts (maximal five) were made, to contact all 63 patients by telephone during summer 2014. All medical records were checked for postoperative radiographic examinations, reoperations and complications. If patients could be reached, they were asked to complete questionnaires about their medical history, especially about any possible reoperation or radiographic examination elsewhere. Patients were not evaluated in the outpatient clinic. The criteria for failure were partial or (sub)total meniscectomy of the previous sutured meniscus or failure (re-tear or partial healing) proven by radiological examination (MRI or Computed Tomography (CT) arthrography).

Surgical technique

At arthroscopy, criteria for meniscal repair were: a vertical tear in red zone or red-white zone (vascularized peripheral zone of the meniscus), a tear length > 1 cm, and non-degenerative, homogenous meniscal tissue. A millimeter ruler to measure tear length and rim width was not available. The standard procedure for isolated meniscal repair included rasping of the peripheral rim and meniscus, suturing the posterior horn with all-inside sutures and the middle section with inside-out sutures, and drilling holes in the intercondylar notch to provide blood and growth factors.

MRI technique

MRI examinations were performed using a 1.5 Tesla (T) Siemens Avanto MRI scanner in 12 patients, a 1.5 T Siemens Magnetom Essenza MRI scanner in 22 patients, and a 1.5 T Siemens Harmony MRI scanner in 29 patients (all Siemens Medical Systems, Erlangen, Germany). For all examinations, a 16 cm field of view was used and patients were scanned in supine position using a phased array knee coil. The examinations performed on the Magnetom Essenza MRI scanner included coronal and sagittal T2-weighted images and with repetition times (TR) of 800 to 1130 ms and echo times (TE) of 27 ms, slice thickness (ST) was 4 mm with a gap/slice spacing (SS) of 0.8 mm, and a matrix size of 384 x 234. On the Siemens Avanto MRI scanner a coronal and sagittal T2 Medic were performed with a TR of 700 ms, TE of 23 ms, ST of 4 mm with a SS of 0.8 mm and a matrix size of 320 X 256. The protocol on the Siemens Symphony included a coronal and sagittal T2 Medic with a TR of TR of 976 to 997 ms, TE of 27 ms, ST of 4 mm and a SS of 0.8mm and a matrix size of 256 x 156, and 320 x 216 respectively. The examinations performed on the Siemens Harmony scanner included a coronal and sagittal T2 Medic having a TR of 867 ms, TE of 26 ms, ST of 4 mm, SS of 0.8 mm and matrix size of 256 x 179.

Image evaluation

Review of images was performed on a Picture Archiving and Communication System (PACS) workstation (GE Healthcare, Hoevelaken, Netherlands). Three orthopaedic surgeons and three musculoskeletal radiologists independently evaluated the MRI images in two rounds. The orthopaedic surgeons had 17 years, 8 years and 6 years of experience. The radiologists had 22 years, 20 years and 11 years of experience in musculoskeletal imaging. The observers were aware of the patients' meniscal injury, but had no additional information about the MRI report, patients' demographics, clinical findings and orthopaedic treatment. They were blinded for the fact that only repaired longitudinal, peripheral meniscal tears were included. After the first review session the patients' MRI images were shuffled randomly and evaluated for a second time. The minimal interval between the two observation rounds had to be at least six weeks.

The observers were asked to measure the width of the peripheral rim and the length of the meniscal tear in millimeters (mm), and to describe the aspect of the meniscal tissue and tear morphology to determine intraobserver and interobserver agreement on meniscal reparability using the following criteria: (1) a bucket handle rim segment less than 4 mm wide; (2) tear length of $\geq$ 1 cm, regardless of the total tear length; and (3) minimal damage to the inner and peripheral meniscal fragments. Tear length was measured by counting the number of slices on which the tear was seen multiplied by the slice thickness in mm. The distance from the meniscosynovial junction to the meniscal tear as seen on the sagittal and coronal MRI images were estimated using standard ruler divided in mm increments. Aspect of the meniscal tissue of the inner and peripheral meniscal tear fragments was compared with the normal, contralateral meniscus of the same knee to determine homogeneity (low signals or isosignals). Meniscal aspect was scored as homogeneous (low signal) or heterogeneous (high signal). Tear morphology was classified by the ISAKOS classification: longitudinal-vertical (extension of this tear is a bucket handle tear), horizontal, radial, vertical flap, horizontal flap, and complex.[1] With six items in the ISAKOS classification for meniscal tears, 63 patients included in this study was enough to get a reliable intraobserver and interobserver agreement.[4]

At the end all observers were asked to answer a key question, whether they would perform a meniscal repair or not, based on their own experience and daily practise and not (only) based on the given three criteria.

Statistics

Data of tear length and rim width were tested for normality. We evaluated the mean length of peripheral rim and meniscal tear length scored by each examiner for both rounds. A weighted Kappa (κ) coefficient was performed to determine consistency among observers for categorical data. For both rounds the Fleiss' Kappa was calculated to show the overall agreement for the six observers. For continuous data, including tear length and peripheral rim width, the intraclass correlation coefficient (ICC) using a 2-way random effects model was calculated to estimate intra- and interobserver reliability.[18] Wilcoxon signed rank test was used to compare paired data between groups. The strength of examiner agreement was defined according to the guidelines of Landis and Koch as follows: poor, $\kappa \leq 0.20$; fair, $\kappa = 0.21$ to 0.40; moderate, $\kappa = 0.41$ to 0.60; good, $\kappa = 0.61$ to 0.80; and excellent, $\kappa = 0.81$ to 1.00.[9] A Student's T-test was used to calculated statistical differences in rim width and tear length between meniscal repair failures and survivors. Statistical analysis was performed using SPSS statistical software (version 20, SPSS Inc, Chicago, IL).

RESULTS

Our study population of 63 patients contained slightly more patients with a displaced meniscal tear (n = 34) than with a non-displaced tear (n = 29), and slightly more medial tears (n = 38) than lateral tears (n = 25). Twenty-two of 38 (58%) medial meniscal tears were displaced and 12 of 25 (48%) lateral meniscal tears were displaced.

Time interval between the two observation rounds varied from 3 months to 5.5 months. According to the measurements and reviews of the observers, 35% to 60% (average 48%) of the patients met all three MRI criteria for reparability. This percentage was lower than the average of 61.4% measured with the key question on meniscal repair of patients considered suitable for meniscal repair according to the 'key question'.

Meniscal Aspect

Results of intraobserver agreement on meniscal aspect were evaluated for all patients and results are shown in Table 1. Intraobserver agreement for orthopaedic surgeons was moderate to good, while the radiologists had a poor to moderate intraobserver agreement of the meniscal aspect, all results are shown in Table 1. Intraobserver agreement did not change when dividing the tears on bases of displacement: displaced tears versus non displaced tears. Intraobserver agreement, was higher for medial tears compared to lateral tears. Interobserver agreement on meniscal aspect in both rounds was fair with a Fleiss' Kappa of 0.34 and 0.31, in respectively round 1 and 2. Kappa coefficient varied from 0.15 to 0.53 in round 1 and 0.09 to 0.53 in round 2 (Table 2).

Table 1. Intraobserver agreement of the meniscal aspect in all patients, in patients divided by tear displacement (displaced versus non displaced) and in patients divided by knee compartment (medial versus lateral).

	All tears (n = 63)			
	κ	95% CI		
OS 1	0.63	0.53 – 0.73		
OS 2	0.72	0.63 – 0.80		
OS 3	0.42	0.31 – 0.54		
Rad 1	0.30	0.20 – 0.41		
Rad 2	0.12	0.08 – 0.16		
Rad 3	0.41	0.25 – 0.56		
	Displaced tears (n = 34)		**Non displaced tears (n = 29)**	
	κ	95% CI	κ	95% CI
OS 1	0.64	0.50 – 0.77	0.61	0.45 – 0.77
OS 2	0.71	0.59 – 0.83	0.73	0.61 – 0.85
OS 3	0.30	0.12 – 0.47	0.52	0.36 – 0.68
Rad 1	0.31	0.19 – 0.44	0.30	0.12 – 0.49
Rad 2	0.07	0.02 – 0.13	0.18	0.13 – 0.23
Rad 3	0.46	0.25 – 0.66	0.34	0.11 – 0.58
	Medial tears (n = 38)		**Lateral tears (n = 25)**	
	κ	95% CI	κ	95% CI
OS 1	0.63	0.50 – 0.75	0.60	0.42 – 0.78
OS 2	0.68	0.56 – 0.80	0.76	0.63 – 0.89
OS 3	0.44	0.28 – 0.60	0.36	0.17 – 0.55
Rad 1	0.52	0.39 – 0.65	0.06	-0.08 – 0.19
Rad 2	0.11	0.06 – 0.16	0.09	0.03 – 0.16
Rad 3	0.42	0.24 – 0.60	0.34	0.04 – 0.63

OS = Orthopaedic Surgeon; Rad = Radiologist. κ = Kappa coefficient. 95% CI = 95% Confidence Interval.

Table 2. Interobserver agreement of the meniscal aspect and tear type in both observation rounds (round 1 and round 2).

	Meniscal aspect				Tear type			
	Round 1		Round 2		Round 1		Round 2	
	κ	95% CI	κ	95% CI	κ	95% CI	κ	95% CI
OS 1 vs OS 2	0.53	0.43 –0.63	0.38	0.27 – 0.50	0.30	0.17 – 0.43	0.38	0.22 – 0.54
OS 1 vs OS 3	0.46	0.36 – 0.55	0.24	0.14 – 0.34	0.25	0.12 – 0.38	0.31	0.06 – 0.57
OS 2 vs OS 3	0.45	0.34 – 0.56	0.53	0.44 – 0.63	0.41	0.28 – 0.54	0.49	0.26 – 0.69
Rad 1 vs Rad 2	0.39	0.28 – 0.51	0.16	0.12 – 0.20	0.06	-0.05 – 0.17	0.03	-0.01 – 0.08
Rad 1 vs Rad 3	0.31	0.18 – 0.41	0.24	0.14 – 0.34	0.09	-0.03 – 0.15	0.03	-0.06 – 0.11
Rad 2 vs Rad 3	0.24	0.13 – 0.36	0.10	0.07 – 0.13	0.10	-0.03 – 0.23	0.04	0.02 – 0.05
OS 1 vs Rad 1	0.49	0.33 – 0.55	0.34	0.23 – 0.46	0.04	-0.07 – 0.15	0.01	-0.09 – 0.11
OS 1 vs Rad 2	0.37	0.25 – 0.49	0.20	0.16 – 0.23	0.17	0.15 – 0.29	0.07	-0.0 – 0.161
OS 1 vs Rad 3	0.37	0.27 – 0.48	0.28	0.16 – 0.40	0.01	-0.09 – 0.19	0.05	0.03 – 0.07
OS 2 vs Rad 1	0.19	0.10 – 0.29	0.26	0.14 – 0.39	0.10	-0.00 – 0.20	0.17	0.06 – 0.27
OS 2 vs Rad 2	0.38	0.27 – 0.49	0.12	0.08 – 0.16	0.10	0.00 – 0.20	0.19	-0.00 - 0.38
OS 2 vs Rad 3	0.22	0.14 – 0.30	0.30	0.20 – 0.39	0.21	0.10 – 0.32	0.55	0.32 – 0.78
OS 3 vs Rad 1	0.22	0.14 – 0.30	0.26	0.15 – 0.37	0.24	0.12 – 0.36	0.18	0.07 – 0.29
OS 3 vs Rad 2	0.43	0.33 – 0.53	0.10	0.06 – 0.15	0.25	0.20 – 0.39	0.12	0.01 – 0.22
OS 3 vs Rad 3	0.15	0.09 – 0.22	0.09	0.02 – 0.16	0.27	0.13 – 0.41	0.38	0.10 – 0.66
Fleiss' Kappa	0.34		0.31		0.19		0.19	

OS = Orthopaedic Surgeon; Rad = Radiologist. κ = Kappa coefficient. 95% CI = 95% Confidence Interval.

Rim width and tear length

Intraobserver reliability for meniscal tear length and the peripheral rim width was moderate to excellent for all observers in both rounds. Absolute values and the intraclass correlation coefficients are shown in Table 3. In all except five (0.007%) observations, tear length was measured longer than 1 cm. Interobserver agreement on tear length was moderate (ICC round 1 = 0.58 and ICC round 2 = 0.52). Interobserver agreement on rim width was moderate (ICC round 1 = 0.50 and ICC round 2 = 0.50).

Tear type

In two rounds, the right tear type (a longitudinal tear as described intraoperatively) was scored in 85.5% of the cases (Table 4). The number of correct scored tear types was slightly higher in the group of orthopaedic surgeons compared to the group of radiologists (89.2% versus 81.7%, $p = 0.09$). A horizontal meniscal tear was the second most scored tear type. The intraobserver reliability for tear type using the ISAKOS classification for meniscal tears was poor to moderate, as shown in Table 4. Interobserver agreement on tear type in both rounds was poor with a Fleiss' Kappa of 0.19 in both rounds. Kappa coefficient varied from 0.01 to 0.41 and 0.03 to 0.55, in respectively round 1 and round 2 (Table 2).

Table 3. Intraobserver agreement of the tear length and of the peripheral rim in both rounds. Tear length and rim width (median and interquartile range (IQR)) in millimeters.

	Tear length[1]	Tear length[2]	ICC	95% CI	Peripheral rim width[1]	Peripheral rim width[2]	ICC	95% CI
OS 1	28.8 (24.0 – 33.6)	33.6 (28.8 – 33.6)	0.51	0.19 – 0.70	3.8 (2.5 – 4.4)	3.7 (3.1 – 4.5)	0.72	0.57 – 0.73
OS 2	38.4 (28.8 – 43.2)	38.4 (28.8 – 43.2)	0.71	0.57 – 0.82	3.8 (2.5 – 4.9)	3.8 (2.3 – 4.7)	0.73	0.59 – 0.83
OS 3	33.6 (24.0 – 38.4)	33.6 (28.8 – 38.4)	0.80	0.70 – 0.88	3.1 (1.9 – 4.0)	3.2 (1.9 – 4.1)	0.73	0.59 – 0.83
Rad 1	33.6 (28.8 – 43.2)	28.8 (28.8 – 38.4)	0.58	0.39 – 0.72	2.8 (1.5 – 4.0)	3.6 (2.2 – 4.8)	0.64	0.46 – 0.77
Rad 2	33.6 (24.0 – 38.4)	33.6 (24.0 – 38.4)	0.79	0.68 – 0.87	3.0 (2.0 – 4.0)	3.4 (2.2 – 4.1)	0.59	0.40 – 0.73
Rad 3	28.8 (24.0 – 33.6)	28.8 (24.0 – 33.6)	0.51	0.30 – 0.67	3.0 (2.0 – 4.0)	3.6 (2.8 – 4.7)	0.69	0.54 – 0.80

1 = round 1, 2 = round 2. OS = Orthopaedic Surgeon; Rad = Radiologist. ICC = intraclass correlation coefficient. 95% CI = 95% Confidence Interval.

Table 4. Tear morphology. Absolute numbers and average percentage (%) of correct estimates of tear morphologic type by examiner in two rounds and intraobserver agreement on tear morphology using the ISAKOS classification.

Longitudinal tear (n = 63)					
	Round 1	Round 2	%	κ	95% CI
OS 1	54	59	89.7	0.17	0.03 – 0.31
OS 2	49	59	85.7	0.40	0.26 – 0.54
OS 3	55	61	92.1	0.34	0.16 – 0.52
Rad 1	46	44	71.4	0.51	0.39 – 0.62
Rad 2	54	58	85.7	0.20	0.05 – 0.35
Rad 3	50	60	88.1	0.19	0.06 – 0.33
Average			85.5		

OS = Orthopaedic Surgeon; Rad = Radiologist. κ = Kappa coefficient. 95% CI = 95% Confidence Interval.

Failure

Median follow-up was 52 months (IQR, 45 – 58 months). Data of 57 patients were available for evaluation (90.5%). Up to date personal data of 4 patients were not available, so they could not be reached by phone or mail, not even after contacting their general practitioner. One patient was excluded because he did not speak Dutch or English and therefore was unable to complete our Dutch or English evaluation. One patient did not return the questionnaires.

In these 57 evaluable patients 14 meniscal repairs failed (25%). No significant differences in tear length and rim width were found between the groups of patients with or without a failed meniscal repair for all observers. Intraobserver agreement of tear length varied from moderate to good (0.46 – 0.80) for patients with a failed meniscal repair and varied from fair to good for patients with an intact meniscal repair (0.34 - 0.76). Intraobserver agreement on rim width varied from moderate to good for both groups (0.49 – 0.74 and 0.52 – 0.78). Interobserver agreement on tear length was fair (ICC round 1 = 0.29 and ICC round 2 = 0.27) for the failed meniscal repairs and moderate to good for meniscal repair survivors (ICC round 1 = 0.59 and ICC round 2 = 0.63). Interobserver agreement on rim width was moderate to good (ICC round 1 = 0.47 and ICC round 2 = 0.66) for the failed meniscal repairs and moderate (ICC round 1 = 0.42 and ICC round 2 = 0.47) for meniscal repair survivors.

DISCUSSION

The results of this study showed that meniscal aspect has poor intraobserver and interobserver agreement. Furthermore, rim width and tear length have moderate to good intra- and interobserver agreement. For that reason, rim width and tear length may be more valuable criteria for reparability of longitudinal meniscal tears on MRI, especially because the meniscal aspect is not only influenced by meniscal damage.

In our study, agreement on meniscal aspect was low especially in lateral meniscal tears. Sensitivity is shown to be related to the location and tear pattern for the lateral meniscus, with peripheral longitudinal tears involving the posterior third of the meniscus demonstrating the lowest sensitivities.[16] False-negatives are more common in the lateral meniscus as well, especially with tears of the posterior horn or if less than one-third of the meniscus is involved.[5] High signal intensity in the body of the meniscus in MRI is a well-established criterion for diagnosing a meniscal tear or degeneration. However, an increased signal in the posterior horn of the lateral meniscus can be due to the magic-angle phenomenon rather than to meniscal degeneration or a meniscal tear.[15] Given the very specific criteria based on signal-intensity on MRI to predict spontaneously healing,[8] using criteria based on signal-intensity to predict reparability instead of meniscal healing may be difficult to use as well. All this can be an explanation for the low agreement on this item, so we have to conclude that a heterogeneous or high MRI signal of the axial part of the meniscus does not compromise arthroscopic reparability.

The displaced fragment of a bucket handle meniscal tear can have a high-intensity signal, which changes to low after reduction of the meniscus to its original position and may therefore be described as degenerative.[7] Low agreement on meniscal aspect in both patients with a displaced and without a displaced bucket handle tear and the possibility to wrongly assess a displaced fragment as degenerative, are two other reasons why meniscal aspect is less valuable as a criterion for reparability.

As mentioned earlier, according to our observers 48% of the patients met all three MRI criteria for reparability. Median measured rim width varied little from 2.8 to 3.8 mm in our study. When using rim width with the cut-off point of 4 millimeters, 68.2% of our would have a reparable meniscus. Of course, enlarging the criterion rim width in millimeters will increase this amount of patients. However, this remains controversial based on meniscal size and blood supply. Capillaries are penetrated in up to 25% of the lateral meniscus and in up to 30% of the medial meniscus.[2] Together with the size of medial and lateral meniscus in people without osteoarthritis measured on MRI, using the central 5 MRI slices representing the meniscus body, a peripheral rim of 3 mm is expected to have good blood supply. Probably for this reason a maximum distance of 3 mm from tear to meniscosynovial junction was chosen as criterion in other studies.[3,10,17] When we would have used this cut-off point of 3 mm in our study population, only 42.2% of the patients would have met this criterion. Matava and co-workers were uncertain about reparability of meniscal tears having a peripheral rim width of 3 to 5 mm, but they did not find those tears irreparable.[10] All of this makes the use of rim width as a criterion for reparability doubtful. Despite the moderate to excellent agreement, only there 68% of the patients in this study met this criterion. Increasing the rim width is not consistent with meniscal vascular anatomy, while decreasing rim width will lead to a large population who will wrongly be rejected for a meniscal repair based on MRI images.

The meniscal tear length gives an indication about its stability and is an important criterion for meniscal repair. In all except five out of 756 observations, tear length was measured longer than 1 cm. This confirms the inclusion criteria for this study.

We have found an average of 85.5% correct scored tears using the ISAKOS classification for meniscal tears, which we find a reasonable score. Radiologists are less familiar with the ISAKOS classification, which could be a possible explanation for their lower score (81.7%) compared to the orthopaedic surgeons (89,2%). A horizontal meniscal tear was the second most scored tear type in this patient group with only longitudinal tears. If a tear appeared in an oblique configuration, this may be scored as a horizontal, instead of a longitudinal tear, this could have decreased the number of correct scored tears. The low intra- and interobserver agreement suggests that the use of this classification is not valuable for describing tear morphology on MRI.

There are two possible explanations for the higher score on reparability according to the key question (61%) compared to the score based on meeting all three MRI criteria (48%). First, because of the consequences of a lateral meniscectomy,[14] the threshold performing a meniscal repair might be lower when facing a lateral meniscal tear. Second, patient's young age, indirectly given by the presence of open epiphysis on MRI, may influence the decision about reparability because of the consequences of (partial) meniscectomy in the young patient.

There was no significant difference in tear length and rim width between the group with a failed meniscal repair and the group without a failed meniscal repair, which contradicts an eventually low threshold for meniscal repair in some patients in this study population. Together with the fair to good interobserver agreement on tear length and a moderate to good agreement on rim width between these two groups, we can conclude that the criteria tear length and rim width measured on MRI cannot predict survival of a meniscal repair.

Our study has some limitations. We were unable to consistently correlate the observers' estimation of tear length and minimum distance from the meniscosynovial junction with actual intraoperative measurements because this information was occasionally missing from the operative records. Software to measure the precise tear length on MRI in three dimensions, using X, Y, Z coordinates, was lacking and is not used on a routine base. Calculation tear length by multiplying number of slices with slice thickness does not give the exact tear length. On the other hand is it a reliable way with a moderate to excellent observer agreement. Three MRI scanners were used in this study. All were 1.5 Tesla using the same slice thickness and gap/slice spacing, but they slightly differ in repetition times, echo times and matrix size. Finally, we used these 1.5T scanners, while the improved resolution on 3T scanners now more and more used, may improve predicting meniscal reparability in the future. However, Grossman et al showed no improvements in the sensitivity of 3T MRI for detecting meniscal tears when compared with 1.5T scanners.[6]

CONCLUSION

A tear length and a rim width are the only two measurements with good agreement. However, these measurements do not predict reparability of a longitudinal meniscal tear on MRI images. Based on the function of the meniscus, and the deleterious biomechanical and long-term clinical effect of removing part of the meniscus, we advise to always consider meniscal repair first and take the risk of failure when facing a longitudinal, peripheral meniscal tear on MRI.

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5

Long-term clinical outcome of open meniscal allograft transplantation.

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ABSTRACT

Background: Meniscal allograft transplantation for the symptomatic post-meniscectomized knee in younger patients has become an accepted treatment. However, long-term data on the clinical outcome of this procedure are scarce.

Hypothesis: Cryopreserved meniscal allograft transplantations can be in the long-term a good alternative for the symptomatic post-meniscectomized knee in younger patients.

Study Design: Case series; Level of Evidence, 4.

Methods: Sixty-three meniscal allografts were transplanted with an open procedure in 57 patients. Clinical outcome and failure rate of 40 lateral and 23 medial meniscal allografts were evaluated at a mean follow-up of 13.8 years ± 2.8 years. Mean age at time of transplantation was 39.4 years ± 6.9 years.

Results: Eight medial allografts (35%) and ten lateral allografts (25%) failed. Overall failure rate was 29%. A significant improvement in overall mean Lysholm score was seen, from 36 ± 18 points (range, 5-86 points) preoperatively to 61 ± 20 points (range, 21-91 points) at long-term follow-up. Long-term and preoperative Lysholm scores were not significantly different in the following subgroups; medial allografts, female patients and left treated knees. All subgroups had a poor Lysholm score at mean follow-up of 13.8 years, except the male patient group which had a fair Lysholm score. Short-term Lysholm scores at a mean follow-up of 3.1 ± 1.5 years (range, 0.5-7.3 years) was overall 79 ± 19 points (range 19-100). A significant difference between short- and long-term Lysholm scores was found for all subgroups. Significant differences for KOOS and IKDC scores were only present between male and female patients. No significant differences in Lysholm scores were seen between post-transplanted survivors and post-transplanted non-survivors who received a total knee arthroplasty.

Conclusions: Long-term follow-up results show that meniscal allograft transplantation is a beneficial procedure. Good improvements in clinical function and pain relief have previously been shown at short-term follow-up in this population. Despite the deterioration over time in function scores, there is still improvement in level of function at long-term follow-up, but not at high level. This means that meniscal allograft transplantation is a good option for the treatment of degenerative arthritis of the symptomatic, post-meniscectomized knee. Meniscal allograft transplantation can be used to postpone total knee arthroplasty in younger patients.

INTRODUCTION

Menisci have an important role in load transmission, shock absorption, joint stability, lubrication and nourishment of the joint. In the initial report of Fairbank, the natural clinical history of meniscectomy on the knee was demonstrated.[7] Since then many clinical and biomechanical investigations have shown that meniscectomy can lead to progressive degenerative changes in the knee.[11,12,24] In addition it has been shown that the risk of post-meniscectomy arthritis correlates with the amount of meniscal tissue resected.[1,18] Arthritic disease after meniscectomy in active, younger patients (<55 years) is not uncommon and its prevalence is expected to increase. Surgical options for these patients by placing a total knee arthroplasty (TKA) or unicompartmental knee arthroplasty (UKA) remain controversial. The survival rate of TKA for younger patients (<55 years) in literature is scarce and varies between 85 and 99 at a minimum of 13 years follow-up.[6,8] In younger patients with a normal aligned knee, intact cruciate ligaments and disabling compartmental osteoarthritis meniscal allograft transplantation is another treatment option. Since the first human meniscal allograft transplantation in 1984 by Milachowski et al.[19], meniscal allograft transplantation has become an acceptable option for treatment of the post-meniscectomized arthritic knee. Short- and mid-term studies showed pain relief, functional improvement and improvement in the clinical and radiological survival of the allograft after transplantation.[4,23,25] Van Arkel et al. have already published an extended report about the short-term and mid-term results of this study population.[2,3] However, data on long-term follow-up of meniscal allografts is scarce.

The purpose of this study was to report the long-term results of 63 meniscal allograft transplantations with a mean follow-up of 13 years. We evaluated if meniscal allograft transplantation is an effective manner to improve patients' satisfaction and clinical outcome in younger patients because total knee arthroplasty has to be postponed. We paid special attention to the failure rate at long-term follow-up.

MATERIALS AND METHODS

Between 1989 and 1999, 57 patients received 63 cryopreserved non-tissue-antigen-matched human meniscal allografts. The study group consisted of 40 men and 17 women with a mean age of 39.4 ± 6.9 years (range, 26-55 years) at time of transplantation. The medial meniscus was transplanted in 17 patients (with and without sufficient ACL), the lateral meniscus in 34 patients, and six patients were transplanted with both menisci in the same knee. The mean interval period between total meniscectomy and meniscal allograft transplantation was 16.2 ± 7 years (range, 2-33 years). Details of the meniscal allografts and patient characteristics are given in Table 1 and 2. The indication, preoperative planning, surgical procedure and postoperative management were described in detail in 1995.[2] Briefly; in the first series of 23 transplantations an open procedure was used to transplant unmatched, cryopreserved meniscal allografts in patients under the age of 55 years with disabling compartmental osteoarthritis after meniscectomy. No further inclusion criteria were used here. Inclusion criteria changed after the first series of 23 transplantations. In this first series 8 patients had an abnormal aligned knee (3˚ varus to 6˚ valgus) and 6 patients had a ruptured ACL. In the second series only patients under the age of 45 years with disabling compartmental osteoarthritis after meniscectomy and a stable, normal aligned knee were included. A diagnostic arthroscopy was performed before transplantation and routine radiographs were taken. Joint space narrowing was not scored. The grafts were fixed, without bony fixation, using six to nine absorbable and non-absorbable sutures. No immunosuppression was used. Intra-operative cartilage damage was scored using the Outerbrigde classification.[20]

Multiple attempts were made to contact all 57 patients by telephone. If they could be reached they were asked to complete postal questionnaires after they had given their informed consent. If patients could not be reached, their general practitioner was requested to give information about the patients' medical history. The patients were not evaluated in the outpatient clinic. Study instruments included the Knee injury and Osteoarthritis Outcome Score (KOOS), Lysholm and the International Knee Documentation Committee (IKDC) scoring system.

The criteria for failure of an allograft were complete resection of the graft, with or without placement of UKA or TKA.

Statistical analyses were performed using the paired samples *t* test, Spearman's rank correlation test and Levene's test. Survival rates were calculated using the Kaplan-Meier survival function. Alpha was set on 0.05 for statistical significance.

RESULTS

Eleven patients (two died and nine could not be traced) were lost to follow-up, three of them were known to have a TKA and their failure was included with the failures reported. The mean follow-up after meniscal transplantation was 13.8 ± 2.8 years (range, 9-18 years). Two patients had a total resection of a meniscal allograft and received a new meniscal allograft. The remaining 46 patients (81%) representing 49 allografts (78%) completed KOOS, Lysholm and IKDC-scores. The Lysholm score was categorized in four groups: excellent (94-100 points), good (84-94 points), fair (65-83 points) and poor (less than 65 points). Preoperatively eight patients (2 lateral and 6 medial) showed instability of the joint due to an insufficient ACL. In two patients an ACL reconstruction with the Slocum procedure was performed simultaneously with a medial allograft transplantation.[21] In the remaining six patients no ACL reconstruction was performed.

Data of preoperative arthroscopy showed at least 19 patients (33%) with grade IV chondropathy and 24 patients with grade III, while preoperative arthroscopic data of 14 patients could not be retrieved (Table 1).

Table 1. Patient characteristics. Variables are presented as mean and range.

Allograft	Medial	Lateral	Combined	Total
N	17	34	6	57
Sex (female/male)	6/11	9/25	2/4	17/40
Mean age (yrs)	41 (30-55)	39 (26-51)	40 (31-47)	39 (26-55)
Mean interval (yrs)	16 (3-33)	16 (2-27)	15 (6-25)	16 (2-33)
Lost to follow-up	1	7	3	11
Mean follow-up (mths)	162 (105-206)	171 (106-221)	133 (107-183)	165 (105-221)
Number of ACL insufficiency (reconstructed)	6 (2)	2 (0)	0 (0)	8 (2)
Degree of chondropathy 3/4	9/4	13/14	2/1	24/19
Number of failure	5	7	3	15
Mean time to failure	82 (51-97)	161 (100-208)	95 (67-140)	123 (51-208)

Overall, eight medial allografts (35%) and ten lateral allografts (25%) failed. The combined failure rate was 29% (Table 2). Twelve patients (21%) were converted to TKA at mean follow-up of 10.8 ± 4.1 years (range, 5.6-17.3 years). Three patients (5%) had a resection of the graft at mean follow-up of 8.4 ± 4.8 years (range, 4.3-13.7 years). Four medial allografts (67%) failed in an ACL insufficient knee. A survival point of 52.5% was found after 16 years of follow-up (Figure 1).

Table 2. Failure rates of meniscal allografts.

Allograft	Right	Left	Total	Number of failure
Medial	12 (19%)	11 (18%)	23 (37%)	8 (35%)
Lateral	31 (49%)	9 (14%)	40 (63%)	10 (25%)
Total	43 (68%)	20 (32%)	63 (100%)	18 (29%)

A significant improvement in the overall mean Lysholm score was seen, from 36 ± 18 points (range, 5-86 points) preoperatively to 61 ± 20 points (range, 21-91 points) at long-term follow-up. The long-term and preoperative Lysholm scores were not significantly different in the following subgroups; medial allografts, female patients and left treated knees. All subgroups had a poor Lysholm score at a mean follow-up of 13.8 years, except the male patient group which had a fair Lysholm score. A significant difference between Lysholm scores of male and female patients was found (*P<0.001*). No significant differences for Lysholm scores at long-term follow-up were found between lateral and medial

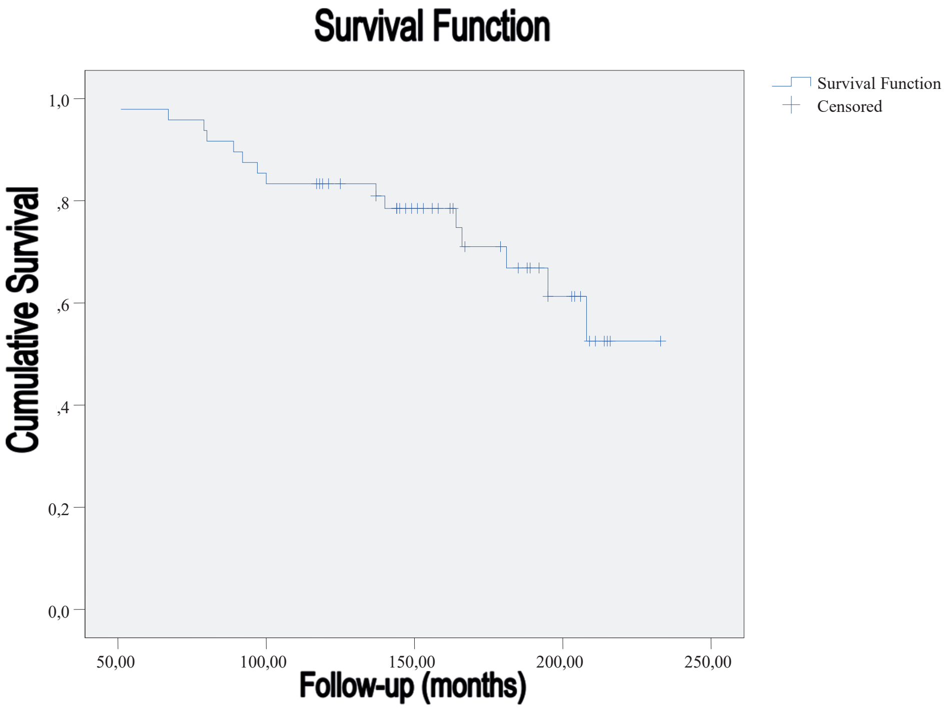

Figure 1. Survival curve of meniscal allografts

transplanted allografts or between right and left knees. No significant difference in Lysholm scores were seen between patients still having an allograft in situ at long-term and patients already converted to TKA at long-term follow-up (Table 3). A comparably significant difference between male and female patients was seen for the IKDC score (P=0.002) and three subgroups of the KOOS score: pain, symptoms and function, daily living (*P=0.014*).

In spite of the difference in function of both menisci; where a medial meniscus has a function as secondary stabilizer of the knee joint, the replacement of either a medial or lateral menisci had no effect on the final result. There were no significant differences between the lateral and medial allografts in long-term Lysholm, KOOS and IKDC scores. Likewise, no statistically significant difference was found between left and right treated knees.

Short-term Lysholm scores of the same population at a mean follow-up of 3.1 ± 1.5 years (range, 0.5-7.3 years) were used to compare with the long-term data. At short-term follow-up overall Lysholm score was 79 ± 19 points (range 19-100). As shown in table 3 a significant difference between short- and long-term Lysholm score was found for all subgroups. Lysholm scores were significantly improved at short-term follow-up compared to preoperative Lysholm scores for all subgroups (*P<0.001*). Patients with TKA after meniscal allograft transplantation presented the same scores at long-term follow-up as patients

Table 3. Function and pain scores at long-term follow-up.

Allograft	Med (n=17)	Lat (n=34)	p value	M (n= 40)	F (n=17)	p value	R (n=43)	L (n= 20)	p value	Allograft (n=33)	TKA (n=10)	p- value	Overall
Lysholm preop	44.00 (15-86)	37.10 (6-65)	0.304	38.52 (6-86)	43.40 (28-68)	0.465	37.77 (6-86)	44.45 (15-65)	0.302	40.00 (6-86)	27.50 (5-66)	0.127	36.36
Lysholm short-term	78.50 (55-100)	81.11 (34-100)	0.191	84.43 (55-100)	72.60 (34-99)	0.071	82.75 (34-100)	76.73 (55-100)	0.444	N/A	N/A	N/A	79.22
Lysholm long-term	55.36 (23-90)	63.90 (21-91)	0.278	68.74 (37-91)	43.40 (21-71)	**0.0001**	62.86 (21-91)	57.45 (23-90)	0.475	61.10 (21-91)	61.30 (18-100)	0.501	61.06
p value PO vs ST	**0.0001**	**0.0001**		**0.0001**	**0.005**		**0.0001**	**0.0001**		**0.0001**	NA		NA
p value PO vs LT	0.134	**0.000**		**0.0001**	1.000		**0.001**	0.053		**0.0001**	**0.001**		**0.001**
p value ST vs LT	**0.001**	**0.000**		**0.0001**	**0.000**		**0.000**	**0.001**		**0.0001**	NA		NA
IKDC long-term	37.20 (8-92)	50.98 (12-86)	0.115	53.92 (26-92)	27.93 (8-64)	**0.002**	48.85 (12-91)	40.44 (8-92)	0.328	46.50 (8-92)	51.12 (9-82)	0.265	39.99
KOOS long-term													
Pain	52.64 (19-100)	66.70 (22-100)	0.143	70.78 (42-100)	44.30 (19-83)	**0.003**	37.77 (22-100)	44.45 (19-100)	0.413	62.76 (19-100)	63.20 (22-100)	0.582	64.72
Symptom	54.09 (29-100)	60.10 (32-96)	0.448	65.43 (29-100)	46.00 (32-71)	**0.014**	59.00 (29-96)	60.63 (29-100)	0.839	59.55 (29-100)	63.30 (18-93)	0.255	61.41
ADL	61.09 (34-100)	72.75 (37-100)	0.219	77.17 (41-100)	50.70 (26-90)	**0.003**	71.64 (26-100)	64.18 (41-100)	0.418	69.15 (26-100)	70.00 (31-100)	0.560	71.31
S&R	23.18 (0-100)	40.00 (0-100)	0.132	40.00 (5-100)	23.50 (0-90)	0.157	34.77 (0-100)	35.45 (0-100)	0.953	35.00 (0-100)	44.50 (0-100)	0.239	36.09
QoL	27.36 (0-100)	43.00 (6-100)	0.127	43.96 (6-100)	26.30 (0-75)	0.810	41.64 (6-100)	32.55 (0-100)	0.372	38.61 (0-100)	41.40 (0-100)	0.498	39.81

PO = preoperative Lysholm score, ST = short-time Lysholm score, LT = long-term Lysholm score, NA = not available.

with initial meniscal allograft transplantation. No significant differences in Lysholm, KOOS and IKDC scores were found between these groups. Patients with TKA after meniscal allograft transplantation had a significantly better Lysholm score compared to the preoperative situation. Lysholm scores of patients with a TKA were not available at short-term.

A weak negative correlation (-0.017) between preoperative cartilage grades and preoperative Lysholm scores was found. A positive correlation (0.149 and 0.058) between was found between postoperative cartilage grades and Lysholm scores at mid-and long-term follow-up. None of the correlations found, were significant.

DISCUSSION

Meniscal allograft transplantation is a procedure that can be used to treat young patients with a disabling and painful post-meniscectomized knee joint. Since the first meniscal allograft transplantation, numerous studies related to meniscal transplantation have been published.[3,4,19,23] Long-term data however, are scarce and most report follow-up of small numbers of patients.[14,26,27]

With this study we showed, after more than nine years of follow-up, that the life span of meniscal allografts is restricted, despite the ability of the allograft to attach to the knee capsule followed by revascularization and restoration of adequate biomechanical status.[2]

Other factors like graft size, graft selection, surgical techniques, fixation of the graft and patient selection play an important role in the durability of the graft.[15] Besides that, long-term follow-up results are expected to be affected by the initial condition of the cartilage. This could be an explanation of the deterioration in clinical function score over time as we showed in our study.

In our study 21% of the patients (= 24% of the allografts) received TKA after meniscal transplantation at mean follow-up of ten years. However, 79% of the patients (= 76% of the allografts, re-implanted allografts included) are still expected to have at least one meniscal allograft in situ, with a function better than prior to meniscal allograft transplantation. This survival rate is equivalent to those of TKA in young patients as reported in the available literature.[19] However, some of the in situ allografts could be extruded or worn down. To confirm the presence of the allografts radiographic evaluation using MRI would be needed.

Survival analysis of this population showed a survival point of 52.5% after 16 years. Surviving data of 15 years or longer of an equal population having a TKA at young age are very scarce in literature, varying from 87 to 95%.[5,6] However, it would be interesting to have life-time follow-up of both groups to see the overall quality of life after revision or primary TKA. The difference between both groups is that the patients after meniscal allograft transplantation still have the possibility to receive a primary TKA. Patients with a failed primary TKA need revision surgery at younger age which could give problems later in life. As far as we know no studies are published about re-revisions of TKA. This is the reason that primary TKA in younger patients is still controversial in orthopedic surgery.

We also showed that patients with TKA after meniscal allograft transplantation function as well as those patients who still have a meniscal allograft in situ. The Lysholm scores for both groups should be compared with young patients having primary TKA after meniscectomy in a randomized controlled trial to examine the effect of meniscal allograft transplantation on TKA.

The failure rate, pain scores and function scores at long-term follow-up for this population is expected to be affected by the interval between meniscectomy and transplantation. Besides that, clinical outcome of this population is also affected by the amount of preoperative chondropathy, fixation of the allograft, ACL insufficiency and patient selection, as shown in earlier literature.[3, 16, 17]

The mean interval of 16 years between meniscectomy and meniscal allograft transplantation is long, leading to a higher level of chondropathy prior to transplantation. As seen in this population at least 33% of the patients had grade IV chondropathy of the tibia and/or femur. A high grade of chondropathy on the femur negatively influenced the pain and function outcomes at long-term follow-up.[16] That is why we see grade IV chondropathy, especially on the femur condyle, as a contraindication for transplantation. We expect that, to make meniscal allograft more successful, the interval between meniscectomy and meniscal allograft transplantation should be smaller than at least 16 years to prevent the progression of chondropathy at time of transplantation.

By improving the indication for meniscal allograft transplantation, improvement in long-term results can be achieved. An intact ACL is very important, because laxity of the knee leads to higher demands on menisci.[13] That is also the reason for fewer failures in lateral allografts compared with medial allografts. These differences can be explained by the anatomical and functional differences between both menisci. The medial meniscus is a secondary stabilizer of the knee joint. In the ACL insufficient knee, the medial meniscus plays an even more important role in joint stability.[13] Absence of the ACL leads to damage or detachment of the allograft. This explains the negative correlation found between success of the medial meniscal allograft and presence of intact ACL in our population. The difference between preoperative and increased long-term follow-up Lysholm scores between medial and lateral menisci is probably due to the difference in the presence of an insufficient ACL in both groups. Based on published literature[16] and our own results we know that ACL instability should be addressed either prior to or concurrent with meniscal allograft transplantation. We state that ACL insufficiency is an absolute contraindication for meniscal allograft transplantation.

As described earlier we used peripheral suturing to fixate the allograft. This fixation technique produces more peripheral extrusion and leads to a higher contact pressure between the tibia and femur.[16] Higher contact pressure probably has a negative influence on pain and function at long-term follow-up. By using bony fixation of the allograft and by preserving the outer rim of the damaged meniscus, particularly on the medial side, extrusion and contact pressure will decrease[16] and clinical outcomes at long-term are expected to improve. Nowadays indications for surgery have changed. Only patients younger than 50 years with symptomatic compartmental osteoarthritis (≤ grade III) after meniscectomy in a stable knee with normal alignment are suitable for transplantation.[16] Surgical techniques have also changed and have advanced along with instrumentation. Current meniscal allograft transplantation is performed arthroscopically using bony fixation. Results at long-term follow-up for these indications and surgical technique have not been reported, but improvement on survival, pain and function scores are expected.

The significant differences between male and female are hard to explain. Probably the differences in anatomical dimensions play a role in meniscal allograft transplantation. Differences in anatomical dimensions of the distal femur, proximal tibia and patella between both sexes are well described.[9,10] To prevent potential clinical differences based on sex, femoral implants are now designed with the known sex differences in mind. But further analysis on this topic in meniscal transplantation is still necessary.

Differences in level of activity could be an explanation for the significant differences between male and female. Because of lack of preoperative IKDC-scores and incomplete preoperative and long-term Tegner-scores further comparison on these topics was restrained.

As in all meniscal allograft studies, a lack of a control group, consisting of matched conservatively treated patients, limits the power of this study to detect a chondroprotective effect and the possibility to delay TKA or even on long-term an early revision. Additional and long-term studies are needed to evaluate the optimal timing and technique for meniscal allograft transplantation. Evaluation of long-term results of arthroscopic assisted meniscal allograft transplantation should follow to see if it is superior to an open procedure. The most important question is whether or not this procedure provides long-term prevention or delay of articular cartilage degeneration and osteoarthritis.

In conclusion, open meniscal allograft transplantation is a salvage treatment option for postponing TKA in the young patient with post-meniscectomy arthritis. There is a significant reduction of pain and improvement in function, clinical and radiological survival of the allograft after transplantation at short-term. At long-term follow-up both significant and insignificant improvement is seen after meniscal allograft transplantation. Patients younger than 50 years, with a normally aligned, stable knee joint with sufficient ACL are the best candidates for meniscal allograft transplantation. The aim of this treatment option is to delay the need for total knee arthroplasty.

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6

Two years follow-up of bone mineral density changes in the knee after meniscal allograft transplantation; results of an explorative study.

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ABSTRACT

Background

A potential chondroprotective effect of meniscal allograft transplantation (MAT) remains still unclear. Subchondral bone mineral density (BMD) and subchondral bone remodelling play important roles in development of osteoarthritis. Evaluation of subchondral BMD after MAT might give more insight in the potential chondroprotective effect. The purpose of our study was to determine early BMD changes in the knee after MAT.

Methods

From 2010 to 2013 twenty-six consecutive patients underwent a MAT. BMD was measured using Dual-energy X-ray Absorptiometry (DXA) scan preoperative and 6 months, 1 and 2 years postoperative. BMD was measured in six regions of interest (ROIs) of tibia and femur (medial, central, lateral) in both treated and healthy contralateral knees.

Results

BMD levels of MAT knees did not significantly change during 2 years follow-up in almost all ROIs. BMD was significant higher in nearly all ROIs in MAT knees at almost all follow-up moments compared to healthy contra-lateral knees. In the healthy contralateral knees BMD slightly, but not statistically, decreased in the first year postoperative, where after BMD normalized to baseline values at 2 years follow-up. BMD levels in all ROIs did not significantly differ between the patients with or without chondropathy at baseline and at 2 years follow-up.

Conclusion

Based on our findings MAT did not show a significant influence on BMD in the first 2 years postoperative. Longer follow-up is necessary to prove the potential chondroprotective effect of MAT using BMD measurements.

INTRODUCTION

Since the first meniscal allograft transplantation (MAT) in 1984,[1] many papers are published in literature regarding different aspects of MAT: indications and contraindications,[2] preoperative graft sizing,[3] methods of graft preservation,[4] surgical techniques,[5] fixation of the allograft,[6] relevance of associated chondral and ligamentous damage,[7] concomitant procedures,[8,9] histologic evaluation,[10] clinical and radiographic outcomes,[11-13] and rehabilitation.[14]

Despite all this research, a chondroprotective effect, as shown in sheep,[15] remains still unclear in humans.[11,16] This may partially be caused of the lack of standardized evaluation methods and the lack of high-quality studies. Nonetheless, MAT seems to provide good clinical results at the short- and long-term, with improvement in knee function and acceptable complication and failure rates.[16]

Concerning the development of osteoarthritis (OA) previous studies suggest that changes in subchondral bone play a key role in the pathogenesis and progression of OA.[17-21] Subchondral bone changes are potentially both a result and a cause of cartilage damage and cartilage loss.[21,22] Even in patients after partial or total medial meniscectomy an increased bone mineral density (BMD) has been seen.[23] The difference in BMD that leads to clinical relevant differences in patients is not known. Some studies have demonstrated that knee OA was associated with lower BMD,[24,25] while another study documented that patients with high tibial BMD had increased joint space narrowing after 1 year.[26] These findings suggest a biphasic process of BMD changes in OA: a reduction in BMD early on followed by an increase during more advanced phases.[27]

We are interested in the effect of MAT on BMD early in the process of OA development. To our knowledge, the effect on BMD of MAT was never investigated using Dual-energy X-ray Absorptiometry (DXA) scans. The purpose of our observational prospective explorative study was to determine BMD changes in the knee after arthroscopic MAT without bone plugs during a 2 year follow-up period and to compare the possible changes with the healthy contralateral knee. Furthermore, we wanted to evaluate if correlations could be found between clinical outcome and BMD findings during follow-up. As MAT can restore mechanical alignment,[28] this might restore biological anatomy as well, so we hypothesized no difference in BMD after 2 years between MAT knees and healthy contralateral knees. We hypothesized that possibly changes in BMD are not related to clinical outcome measured with patient related outcomes measurements (PROMs).

MATERIALS AND METHODS

This study has been approved by the local medical ethical review board (METC number: 15–069) and was registered in the Dutch Trial Register (NTR: NTR5633).

Population

Between March 2010 and October 2013, 26 patients received a cryopreserved non-tissue-antigen-matched and non-irradiated human meniscal allograft. All of the patients were recruited at the outpatient department of the Haaglanden Medical Center (HMC) and were operated by the senior author (EvA). Inclusion criteria were: disabling unicompartmental pain after a (sub)total meniscectomy, patient under the age of 55 years, stable knee joint or stabilized by concomitant anterior cruciate ligament reconstruction (ACLR) and normal knee alignment (5 degrees valgus – 5 degrees varus). Exclusion criteria were: > grade II chondropathy (according to the Outerbrigde classification[29]), PCL insufficiency, abnormal and uncorrected knee or lower limb alignment, complex regional pain syndrome of the knee, arthrofibrosis, muscular atrophy and a history of knee sepsis. Patients with previous operations or signs of chondropathy on the contralateral knee were also excluded. Radiographic measurements and anthropometric parameters (height and weight of the patient) were used to establish the correct size of the graft. All patients gave their written informed consent before participating in this study.

Study design

All patients were clinically evaluated preoperatively and during a minimum follow-up of 2 years. Accordant to our standard care patients were asked to complete questionnaires. Questionnaires included the Knee injury and Osteoarthritis Outcome Score (KOOS),[30] International Knee Documentation Committee subjective knee form (IKDC)[31] and Tegner activity score.[32] All questionnaires were filled in at baseline (preoperative) and 6 months, 1 and 2 years postoperative, except for the Tegner activity score. This score was not completed at 6 months postoperative, because of the rehabilitation protocol. During these follow-up moments a DXA scan was performed in the Erasmus Medical Centre, Rotterdam.

BMD measurement

BMD measurement was performed as described by van Meer et al.[33] In short, a Lunar Prodigy scanner (GE Lunar Corp., Madison, WI, USA) was used with “the spine protocol”. The lower extremity was fixed in a plastic device and the knee was slightly flexed (10 degrees). The positioning laser light was used to position the centre of the scanner arm 8 cm below the tibial tubercle. This resulted in anteroposterior views. Contours of the femur and tibia were outlined by placing anatomical landmark points using the freely available active shape model toolkit software package (Manchester University, Manchester, UK).

With these landmark points, six regions of interest (ROIs) were extracted: medial, central, lateral in the tibia, and medial, central and lateral in the femur. Anatomical landmark point placing for all DXA scans was done by one person (DA). The height and placement of the regions were based on reference lines between landmark points that indicated the medial and lateral sides of the tibia and femur (Figure 1). In the tibia, the regions run from the lower point of these lines up to a point 30% beneath the top of the line. This was to assure that the regions were positioned below the subchondral bone. In the femur, the bottom of the regions was positioned 10% of the length of the reference line above the lowest point, while the top was placed at 50%. The regions in the femur were positioned such that the medial and lateral ROIs were placed inside the respective condyles. The most lateral and medial border of the ROIs in the tibia and femur were positioned parallel to the outline of the tibia and femur, at a distance from the outline of 5% of the width of the bone. The area without bone in the central region of the femur, which interfered with the femoral notch, was excluded from BMD analysis.

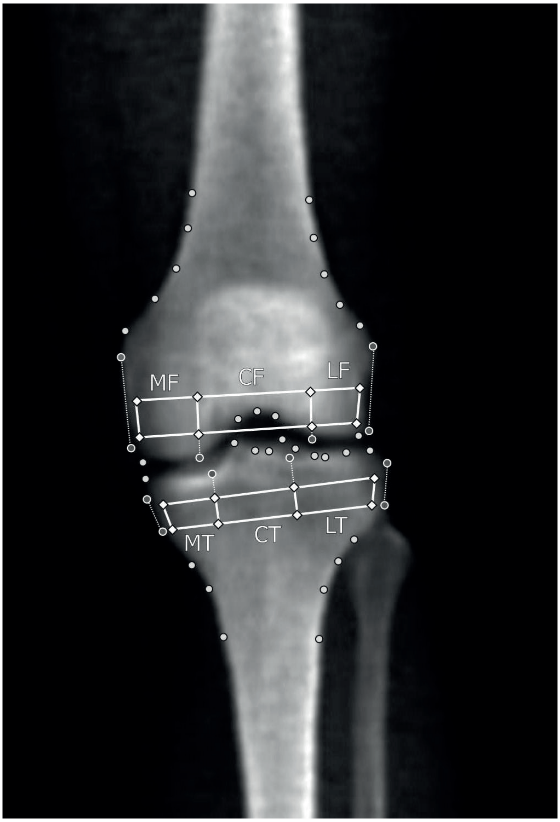

Figure 1. Determination of six regions of interest (ROIs) by using landmark points. 1: medial tibia (MT), 2: central tibia (CT), 3: lateral tibia (LT), 4: medial femur (MF), 5: central femur (CF), 6: lateral femur (LF). (Published with permission of B.L. van Meer)

Surgical technique

The meniscal allograft was delivered on the donor tibia plateau and was dissected leaving the posterior and anterior meniscal ligaments intact, no bone block was used. Fiberwire sutures 2.0 (Arthrex, Naples, Florida) were placed through the posterior and anterior meniscal ligament. Another two sutures were placed at the posterior and anterior horn. The MAT was performed arthroscopically using one tibia tunnel. Needling of the remnant of the peripheral rim was performed to provide blood at the attachment site. A FlipCutter (Arthrex, Naples, Florida) was used to create an inside-out socket in the tibia plateau with the same diameter as the posterior horn attachment. There through a passing suture was brought intra articular and taken out of the joint through a posterior portal. On this suture a second passing suture was attached extra articular and both were pulled through the anterior arthrotomy opening, resulting in a passing suture through the tibia tunnel and one through the posterior portal. The posterior sutures of the donor meniscus were fixed to the passing sutures and the graft was gradually pulled into the joint. The posterior horn suture was fixed over an anteriorly placed button on the tibial cortex. By pulling the suture through the portal tension on the meniscus was adjusted. The posterior side of the allograft was attached with two or three all inside meniscal repair systems (Fast-fix, Smith & Nephew, Memphis, Tennessee). Using meniscal repair needles (Arthrex, Naples, Florida) with two or three inside out meniscal sutures the middle part of the allograft was fixed. Using a self-punching SwiveLock anchor (Arthrex, Naples, Florida) the anterior horn suture was fixed to the tibia plateau. The arthrotomy wounds were closed after the knee was arthroscopically inspected for the final time.

Rehabilitation

The rehabilitation period started with 3 weeks of partial weight bearing (25%) with mobilization on crutches with a limit of 60º of flexion. After the first three weeks partial weight bearing was allowed till 50% and knee flexion to 90º. From week 9 till 12 the knee was progressively loaded more and flexed until 120º. During week 13 – 24 postoperative patients were allowed to progressively train their knees. When the knee had 80% of its former strength back, the patients were allowed to exercise and move without restrictions. However, it was advised to avoid high-impact activities and contact sports.

Reproducibility

Test-retest for placing landmark points was assessed. Landmark points were placed in 25 scans of randomly chosen patients from the study from van Meer et al[32] to determine interobserver agreement. Intraobserver agreement was determined by placing landmark points twice in 25 randomly chosen patients from this study with a time interval of two weeks.

Statistical analysis

All statistical analyses were performed with the use of SPSS (version 22.0, SPSS Inc, Chicago, IL). The statistical significance was set at alpha of <0.05. Data was tested for normality with the Shapiro-Wilk test. Normally distributed data is presented in mean and standard deviation (SD), non-normally distributed data is presented in median and interquartile range (IQR). The reproducibility of the DXA scan measurements was assessed by determining the intraclass correlation coefficient (ICC; two-way random effects model, absolute agreement). The strength of examiner agreement was defined according to the guidelines of Landis and Koch.[34] Linear mixed model analyses (repeated covariance type: compound symmetry) were applied to analyse differences in BMD levels regarding time of measurement, side and compartment and to evaluate changes in KOOS, IKDC and Tegner scores. Correlation between Tegner activity score and BMD was analysed using Pearson's correlation.

RESULTS

Baseline patient characteristics are shown in Table 1. One patient missed DXA scan at 6 months and 1 year follow-up because of pregnancy. Logistical problems were the reason for missing two other DXA scans (one at 6 months and one at 2 years follow-up). So 100 of a potential 104 DXA scans (96%) were available for evaluation.

Table 1. Patient characteristics. Data are presented in median and inter quartile range (IQR) unless otherwise indicated, n = number, ACL = anterior cruciate ligament, MAT = meniscal allograft transplantation.

Baseline characteristics	**n = 26**
Gender (female) – n (%)	15 (58)
Age (years)	39 (26 – 45)
BMI (kg/m^2)	24.3 (21.8 – 25.9)
Compartment (medial) – n (%)	10 (39)
Chondropathy – n (%) - Grade 0 - Grade 1	 12 (46) 14 (54)
No. of operations previous to MAT	3 (2 – 4)
No. of concomitant ACL reconstructions – n (%) medial / lateral - n	4 (15) 3 / 1
Interval between (sub)total meniscectomy and MAT (months)	29 (18.5 – 61.8)

Reproducibility

Interobserver agreement for landmark point placing was excellent (ICC = 0.826 to 0.976). Intraobserver agreement for landmark point placing ranged from good to excellent (ICC = 0.757 to 0.980).

BMD changes

The BMD levels of the MAT knees did not significantly change during the 2 year follow-up in almost all ROIs. A significantly decrease (P = 0.002, 95% CI = 0.74 – 0.92) in BMD was only seen at the central tibia (CT) 6 months postoperative compared to baseline for medial MAT knees. In lateral MAT knees no significant changes in BMD during follow-up was seen. In contrast, several BMD changes were seen in the compartments of healthy contralateral knees. After 6 months, a significant decrease in BMD was seen in all ROIs, except the medial femoral (MF) compartment. From this point, BMD gradually increased after 1 and 2 years follow-up, but never reached baseline level (Table 2).

The BMD levels in all ROIs at all time points were significantly higher in the MAT knee than the BMD levels of the contralateral healthy knee (Table 2).

BMD levels in all ROIs did not significantly differ between the patients with or without chondropathy at baseline and at 2 years follow-up. Baseline BMD levels in the MAT knees were higher for both patients with (grade 1) or without (grade 0) chondropathy compared to the healthy contralateral knees (Table 3).

Table 2. Bone mineral density levels (g/cm^2) of the knee after meniscal allograft transplantation (MAT) and in the contralateral healthy knees based on Linear Mixed Model analyses (medial versus lateral MAT).

ROI		Baseline (T0)	6 months (T1)	1 year (T2)	2 years (T3)
Medial MAT		n = 10 Mean (SD, 95% CI)	n = 10 Mean (SD, 95% CI)	n = 10 Mean (SD, 95% CI)	n = 10 Mean (SD, 95% CI)
MT	MAT	0.93 (0.16, 0.87 – 0.99)	0.92 (0.15, 0.86 – 0.98)	0.92 (0.15, 0.86 – 0.98)	0.92 (0.18, 0.86 – 0.98)
	Healthy	0.88 (0.16, 0.81 – 0.94)	0.83 (0.21, 0.77 – 0.90)*	0.83 (0.16, 0.77 – 0.90)	0.86 (0.16, 0.80 – 0.92)
P value#		**<0.001**	**<0.001**	**<0.001**	**<0.001**
CT	MAT	0.86 (0.18, 0.80 – 0.93)	0.85 (0.18, 0.79 – 0.92)*	0.86 (0.17, 0.79 – 0.92)	0.85 (0.18, 0.78 – 0.91)
	Healthy	0.84 (0.16, 0.78 – 0.90)	0.75 (0.17, 0.69 – 0.82)*	0.77 (0.15, 0.70 – 0.83)	0.79 (0.16, 0.73 – 0.86)
P value#		**<0.001**	**0.016**	**<0.001**	**0.031**
LT	MAT	0.89 (0.15, 0.83 – 0.95)	0.89 (0.15, 0.83 – 0.94)	0.88 (0.16, 0.82 – 0.94)	0.88 (0.15, 0.82 – 0.94)
	Healthy	0.86 (0.13, 0.80 – 0.92)	0.78 (0.15, 0.72 – 0.84)*	0.79 (0.14, 0.73 – 0.85)	0.81 (0.15, 0.75 – 0.87)
P value#		**<0.001**	**<0.001**	**<0.001**	**<0.001**

Table 2. Bone mineral density levels (g/cm^2) of the knee after meniscal allograft transplantation (MAT) and in the contralateral healthy knees based on Linear Mixed Model analyses (medial versus lateral MAT). (*continued*)

ROI		Baseline (T0)	6 months (T1)	1 year (T2)	2 years (T3)
MF	MAT	1.12 (0.16, 1.05 – 1.20)	1.12 (0.17, 1.04 – 1.19)	1.08 (0.16, 1.00 – 1.16)	1.11 (0.16, 1.04 – 1.19)
	Healthy	1.04 (0.16, 0.97 – 1.12)	0.99 (0.19, 0.91 – 1.06)	0.98 (0.19 ,0.90 – 1.05)	0.99 (0.18, 0.92 – 1.07)
P value#		**<0.001**	**<0.001**	**<0.001**	**<0.001**
CF	MAT	1.37 (0.20, 1.3 – 1.45)	1.35 (0.21, 1.27 – 1.42)	1.36 (0.16, 1.29 – 1.44)	1.38 (0.20, 1.29 – 1.44)
	Healthy	1.34 (0.17, 1.27 – 1.42)	1.23 (0.28, 1.16 – 1.31)*	1.22 (0.20, 1.15 – 1.30)	1.24 (0.22, 1.15 – 1.30)
P value		**0.020**	**<0.001**	**0.001**	**<0.001**
LF	MAT	1.14 (0.20, 1.06 – 1.22)	1.14 (0.18, 1.06 – 1.22)	1.15 (0.19, 1.07 – 1.23)	1.15 (0.16, 1.07 – 1.23)
	Healthy	1.12 (0.18, 1.05 – 1.20)	1.00 (0.20, 0.92 – 1.08)*	1.06 (0.30, 0.98 – 1.14)	1.11 (0.22, 1.03 – 1.19)
P value#		**<0.001**	**<0.001**	**<0.001**	**0.005**
Lateral MAT		n = 16 Mean (SD, 95% CI)	n = 14 Mean (SD, 95% CI)	n = 15 Mean (SD, 95% CI)	n = 16 Mean (SD, 95% CI)
MT	MAT	0.89 (0.14, 0.82 – 0.96)	0.89 (0.14, 0.82 – 0.96)	0.89 (0.15, 0.82 – 0.97)	0.90 (0.15, 0.83 – 0.97)
	Healthy	0.82 (0.13, 0.75 – 0.90)	0.80 (0.13, 0.72 – 0.87)*	0.80 (0.14, 0.73 – 0.87)	0.81 (0.12, 0.73 – 0.88)
P value#		**<0.001**	**<0.001**	**<0.001**	**<0.001**
CT	MAT	0.83 (0.15, 0.75 – 0.92)	0.83 (0.16, 0.75 – 0.91)	0.83 (0.16, 0.75 – 0.92)	0.83 (0.17, 0.75 – 0.91)
	Healthy	0.81 (0.16, 0.73 – 0.90)	0.73 (0.15, 0.65 – 0.82)*	0.74 (0.14, 0.66 – 0.82)	0.77 (0.130, .69 – 0.85)
P value#		**0.030**	**<0.001**	**<0.001**	**0.005**
LT	MAT	0.88 (0.16, 0.80 – 0.96)	0.88 (0.16, 0.8 – 0.96)	0.88 (0.16, 0.80 – 0.96)	0.88 (0.17, 0.80 – 0.96)
	Healthy	0.85 (0.15, 0.77 – 0.93)	0.77 (0.14, 0.69 – 0.85)*	0.79 (0.19, 0.71 – 0.87)	0.81 (0.14, 0.73 – 0.89)
P value#		**<0.001**	**<0.001**	**<0.001**	**<0.001**
MF	MAT	1.08 (0.18, 0.99 – 1.17)	1.09 (0.19, 1.00 – 1.18)	1.05 (0.17, 0.96 – 1.14)	1.07 (0.15, 0.98 – 1.16)
	Healthy	0.96 (0.18, 0.87 – 1.05)	0.94 (0.19, 0.84 – 1.03)	0.93 (0.19, 0.83 – 1.02)	0.93 (0.18, 0.84 – 1.02)
P value#		**<0.001**	**<0.001**	**<0.001**	**<0.001**
CF	MAT	1.35 (0.17, 1.26 – 1.44)	1.31 (0.20, 1.22 – 1.41)	1.35 (0.20, 1.25 – 1.44)	1.36 (0.18, 1.26 – 1.45)
	Healthy	1.33 (0.17, 1.24 – 1.43)	1.22 (0.20, 1.12 – 1.31)*	1.23 (0.19, 1.13 – 1.31)	1.24 (0.16, 1.14 – 1.33)
P value#		**0.047**	**<0.001**	**<0.001**	**<0.001**
LF	MAT	1.14 (0.18, 1.04 – 1.24)	1.11 (0.16, 1.01 – 1.21)	1.14 (0.21, 1.03 – 1.24)	1.15 (0.19, 1.05 – 1.26)
	Healthy	1.12 (0.24, 1.02 – 1.23)	0.98 (0.17, 0.88 – 1.09)*	0.99 (0.18, 0.89 – 1.10)	1.09 (0.22, 1.00 – 1.19)
P value#		**<0.001**	**0.001**	**<0.001**	**0.020**

ROI = region of interest. MT: medial tibia, CT: central tibia, LT: lateral tibia, MF: medial femur, CF: central femur, LF: lateral femur. SD = standard deviation. 95% CI = 95% Confidence Interval. * = significant difference between baseline and 6 months follow-up. # = P value for bone mineral density levels between MAT and healthy knees for each time interval.

Table 3. Bone mineral density levels (g/cm^2) of the knee after meniscal allograft transplantation (MAT) and in the contralateral healthy knees based on Linear Mixed Model analyses (for grade 0 versus grade 1 chondropathy) at baseline and at 2 years follow-up.

ROI	Baseline (T0)		2 years (T3)	
Medial MAT	Mean (SD, 95% CI)		Mean (SD, 95% CI)	
Grade of chondropathy	0	1	0	1
MT MAT	0.94 (0.16, 0.88 – 0.97)	0.92 (0.15, 0.86 – 0.99)	0.93 (0.15, 0.86 – 0.97)	0.95 (0.18, 0.90 – 1.01)
Healthy	0.87 (0.15, 0.80 – 0.93)	0.85 (0.19, 0.79 – 0.90)	0.83 (0.16, 0.77 – 0.90)	0.85 (0.16, 0.79 – 0.92)
P value#	<0.001	<0.001	<0.001	<0.001
CT MAT	0.86 (0.17, 0.81 – 0.93)	0.88 (0.16, 0.80 – 0.94)	0.86 (0.15, 0.80 – 0.93)	0.89 (0.18, 0.83 – 0.95)
Healthy	0.84 (0.15, 0.79 – 0.91)	0.75 (0.15, 0.68 – 0.82)	0.77 (0.15, 0.71 – 0.83)	0.79 (0.16, 0.72 – 0.88)
P value#	<0.001	<0.001	<0.001	<0.001
LT MAT	0.89 (0.16, 0.83 – 0.96)	0.91 (0.16, 0.86 – 0.98)	0.87 (0.16, 0.81 – 0.93)	0.89 (0.15, 0.82 – 0.93)
Healthy	0.83 (0.14, 0.81 – 0.92)	0.80 (0.15, 0.76 – 0.86)	0.78 (0.14, 0.70 – 0.82)	0.82 (0.14, 0.75 – 0.87)
P value#	<0.001	<0.001	<0.001	0.016
MF MAT	1.14 (0.17, 1.06 – 1.20)	1.10 (0.16, 1.03 – 1.18)	1.12 (0.16, 1.05 – 1.20)	1.13 (0.17, 1.05 – 1.19)
Healthy	1.02 (0.16, 0.96 – 1.12)	0.99 (0.18, 0.91 – 1.05)	0.99 (0.19 ,0.90 – 1.06)	0.99 (0.17, 0.92 – 1.08)
P value#	<0.001	<0.001	<0.001	<0.001
CF MAT	1.38 (0.20, 1.30 – 1.46)	1.35 (0.19, 1.28 – 1.42)	1.34 (0.16, 1.28 – 1.42)	1.36 (0.20, 1.27 – 1.43)
Healthy	1.33 (0.17, 1.28 – 1.42)	1.25 (0.28, 1.15 – 1.31)	1.25 (0.20, 1.16 – 1.33)	1.24 (0.19, 1.14 – 1.28)
P value#	<0.001	<0.001	<0.001	<0.001
LF MAT	1.10 (0.19, 1.06 – 1.19)	1.14 (0.17, 1.05 – 1.22)	1.12 (0.17, 1.07 – 1.20)	1.09 (0.16, 1.02 – 1.20)
Healthy	1.02 (0.18, 0.92 – 1.11)	1.03 (0.20, 0.92 – 1.08)	1.06 (0.25, 0.91 – 1.16)	1.01 (0.19, 0.94 – 1.09)
P value#	<0.001	<0.001	<0.001	<0.001
ROI	Baseline (T0)		2 years (T3)	
Lateral MAT	Mean (SD, 95% CI)		Mean (SD, 95% CI)	
Grade of chondropathy	0	1	0	1
MT MAT	0.90 (0.15, 0.84 – 0.96)	0.93 (0.15, 0.87 – 1.00)	0.89 (0.15, 0.83 – 0.96)	0.90 (0.16, 0.84 – 0.99)
Healthy	0.83 (0.13, 0.73 – 0.90)	0.84 (0.17, 0.78 – 0.91)	0.81 (0.16, 0.74 – 0.90)	0.82 (0.13, 0.77 – 0.92)
P value#	<0.001	<0.001	<0.001	<0.001
CT MAT	0.85 (0.14, 0.80 – 0.92)	0.87 (0.16, 0.80 – 0.96)	0.83 (0.15, 0.76 – 0.93)	0.88 (0.18, 0.80 – 0.96)
Healthy	0.80 (0.15, 0.72 – 0.90)	0.78 (0.14, 0.65 – 0.81)	0.74 (0.14, 0.69 – 0.83)	0.81 (0.16, 0.74 – 0.89)
P value#	<0.001	<0.001	<0.001	<0.001
LT MAT	0.88 (0.16, 0.81 – 0.95)	0.89 (0.17, 0.80 – 0.98)	0.88 (0.16, 0.80 – 0.94)	0.90 (0.16, 0.83 – 0.95)
Healthy	0.83 (0.15, 0.75 – 0.91)	0.80 (0.16, 0.75 – 0.88)	0.81 (0.14, 0.72 – 0.85)	0.83 (0.14, 0.77 – 0.90)
P value#	<0.001	0.017	<0.001	<0.001
MF MAT	1.09 (0.18, 1.01 – 1.19)	1.11 (0.16, 1.01 – 1.20)	1.13 (0.17, 1.01 – 1.20)	1.13 (0.16, 1.03 – 1.18)
Healthy	1.03 (0.17, 0.96 – 1.14)	0.97 (0.18, 0.90 – 1.03)	1.00 (0.18 ,0.91 – 1.02)	0.99 (0.17, 0.90 – 1.05)
P value#	0.002	<0.001	<0.001	<0.001
CF MAT	1.35 (0.18, 1.23 – 1.44)	1.35 (0.17, 1.25 – 1.44)	1.35 (0.18, 1.25 – 1.43)	1.34 (0.18, 1.24 – 1.43)
Healthy	1.29 (0.17, 1.23 – 1.42)	1.24 (0.16, 1.14 – 1.31)	1.23 (0.19, 1.13 – 1.33)	1.24 (0.19, 1.14 – 1.30)
P value#	<0.001	<0.001	<0.001	<0.001
LF MAT	1.13 (0.17, 1.03 – 1.19)	1.12 (0.16, 1.01 – 1.22)	1.13 (0.17, 1.07 – 1.20)	1.15 (0.18, 1.02 – 1.22)
Healthy	1.00 (0.19, 0.90 – 1.06)	1.03 (0.18, 0.94 – 1.09)	1.02 (0.18, 0.92 – 1.11)	1.05 (0.22, 0.98 – 1.13)
P value#	<0.001	<0.001	<0.001	0.006

ROI = region of interest. MT: medial tibia, CT: central tibia, LT: lateral tibia, MF: medial femur, CF: central femur, LF: lateral femur. SD = standard deviation. 95% CI = 95% Confidence Interval. # = P value for bone mineral density levels between MAT and healthy knees.

All time points and all knees (MAT or healthy) showed significant higher BMD levels in the femur compared to the tibia in each compartment (medial, central and lateral).

In medial MAT knees, BMD levels were significant higher in the lateral femoral (LF) compartment compared to the medial femoral (MF) compartment. No significant difference was found in BMD levels between medial tibial (MT) and lateral tibial (LT) compartments in medial MAT knees. In the femoral compartments no significant difference in BMD level was found comparing medial and lateral in lateral MAT knees. A significant increased BMD level was found in the medial compartment of the tibia (MT) in lateral MAT knees. No significant differences in BMD were found between both femoral and tibial compartments in the healthy contralateral knees.

Only 4 patients had a concomitant ACLR, 3 patients in combination with medial MAT and 1 in combination with lateral MAT. This number was too small to draw any statistical conclusions about the influence of ACLR on BMD of tibia and femur.

Patient Related Outcome Measurements

A significant improvement in KOOS score compared to baseline was found for all subtypes at all follow-up moments. After 1 year a significant deterioration in KOOS score was found for two subtypes: Sports and Recreation and Quality of Life. The other 3 KOOS items remain on the same level. IKDC score also significantly improved during follow-up compared to baseline. A small increase in Tegner activity score was found, but this was not significantly different (Table 4).

Table 4: Patient Related Outcome scores. Data are presented in mean, standard deviation (SD) and 95% Confidence Interval (95% CI) unless otherwise indicated.

	Baseline Mean (SD, 95% CI)	6 months	1 year	2 years
KOOS Symptoms	55 (16.1, 47.9 – 62.9)	72 (21.7, 62.1 – 81.3)*	77 (13.5, 70.9 – 83.1)*	78 (12.1, 72.4 – 84.0)*
KOOS Pain	50 (18.0, 41.2 – 58.1)	78 (18.0, 65.6 – 85.5)*	82 (17.1, 74.2 – 89.8)*	85 (12.1, 79.4 – 91.0)*
KOOS ADL	63 (21.0, 53.5 – 73.2)	84 (15.7, 77.3 – 91.2)*	78 (14.0, 71.8 – 84.3)*	93 (9.5, 88.5 – 97.7)*
KOOS S&R	26 (21.7, 15.4 – 36.4)	44 (32.2, 29.7 – 58.3)*	82 (17.0, 75.1 – 90.2)*	61 (27.2, 47.8 – 74.0)*#
KOOS QoL	28 (11.7, 10.7 – 44.6)	54 (20.0, 45.5 – 63.2)*	89 (16.3, 81.8 – 96.2)*	64 (16.7, 56.0 – 72.2)*#
IKDC	47 (16.2, 39.7 -55.9)	65 (15.3, 56.7 – 73.6)*	71 (14.0, 63.3 – 79.4)*	75 (14.7, 67.4 – 82.6)*
Tegner (median, IQR)	2 (1.0 – 3.0)	N/A	3 (2.3 – 3.8)	4 (2.0 – 5.0)

ADL = activity in daily living, S&R = sports and recreation, QoL = quality of life. N/A = not applicable. * significantly different from baseline (p<.05), # significantly different from 1 year (p<.05).

We did not find a significant relationship between the Tegner activity score and the BMD levels at 1 and 2 year follow-up in the MAT knees in all ROIs, neither we did find a significant correlation between Tegner activity score and BMD levels in all ROIs in the healthy contralateral knees.

DISCUSSION

Subchondral bone is thought to play a key role in the pathogenesis of OA.[35] Structural changes in subchondral trabecular bone are associated with cartilage loss in OA and these changes are both a result and a cause of cartilage loss.[20,22,36] Investigating BMD after MAT could give more insight in the potential chondroprotective effect of MAT.

This explorative study showed that BMD in the knee after MAT does not change substantially in the first two years after surgery. Because this study is the first to report about BMD changes after MAT we could not compare our results to previous findings regarding BMD and MAT. It is generally known that a decrease in load or physical activity is related to a decrease in BMD.

All patients were rehabilitated according to a standard protocol. Complete weight bearing was prohibited for at least 6 weeks. Hereafter, patients were only allowed to exercise and move without restrictions when the knee had 80% of its former strength back, which usually took a few months. This period of lesser physical activity might explain the decrease in BMD in the healthy knee. Because of reduced weight bearing and disuse BMD in the MAT knee can be expected to be even more decreased. BMD levels did not increase in the MAT knees over time. BMD levels in MAT knees were higher than BMD levels in healthy knees, but stayed the same, while the values in healthy knees decreased. It should be taken into account that the observed difference in BMD levels between MAT knees and healthy knees is due to the decrease in BMD levels of the healthy knees, more than due to the unchanged BMD levels of the MAT knees. This raises questions about the comparability between BMD levels between a MAT knee and a healthy knee, even in the same patient.

Only patients with chondropathy grade ≤ 1 were included in this study. Despite this strict selection criterion, patients in this state of maximal slightly chondropathy, might already have subchondral bone changes resulting in higher BMD. It is known that as cartilage area decreases in the medial joint, bone volume fraction and trabecular thickness in the medial tibia increases,[20] leading to an increased BMD. An increased BMD in both medial and lateral compartment in MAT knees in patients with grade 1 chondropathy compared to the patients without chondropathy can be explained by the slight reduction in cartilage condition and its effect on subchondral bone. However, even in the selection of MAT patients without chondropathy on index surgery or on preoperative MRI a higher

BMD was found. This emphasizes that subchondral bone changes can occur in patients without clinical or radiological signs of OA and also in patients after (sub)total meniscectomy. This is in accordance with the results of the study of Petersen,[23] which showed an increased bone mineral density (BMD) and a specific distribution of BMD in the cortical of the subchondral plates and below in the trabecular bone in the medial compartment after partial or total medial meniscectomy in patients with isolated medial meniscal tears.[23]

The difference in BMD between tibia and femur is in concordance with other studies[33] and is probably physiological. The possibility of patella overlap, giving erroneous measurements of the femoral ROIs should also be taken into account.[37]

Regarding subchondral bone changes one would expect higher BMD levels in the affected compartment. Nonetheless, we could not demonstrate higher BMD in the affected compartment of a MAT knee compared to the non-affected compartment in the same MAT knee. A good explanation was not found. It might be the limb alignment that could play a role here. Although, all our patients have a normal aligned knee before surgery, varying between 5 degrees of valgus and 5 degrees of varus. Because of the axial loading BMD levels could be higher in the medial compartment, in a slightly varus aligned knee a higher BMD even in a lateral MAT knee. In vivo studies are needed to see if mechanical anatomy and mechanical function will restore after MAT.

Differences in BMD between compartments were not found in healthy knees, where we assume mechanical anatomy and mechanical function are normal. In healthy knees BMD in medial compartment compared to lateral compartment in the both femur and tibia were the same (e.g. BMD in medial femoral compartment compared with lateral femoral compartment). In this study three patients had a concomitant ACLR during medial MAT and one patient during lateral MAT. As mentioned before, this number was too small to draw any statistical conclusions about the influence of ACLR on BMD of tibia and femur. However, in the first 6 months we found a significantly decrease in BMD for the central tibial compartment in the group of 10 patients having a medial MAT. The influence of a drilled tunnel in the tibia on BMD, especially on BMD changes of the central tibial compartment, was not described in other studies. One could imagine that drilling a hole in the tibia and removing trabecular and cortical bone would give a decrease in bone mass and a decrease in BMD level at this specific site. This might be an explanation for the significantly decrease in BMD in the central tibial compartment in the group of patients where one-third had a concomitant ACLR. Nevertheless, after 6 months BMD levels of the central tibia compartment were equal the BMD levels of the other compartments. Probably, a 6 months period is long enough to restore BMD and for incorporation of the anterior cruciate ligament (ACL) graft.

Patient related outcome improved during the first two years after MAT as seen in many other studies.[12] Nonetheless, in our study patients score worse on recreation and sports after 1 year. A possible reason is that patients might still have too much complaints of their knee which force them to stop practising sports or renounce recreational activities. This could negatively influence their quality of life, especially in this young patient population, but can help them to function on the same level in activities of daily living (ADL) with the same scores on pain and symptoms like 1 year before.

The overall improvement found in PROMS does not seem to have a relation with BMD levels, since they do not improve. Any literature on clinical influence of BMD changes is not available. Longer follow-up in a bigger group of patients could give some more insight on this topic.

This study has some limitations. First, this is the first study describing BMD level changes after MAT. Baseline or normal values of BMD, clinical relevance of BMD levels and BMD level changes after MAT are not clear yet. Second, the study population consists of 26 patients, which is relatively small. The group of patients having a concomitant ACLR was even smaller. This makes it difficult to draw strong conclusions on the influence of ACLR on BMD. Third, a follow-up time of 2 years might be too short to show any changes in the subchondral bone, especially concerning a long-term process such as developing OA. Fourth, with the lack of any former studies examining the influence of MAT on BMD levels, a power analysis was not possible. At last, there is some heterogeneity among this patient population (left versus right (dominant versus none dominant side), lateral versus medial MAT and ACLR versus intact anterior cruciate ligament (ACL), which has influence on the power of this study. More studies are needed to investigate BMD changes after MAT to investigate the potential chondroprotective effect of MAT. A longer follow-up in a larger group of patients is needed to see whether BMD remains stable or changes over time more than two years after MAT and to see if BMD measurement can be a suitable tool to prove a chondroprotective effect of MAT.

In conclusion, this study is the first prescribing BMD changes after MAT. The results show that BMD levels differ after MAT compared to the healthy contralateral knee and do not change over time after 2 years of follow-up. The difference in BMD between healthy and operated knees can be explained by subchondral bone changes which already occurred as the initial step of the development of OA. This explorative study is a base for further research on BMD in MAT patients and might contribute to a better understanding of the clinical good results of MAT.

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Meniscal allograft transplantation in the Netherlands: long-term survival, patient-reported outcomes, and their association with preoperative complaints and interventions.

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ABSTRACT

Purpose: Evaluation of survival of meniscal allograft transplantation (MAT) and postoperative patient reported outcome (PRO), and their association with prior interventions of the knee.

Methods: A prospective consecutive study of 109 consecutive patients who had an arthroscopic meniscal allograft transplantation (MAT) between 1999 and 2017 by a single-surgeon. Patients were assessed with KOOS scores, preoperative and after a minimal follow-up of 2 years. Furthermore, two anchor questions (whether expectations were met and overall satisfaction, on a 5-point Likert scale) were asked. Additionally, prior interventions to MAT were evaluated.

Results: Prior to MAT, patients had undergone an average of 2.8 (range 1-14) of surgical procedures of the knee. Overall, mean allograft survival was 16.1 year (95%CI: 14.8 to 17.5 year). Higher age at surgery was associated with lower MAT survival: hazard ratio for MAT failure was 1.19 per year increase (95%CI: 1.04 to 1.36, p=0.009). At 4.5 years (IQR, 2 – 9) of follow-up all KOOS score were still improved compared to baseline.

Age below 35 years, simultaneous anterior cruciate ligament reconstruction and number of knee surgeries before MAT were associated with lower KOOS scores. Overall patient expectations and overall satisfaction after MAT were not associated with preoperative patient characteristics nor with the number, or kind of preoperative interventions.

Conclusion: Meniscal allograft transplantation has a good overall survival with a clinically relevant improvement. Both meniscal allograft survival and PRO were associated with age. PRO was lower in patients younger than 35 years at time of MAT and meniscal allograft survival was worse in patients older than 50 years. PRO was associated with preoperative patient characteristics and number of surgical procedures prior to MAT. All patients reported improved postoperative satisfaction and met expectations after MAT. Both independent of the preoperative history of knee interventions.

INTRODUCTION

Partial or total meniscectomy is often performed when damaged meniscal tissue cannot be repaired due to unfavorable conditions, type of meniscal tear, or when conservative treatment failed in presence of a locking knee. Such a (partial) meniscectomy will alter the biomechanical and biological conditions in the knee joint.[5] This can lead to a painful meniscus deficient knee, also referred to as the *postmeniscectomy syndrome*, or eventually to symptomatic osteoarthritis.[14] In the Netherlands about 18.000 to 36.000 arthroscopies for meniscal pathology are performed annually.[21] Subsequently, some of these patients develop a post meniscectomy syndrome.[17]

Currently, meniscal allograft transplantation is a widely accepted and recommended treatment option for patients with a post meniscectomy syndrome.[3,24-26] The first meniscal allograft transplantation (MAT) in the Netherlands was performed in 1989[27] and until 1999 it was performed by an open procedure. Long-term results after open MAT show good clinical results.[29] Since 1999, MAT has been increasingly performed as an arthroscopically assisted procedure in the Netherlands, thus minimizing trauma to the knee joint.[7] Not only the surgical technique has been improved by the arthroscopic MAT, but also indications, patient selection and postoperative rehabilitation have been improved during 30 years of clinical experience. Short- and long-term outcomes of both open and arthroscopic MAT have shown positive results in terms of pain relief and functional improvement.[3,25]

Interestingly, some patients with a poorer clinical outcome still report good levels of satisfaction about the MAT procedure. This suggests that patient satisfaction for MAT is likely multifactorial and poorly understood. Therefore, it is very relevant to obtain knowledge on preoperative patient characteristics which may influence not only clinical outcome, but also patient's satisfaction. These factors can contribute to clinical decision-making on whether or not to perform a MAT.

Little is known on the associations of post-operative clinical results and patient satisfaction of MAT with pre-operative history, symptoms, and prior conservative and surgical interventions. The latter may affect outcome after MAT. Publications reporting on patients' history with respect to knee complaints prior to MAT, as well as interventions prior to MAT are scarce and often very concise.[1,18] However, these factors may not only effect the knee joint and the lower extremity and the outcome of MAT, but also the patient's overall functioning as reflected in the International Classification of Functioning (ICF) model of the World Health Organization (WHO).[30]

Therefore, as first aim of this study, the overall impact of clinical status and interventions prior to MAT on patient's overall functioning after MAT, using long-term patient reported outcome measures (PROMs) was evaluated. As second aim, overall meniscal allograft survival at long-term follow-up was evaluated. Recently, minimal clinically important difference (MCID) and patient acceptable symptom states (PASS) for MAT were determined,[11] however, patients' expectations and satisfaction about this procedure are still unknown and should potentially be considered as significant entities in the overall result of MAT. Thus, as our third aim, patient's expectations and satisfaction about MAT were evaluated.

MATERIALS AND METHODS

This study has been approved by the local medical ethical review board (METC Leiden-Den Haag-Delft, METC number: 17–104) and was registered in the Dutch Trial Register (NTR: NTR6630).

All 109 consecutive patients (111 meniscal allografts) with an arthroscopic assisted MAT between November 1999 and January 2017 were evaluated. All surgeries were performed by a single experienced knee surgeon. Surgical technique is described in detail in earlier research.[28,29] Patients eligible for MAT were 55 years and younger with disabling unicompartmental pain after a (sub)total meniscectomy with a stable knee joint or stabilized by concomitant anterior cruciate ligament reconstruction (ACLR) and normal knee alignment (5 degrees valgus – 5 degrees varus).

Surgical technique: preoperative, size matched, cryopreserved allografts were used. Needling of the remnant of the peripheral rim was performed to enhance MAT ingrowth. The allograft was fixed using six to nine absorbable and non-absorbable sutures in the capsule, no bone block was used. Until 2009 the posterior side of the allograft was attached with inside-out sutures. As of, 2009 all-inside meniscal sutures were used for posterior horn fixation. The middle part of the allograft was fixed with inside-out sutures. One tibia tunnel was used and the anterior horn was fixed to the tibia plateau using a suture anchor. Before 2009 an extra tibia tunnel was used for anterior horn fixation.

Rehabilitation started with 3 weeks of partial weight bearing (25%) with mobilization on crutches with limited flexion of 60º. After the first three weeks partial weight bearing increased to 50% and knee flexion to 90º. From week 9 till 12 progressively loading was allowed and knee flexion to 120º. Between week 13 – 24 patients could progressively increase loading. If 80% of its former strength was reached no restrictions were needed, except the advice to avoid high-impact activities and contact sports.

Baseline characteristics of the patient population are shown in Table 1. All patients had regular yearly clinical follow-up (including physical examination and assessment with PROMs). All patients were evaluated in 2019, with a minimum follow-up of 2 years. All patients gave written informed consent for this study.

At baseline, patients' history on interventions prior to the meniscal transplantation as well as complaints of the knee and social impact of the knee complaints were evaluated at intake for the MAT procedure. For the current study, these data were collected from

Table 1. Baseline patient characteristics prior to meniscal allograft transplantation (MAT). # Worst grade of chondropathy on tibia and/or femur in treated compartment (Outerbrige scale).

Number of patients with meniscal allograft	**n = 109**	
Gender (female) – n (%)	65 (60)	
Age (years) – median (IQR)	41 (29 – 51)	
Medial Compartment – n (%) Bilateral	36 (33) 2 (2)	
No. of concomitant ACL reconstructions – n (%)	16 (15%)	
Median follow-up (months) – median (IQR)	54 (27 – 129)	
Grade chondropathy#	Medial (n=36)	Lateral (n=69)
- Grade 0	15	21
- Grade 1	10	18
- Grade 2	7	16
- Grade 3	4	13
- Grade 4	0	1

ACL: anterior cruciate ligament, IQR= inter quartile range.

the medical records of the hospital's electronic patient record system. Furthermore, at the final follow-up evaluation in 2019, all patients were asked to provide a complete overview of their medical history with respect to the knee prior and after MAT. Questionnaires were send out several times and multiple attempts were made to contact to non-responders.

The Knee injury and Osteoarthritis Outcome Score (KOOS)[20] was used to evaluate functional outcome. Health-related quality of life was assessed using EuroQol five-dimensional questionnaire (EQ-5D).[8] To evaluate the postoperative patient opinion on the MAT procedure, two anchor questions with a five-point Likert scale were used (see appendix). The answers 'to a reasonable degree' (Likert scale 3) and higher were considered as a positive (i.e. satisfied on the postoperative result).

Preoperative data of one patient could not be retrieved. In 108 patients (99%) preoperative history of the knee was analyzed. At the final follow-up, eighty-one (74%) patients returned complete questionnaires. 28 patients were lost to follow-up after a median of 4 years (inter quartile range (IQR) 2 – 13). The two patients with bicompartmental MAT (1 lost to follow-up) were excluded for further analysis due to the small size of this group.

At final follow-up 8 of 47 patients younger than 35 years were lost to follow-up (17%), 6 of 35 patients between 35-50 years were lost to follow-up (17%), 5 of 27 patients older than 50 years at time of MAT were lost to follow-up (18%).

Meniscal allograft failure was defined as removal of the complete allograft (with or without (unicompartmental) knee arthroplasty placement) as defined during the International Meniscus Reconstruction Experts Forum in 2015.[6]

Statistical analysis

Data were tested for normality using Kolmogorov-Smirnov. Survival was assessed using Kaplan-Meier survival function and cox regression analysis (end-point: failure of meniscal allograft, see definition above). Continuous outcome measures were analyzed using a linear mixed-model. This technique is recommended for analysis of repeated measurements; it takes the correlation of values within subjects into account and deals effectively with missing values and loss-to-follow-up. Consequently, statistical inference can be based on the data of more patients then only those who completed the entire follow-up period.[4,16] Continuous and ordinal variables are collapsed into ordinal variables or reduced in number of categories if required for modelling purposes. For example, age is investigated in all models as a continuous variable, an ordinal categorized variable (younger than 35, 35-50, older than 50) and a dichotomized variable (younger than 35, 35 and older). Regarding age, the dichotomized variable was chosen for modelling purpose and its clinical relevance.[12] Model assumptions were checked and models were adjusted accordingly.

In the mixed-model analysis the following predictors were included: sex, age, side treated (left or right), compartment treated (medial or lateral), with or without concomitant anterior cruciate ligament reconstruction (ACLR), chondropathy grade two or more on the Outerbridge scale (yes or no),[13] number of knee surgeries before MAT.

Postoperative ordinal and categorical outcome measures were analyzed using multiple linear, ordinal and logistic regression models with appropriately collapsed outcome categories in order to obtain reliable estimates. Sex, age, side treated, compartment treated, with or without ACLR, chondropathy grade and the number of knee surgeries before MAT were included as factors in the models.

IBM SPSS Statistics (version 25.0; SPSS Inc) was used for the statistical analyses.

RESULTS

Patients' history

Overall, 302 surgical interventions prior to MAT were performed in 108 patients (Table 2).

Meniscal allograft survival

At final follow-up, data on MAT survival data were available in 90 of the 109 patients (83%). In 29 patients (32%), a total of 48 operations were performed after the MAT (Table 2). Failure of the MAT occurred in 11 patients (10%); 2 medial (of 36, 6%) and 9 lateral (of 73, 12%) meniscal allografts failed after a mean of 8.0 years (range, 0.8 – 15.4 years). Eight of these patients (72.3%, or 7% of 109) had a conversion to total knee arthroplasty (TKA) at a median of 7.3 years (IQR, 5.2 – 11.9). The other 3 had a complete resection of the graft.

Mean survival time of the MAT was 16.1 year (95%CI: 14.8 - 17.5). The mean survival of a medial and lateral MAT was comparable and did not significantly differ (Figure 1).

Table 2. Patients' knee operations prior to and after MAT. *Multiple responses (some patients had up to 14 prior procedures of which up to 7 partial meniscectomies).

Patients' history*		
		patients (n = 108)
Number of prior surgical interventions	n = 302	
- 1 operation		20 (19%)
- 2		38 (35%)
- 3-5		44 (40%)
- 6-14		6 (6%)
		per patient (median, IQR)
Operations **prior to** MAT*		2 (2 – 3)
- Partial meniscectomy		1 (1 – 2)
- (Sub)total meniscectomy		0.5 (0 – 1)
- ACL reconstruction		0 (0 – 0)
- Meniscal repair		0 (0 – 0)
- No further specified arthroscopy		0 (0 – 1)
Interval between (sub)total meniscectomy and MAT (months)		28 (13 – 68)
Operations **after** MAT	n = 48	patients (n = 29)[#]
- Partial meniscectomy	12	8
- Refixation of the graft	8	8
- Resection of the graft	3	3
- Total Knee Arthroplasty	8	8
- Other reason (e.g. synovectomy)	17	16

ACL: anterior cruciate ligament, IQR= inter quartile range. [#]Some patients had multiple (different) operations after MAT.

MAT survival was associated with age at baseline (Figure 2, *p*=0.010). In patients between 35-50 years, 3 of 29 (10%) had failure of the MAT and in patients older than 50 years at time of MAT, 8 of 22 (30%) failed. Patient sex, compartment treated, procedure with or without ACLR and intraoperative chondropathy grade two or higher (χ^2 testing, p>0.27) were not associated with survival of the MAT in an univariate analysis.

In a multivariable Cox-regression analysis, patient age at baseline was associated with MAT survival: hazard ratio for MAT failure was 1.19 per increasing person year after the age of 35 years (95%CI: 1.04 to 1.36, *p*=0.009). This corresponds to a 5.2 times higher risk of revision for every 10 years increase in age older than 35 years at time of MAT surgery.

Patient reported outcome

The median follow-up between MAT and final follow-up was 4.5 years (IQR, 2 – 9).

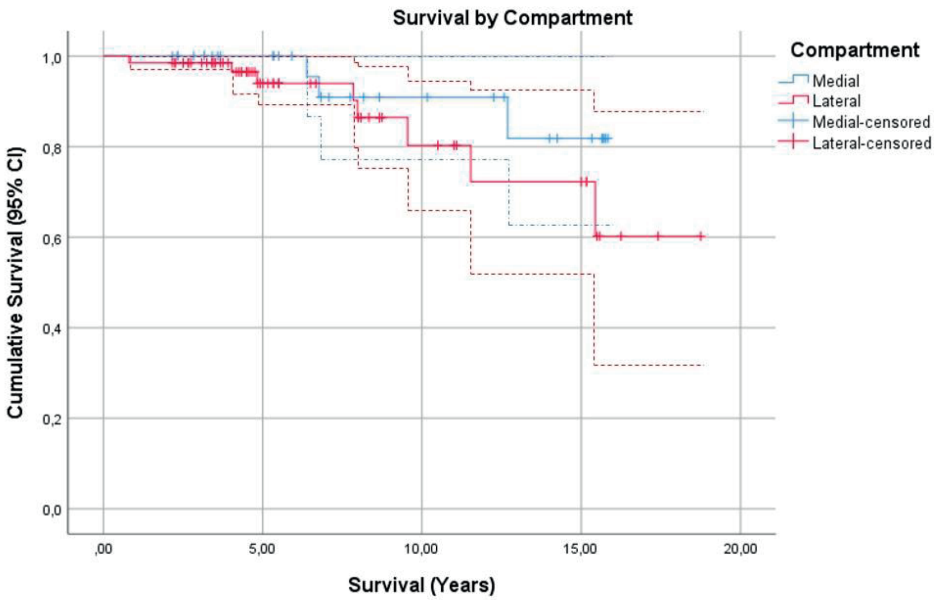

Figure 1. Survival by compartment (95%CI).

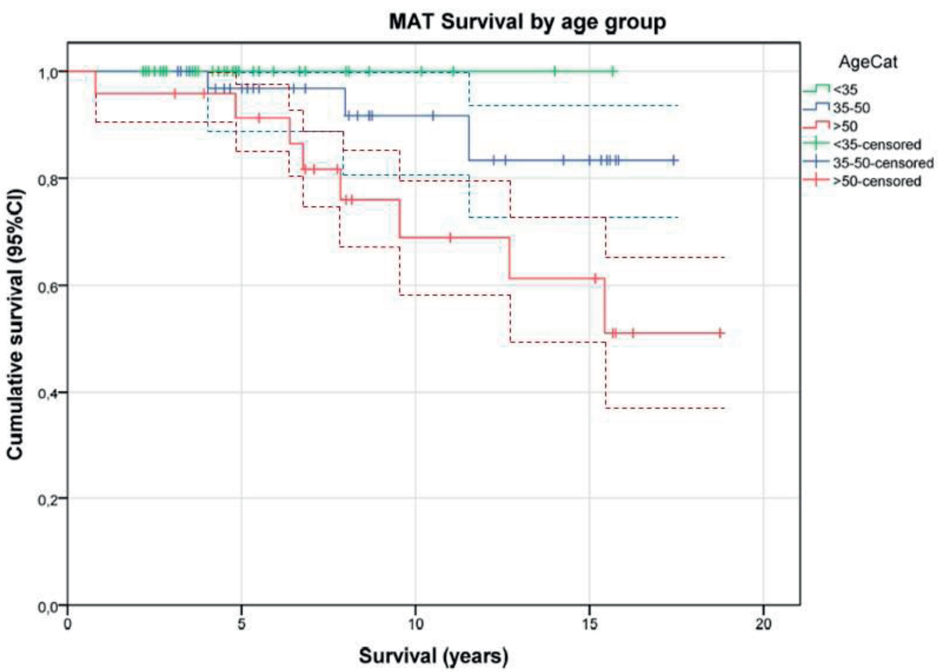

Figure 2. Survival by age (95%CI). AgeCat = Age category.

Overall, PROMs improved compared to the preoperative state and persisted during follow-up, except for a slight increase of symptoms after five years. (Figure 3). For all five domains, a minimal clinically important difference (MCID) was present at one year and at the last follow-up compared to baseline. The mean differences between scores at final follow-up compared to preoperative scores were significant for all five domains. (Figure 3).

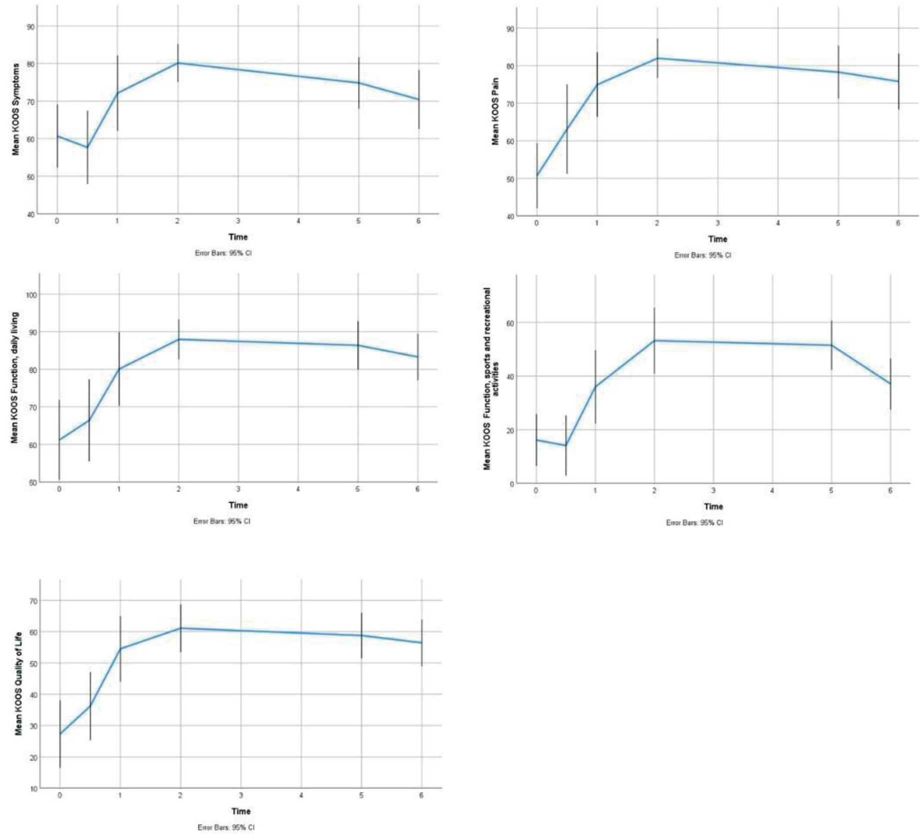

Figure 3. Mean KOOS scores at follow-up (mean / 95%CI).

With univariate analyses, age below 35 years, ACLR in the same session and the number of knee surgeries before MAT were associated with lower improvement in different KOOS domain scores. Surgical side, knee compartment treated with MAT and the degree intraarticular chondropathy were not significantly associated with the postoperative KOOS score (Table 3). Men experienced less improvement than women in the KOOS domain scores for pain (7.4 points, 95%CI: 14.3 to 0.5, p=0.037).

At final follow-up, overall mean postoperative quality of life score, EQ5D, was 0.84 (95%CI: 0.79 to 0.88). The mean patient perceived health state on the EQ5D 0-100 VAS was

Table 3. Association between postoperative KOOS in relation to specified covariates (univariate analyses).

	KOOS symptoms	KOOS pain	KOOS function and daily living	KOOS sports and recreational activities	KOOS quality of life
Age	7.9 (95%CI 14.8 – 0.9) p=0.028	5.6 (95%CI -12.1 – 0.9) n.s	8.5 (95%CI 15.2 – 1.8) p=0.015	14.0 (95%CI 24.7 – 3.6) p=0.013	3.9 (95%CI -13.0 – 5.4) n.s
Compartment (medial or lateral)	6.3 (95%CI -1.5 – 14.2) n.s	1.8 (95%CI -5.6 – 9.2) n.s	2.7 (95%CI -10.6 – 5.2) n.s	2.3 (95%CI -10.0 – 14.6) n.s	1.7 (95%CI -9.2 – 12.5) n.s
Additional ACLR	16.3 (95%CI 5.1 – 27.6) p=0.006	14.2 (95%CI 3.6 – 24.8) p=0.01	2.3 (95%CI -8.8 – 13.5) n.s	9.7 (95%CI -6.5 – 25.9) n.s	8.8 (95%CI -5.8 – 23.2) n.s
Side	0.3 (95%CI -6.6 – 7.3) n.s	3.0 (95%CI -3.6 – 9.5) n.s	3.3 (95%CI -3.4 – 10.0 n.s	2.7 (95%CI -13.3 – 7.9) n.s	2.8 (95%CI -6.2 – 11.8) n.s
Number of surgeries before MAT	3.9 (95%CI 6.1 – 1.8) p=0.001	3.9 (95%CI 6.0 – 1.8) p=0.000	3.1 (95%CI 5.1 – 1.2) p=0.002	2.6 (95%CI -6.0 – 0.8) n.s	3.8 (95%CI 6.3 – 1.3) p=0.003
Intraarticular chondropathy	0.7 (95%CI -10.4 – 8.9) n.s	0.0 (95%CI -9.1 – 9.2) n.s	7.2 (95%CI -1.8 – 16.2) n.s	3.0 (95%CI -10.7 – 16.6) n.s	3.1 (95%CI -8.7 – 14.8) n.s

95%CI= 95% Confidence Interval. n.s = non-significant.

78.5 points (95%CI: 75.1 to 81.9), which was not associated with sex, age, surgical side, compartment, concomitant procedure nor grade of chondropathy (p>0.3).

Eighty patients (of 109, 73%) responded to the anchor questions, 4 questions were answered incomplete. The outcome for all 12 anchor questions was in the vast majority (range 71% to 93%) positive (scored 3 or higher on the Likert scale) (Table 4).

With regards to factors associated with patients satisfaction multivariate analyses showed that patients of 35 years and older indicated they were more willing to undergo the MAT again, compared to patients under 35 years (adjusted odds ratio 4.2, 95%CI: 1.03 – 16.9, p=0.04). Patients' opinions on the outcome (e.g. expectation, satisfaction) of the MAT procedure was not associated with preoperative patient characteristics (e.g. grade of chondropathy), nor characteristics of the MAT procedure as such (e.g. ACL , medial or lateral graft) (Table 5).

Table 4. Patient opinion on MAT procedure.

	Not at all	Little	To a reasonable degree	Much	Very much	Negative/ positive (positive %)
1. Expectations	3	4	15	42	15	7/72 (91%)
2. Confidence	7	14	18	31	8	21/57 (72%)
3. Social life	5	14	24	21	15	19/60 (76%)
4. Satisfaction body	7	15	25	25	7	22/57 (72%
5. Daily activity	5	12	14	35	14	17/63 (79%)
6. Work	9	14	18	25	14	23/57 (71%)
7. Solution to complaints	2	5	22	23	28	7/73 (91%)
8. Satisfaction	2	5	17	32	24	7/73 (91%)
9. Do it again	6	4	6	29	35	10/70 (88%)
10. Recommendation	1	5	12	29	33	6/74 (93%)
11. Physiotherapy	58	5	4	6	6	16/63 (79%)
12. Adjustments at work	28	22	17	9	4	13/67 (84%)

Table 5. Association between satisfaction of the treatment, fulfilment of the expectations, recommendation to undergo MAT again, recommendation of procedure to other patients in relation to specified covariates.

	Anchor questions			
	Preoperative expectation on MAT	Satisfaction on outcome MAT	Willingness to have MAT again	Recommendation to other patients
Sex	-0.26 (95%CI: 0.22 – 2.00, *p*=0.50)	-0.36 (95%CI: -0.24 – 2.00, n.s)	0.21 (95%CI: -0.36 – 4.18, n.s)	-0.35 (95%CI: -0.21 – 2.34, n.s)
Side	0.54 (95%CI: 0.60 – 4.66, *p*=0.33)	0.51 (95%CI: 0.60 – 4.67, n.s)	0.27 (95%CI: -0.40 – 4.32, n.s)	0.91 (95%CI:- 0.75 – 8.16, n.s)
Compartment (medial or lateral)	0.55 (95%CI: -0.44 – 6.8, n.s)	0.72 (95%CI: 0.53 – 8.07, n.s)	0.30 (95%CI: -0.28 – 6.54, n.s)	1.00 (95%CI: -0.50 – 14.84, n.s)
Additional ACLR	0.19 (95%CI: -0.20 – 7.3, n.s)	0.23 (95%CI: -0.21 – 7.47, n.s)	0.26 (95%CI: -0.19 – 8.87 n.s)	1.47 (95%CI: -0.60 – 31.59, n.s)
Number of surgeries before MAT	-0.23 (95%CI: -0.59 – 1.1, n.s)	-0.09 (95%CI: -0.60 – 1.40, n.s)	0.04 (95%CI: -0.77 – 1.41, n.s)	-0.05 (95%CI: -0.71 – 1.27, n.s)
Intraarticular chondropathy	0.09 (95%CI: -0.72 – 1.68, *n.s*)	0.01 (95%CI: -0.68 – 1.51, n.s)	0.04 (95%CI: -0.66 – 1.64, n.s)	0.02 (95%CI: -0.63 – 1.53, n.s)
Age	0.50 (95%CI: -0.53 – 5.04, n.s)	0.13 (95%CI: -0.40 – 3.28, n.s)	1.43 (95%CI: 1.03 – 16.90, *p*=0.04)	0.09 (95%CI: -0.33 – 3.68, n.s)

Data expressed in B coefficient (standardised regression coefficient), 95%CI= 95% Confidence Interval. n.s = non-significant.

DISCUSSION

The most important findings of this study were that both meniscal allograft survival and patient reported outcome were associated with age; PROMs were lower in patients younger than 35 years and MAT failure rate was higher in patients older than 35 years. Patient reported outcome was associated with (pre)operative characteristics: e.g. a higher number of knee surgeries before MAT and simultaneous ACLR were associated with lower PROMs. Nevertheless, all patients reported improved postoperative satisfaction and reported that preoperative expectations after MAT were met. The latter despite, an extensive preoperative history of knee interventions.

This is the first study evaluating all surgical procedures at the knee prior to MAT, using PROMs as well as MAT survival. Our results show a good survival of MAT, with an overall survival of 76% at 15 years. If MAT surgery was done at an age of 35 years and younger meniscal allograft graft survival was better. The risk of removal of the meniscal allograft increased with increasing age at time of MAT surgery. For every 10 years older age than 35 years at time of MAT surgery, the risk for meniscal allograft resection (with or without conversion to TKA) increased 5 times. Other patient and surgical characteristics, including sex, medial or lateral compartment, ACLR or chondropathy were not associated with graft survival.

The finding of a higher failure rate in older patients (>35 years), is in concordance with others.[12] The biological vitality of the knee compartment in this age group might have a negative effect on graft ingrowth and subsequent graft degeneration. This might lead to a higher chance / likelihood of MAT failure. Furthermore, MAT survival is not only influenced by good graft ingrowth and functioning, but also on the decision whether or not to re-operate. This decision is likely age-dependent, as there are relatively few acceptable alternatives (e.g. unicompartmental or total knee arthroplasty) for these patients.

Regarding the high failure rate (30%) in patients >50 years and the worse allograft survival compared to the younger age groups, it should be up for discussion to whether or not to perform MAT in these patients. Despite the positive results on satisfaction and expectations and despite the missing correlation between PROMs and grade of chondropathy in this patient group.

Twice as less failures were seen for medial MAT compared to a lateral MAT, however in relation to allograft survival there was no significant difference. This is probably due to the relative small group of patients. This finding is supported by a meta-analysis by Bin et al, who also did not find a difference in survival between medial and lateral compartment MAT.[2]

We found no inferior survival for concomitant ACLR and MAT, in concordance with previous publications.[2,22] Chondropathy grade three or higher was not associated with survival in our study. Where others[12] report increased mechanical failure of MAT with advanced cartilage damage, we did not find this association. Even more, in our study both patients with and without chondropathy benefit from MAT.

In the current study, all patients experienced a clinical improvement at 1 year until final follow-up after MAT. Noteworthy is that despite a slight deterioration in clinical symptoms over time, the majority (88%) of patients were willing to undergo the MAT again, irrespective of eventual experienced MAT failure. Patients who were 35 years and younger at MAT surgery had lower PROMs, and reported consequently, to be more reluctant to undergo the same procedure again, for the same complaints. The worse KOOS scores in these younger patients probably reflect the higher physical demands and expectations on the effect of MAT surgery of these younger patients.

As mentioned earlier, this is the first study evaluating all surgical procedures at the knee prior to MAT, using PROMs as well as MAT survival. In our study, 82% of patients had two or more operations prior to their MAT. A higher number of knee surgeries before MAT had a negative association with postoperative knee score (KOOS). Multiple prior surgeries might lower the baseline value of patient reported outcome, which also negatively influence the postoperative outcome. It could also be that the number of prior surgeries is related to the severity of injury or concomitant injuries prior to MAT, influencing the postoperative outcomes.

This is also the first study to evaluating patients' expectations and satisfaction of MAT, taking into account prior procedures to the knee. For general meniscal surgery, it has been reported that patients expect fast recovery and a high level of participation in leisure activities.[15] However, in this study less than half of the patients were able to participate at the same competition level as they expected preoperatively. Even more, less than 50% was satisfied with their knee function 3 months after meniscal surgery.[15] Although our MAT cohort with multiple surgical interventions at their knee was difficult to compare with a general meniscal lesion cohort, it was interesting to see that the MAT cohort showed more favorable results. In the current study, 91% of the patients met their preoperative expectations and 67% of patients were satisfied with the postoperative result. The satisfaction after MAT was confirmed by the large number of patients who would recommend the operation to patients with the same problem and who would undergo the same procedure again. Concordantly, Searle et al. also found a high number of patients (32 out of 43 patients, 74%) reporting they would undergo MAT again.[23]

Recently, Liu et al, determined the minimal clinically important difference (MCID) and patient acceptable symptom states (PASS) for MAT.[11] We did not establish PASS or MCID in our population, but positive answers to the questions about patients opinion regarding MAT ranged from 71 to 93%, with 91% in particular regarding patients satisfaction after MAT. We are aware that a PASS thresholds can be patient population specific[11] and can alter in follow-up time.[9,10] Nevertheless, compared to baseline level, all KOOS scores were above both the MCID and the PASS as given by Lui et al[11] at any follow-up moment in our population. This confirms the patient reported success of MAT in our cohort.

There are some limitations when interpreting the results from this study. First, 27% of patients were lost to follow-up, which could have led to selection bias. Although, a 60% threshold seems enough for an acceptable frequency of response.[19] Secondly, the wide range in follow-up since the MAT procedure might have an effect the patient's opinion on the surgical procedure (recall bias). But since we used anchor questions at follow-up, our results are informative on the patients perception of MAT.

Despite these limitations, results of present study could be used for better expectation management in clinical practice. Based on patient characteristics (e.g. number of prior operations or patient's age) expectations of a patient on the effect of a MAT can be better managed during the preoperative consultation prior to a MAT. Patients will be better informed during a shared decision making process on outcome and MAT survival.

CONCLUSION

Our results show a good overall survival of MAT, even in young patients, high patient reported outcomes and successful fulfilling of patient expectations. This makes MAT a good option a good joint preserving option, leaving other conservative and surgical options open. On the other hand, a higher number of previous procedures before MAT, simultaneous ACLR and younger ages are associated with inferior patient reported outcomes. These factors should be taken into account with clinical decision making and expectation management with regards to MAT.

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8

Translation and Validation of the Dutch Western Ontario Meniscal Evaluation Tool (WOMET).

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ABSTRACT

Purpose: The purpose of this study was to translate the Western Ontario Meniscal Evaluation Tool (WOMET) into Dutch and to determine validity, reliability and responsiveness of the Dutch version.

Methods: The WOMET was translated into Dutch according to a standardized forward-backward translation protocol. Eighty-six patients (51 male, 35 female, mean age 52.2 (standard deviation (SD) 11.4)) with isolated meniscal pathology were included. WOMET was completed three times (at baseline around 2 weeks and after 3 months from baseline). Knee injury and Osteoarthritis Outcome Score (KOOS), International Knee Documentation Committee (IKDC) Subjective Knee Form, IKDC Current Health Assessment Form and two anchor questions were also answered. Content validity, construct validity, reliability and responsiveness was determined.

Results: The Dutch WOMET showed good construct validity (good correlation with all other questionnaires and all hypotheses confirmed), content validity (floor and ceiling effects (<30%), internal consistency (Cronbach's alpha = 0.88) and test-retest reliability (intraclass correlation coefficient = 0.78). The Dutch WOMET was found responsive to change (88% confirmation of the predefined hypotheses). The smallest detectable change (SDC) and minimal important change (MIC) for the Dutch WOMET are 15.4 and 14.7, respectively.

Conclusions: The Dutch version of the WOMET is valid and reliable. It can be used as a disease specific tool to evaluate health related quality of life of Dutch patients with meniscal pathology.

INTRODUCTION

Meniscus injuries are the most common knee injury,[32] and can be classified into traumatic tears[37] or degenerative lesions.[31] The most common treatment for meniscal lesion is an arthroscopic partial meniscectomy, making this the most frequent orthopaedic intervention. Each year, almost half a million partial meniscectomies occur annually in the United States and this cost several thousand dollars each.[10,26] In the Netherlands about 30.000 arthroscopies for meniscal pathology were performed in 2000. In 2010 this has increased to about 42.000, of which 65% in the patients who were older than 45 years of age. This represents an increase in ten years' time of 46%. The percentage of meniscal repair is unknown.[7]

To evaluate an intervention, measures of impairment (such as pain, swelling and mechanical problems) as assessed after arthroscopic meniscal treatment, outcomes have to be determined. Surgeons can use objective measures such as range of motion or radiographic imaging to confirm meniscal healing after meniscal repair or the presence of a tear remnant after partial meniscectomy. However, to ensure the intervention satisfies the expectations of the patients, an instrument must measure the patient relevant outcomes, emphasizing health status, disability and function.[43] Therefore, patient reported outcomes measures (PROMs) can be used. Although this instrument does not measure objective outcomes, it can be an important instrument to measure the outcome of an intervention, because an objectively measured good result does not always ensure good patients satisfaction.[4] For instance, the result of a partial meniscectomy can be successful when judged with objective measures like wound healing, range of motion and swelling, but can be disappointing for the patient when there are still functional problems.[4,34]

Although arthroscopic meniscal treatment (partial meniscectomy and meniscal repair) is the most common orthopaedic procedure, there is no validated pathology-specific health-related quality of life outcome measurement for this type of injury in the Netherlands. Nowadays, various instruments have been used to assess the outcome of treatment of knee pathology: the Knee injury and Osteoarthritis Outcome Score (KOOS),[33] the International Knee Documentation Committee (IKDC) Subjective Knee Form,[19] the Lysholm score,[24] the Oxford Knee Score,[11] and the Cincinnati Knee Rating Scale.[29] The KOOS has been validated for patients with multiple knee problems, including meniscal lesions.[35] The Lysholm knee score and the IKDC subjective knee has been specially validated for patients with meniscal pathology.[5,8] However, these instruments do not all measure the outcomes for specific meniscal pathology or are not a specific health-related quality-of-life instrument. Kirkley et al. developed the Western Ontario Meniscal Evaluation Tool (WOMET), which is the first meniscal pathology-specific health-related quality of life instrument.[23] The WOMET is a valid, reliable, and responsiveness disease-specific outcome measure for the assessment of health-related quality of life deficits in patients with meniscal pathology.[23]

To our knowledge, there is no Dutch version of the WOMET available at this moment. Considering the fact that the original version of the WOMET has already been validated in English[23] and recently is translated and validated in Finnish[36] and Turkish,[6] we hypothesized that the Dutch version of the WOMET is also a valid instrument to for the assessment of health-related quality of life deficits in Dutch patients with meniscal pathology. Therefore, the purpose of this study was to translate the WOMET into the Dutch language and determine the validation, reliability, and responsiveness for patients with traumatic or degenerative meniscal injury.

MATERIALS AND METHODS

Study Population

From July 2013 till June 2015, all consecutive patients who had a Magnetic Resonance Imaging (MRI) confirmed symptomatic meniscal tear were assessed for participation in this study. Patients were included at the orthopaedic outpatient clinic of the Medical Center Haaglanden by their orthopaedic consultant. Patients signed an informed consent after meeting all inclusion criteria. Inclusion criteria were: patients between 18 and 70 years old, a MRI confirmed symptomatic, isolated, traumatic or degenerative meniscal tear, no signs of osteoarthritis on plain radiographs, understanding of the Dutch language. Patients were excluded if they had concomitant ligament injuries or previous ligament injury with persistent knee instability, any previous knee operation, chondropathy higher than grade two on the Outerbridge scale[30] seen on MRI or during the operation, or inability to participate due to cognitive impairment. Because of the high prevalence of meniscal lesions among elderly people,[16] it was decided to exclude all patients over 70 years of age.

Study Design

All patients were asked to complete three sets of questionnaires at three time points: T0 (baseline), T1 (around 2 weeks after baseline and before start of intervention) and T2 (at least at 12 weeks after start of intervention; surgery or start of conservative treatment). All sets contained the Dutch WOMET, KOOS, IKDC Current Health Assessment form and IKDC Subjective Knee Form. At T1 an anchor question (one on remembrance of questions) and at T2 two anchor questions (one on remembrance and one about the effect of treatment) were asked as well. Patients received their first questionnaire at the outpatient department or by post to fill in at home. The second and third questionnaire was send by post to fill in at home. For this study the KOOS and IKDC Subjective Knee Form were used because these questionnaires were the second and third best instruments to measure symptoms in patients with meniscal lesions after the WOMET.[39]

Outcome Measures

WOMET

The WOMET consists of 16 questions and is specifically developed to evaluate health-related quality of life in patients with meniscal pathology.[23] The score may be reported as a total overall score and a total score per subscale (symptoms; sport, recreation, work, and lifestyle; emotions). The original questionnaire contains a visual analogue scale (VAS), however in this study we have chosen for numeric rating scale (NRS) from 0-10, with 0 indicating no problems at all, and 10 indicating the worst problems. We divided the WOMET in three different subscales to compare the WOMET with the other questionnaires: pain, function and quality of life (QoL). Questions 1,3,4,5,6,7,9,11 and 12 represented the subscale 'function', questions 2,8,13 represented the subscale 'pain' and the remaining questions 10,14,15,16 represented the subscale 'quality of life'.

The WOMET was translated according to a forward-backward translation protocol.[17,27,28] Two independent bilingual translators, one with a medical background and one without a medical background, and a translation agency created a Dutch version of the WOMET. Any discrepancies between the translators were solved by consensus between all translators. Two other independent bilingual translators, who were blinded for the original version of the WOMET, then translated the Dutch version back to English. Next to that, the forward-backward translated WOMET was compared with the original WOMET, to see if any changes occurred during the translation process. The Dutch version of the WOMET was presented to a focus group, consisting of seven patients with meniscal pathology and one independent orthopaedic surgeon, for feedback on the clarity, content and relevance of the questions. The feedback was used to improve the Dutch version of the WOMET and the final version was composed (see attachment). This final version was pre-tested on 25 patients with isolated meniscal injury to check interpretation, cultural relevance of translation and ease of comprehension.

KOOS

The KOOS is a Swedish questionnaire developed by Roos et al.[33] The KOOS is developed with the purpose of evaluating short-term and long-term symptoms and function in subjects with knee injury and osteoarthritis. The questionnaire consists of 42 questions divided into five subdomains: symptoms (7), pain (9), Activities of Daily Living (ADL) (17), function in Sport and Recreation (S&R) (5) and Quality of Life (QoL) (4). All answers are multiple-choice with a 5-Likert scale from 0 to 4. The score is reported as a total score per domain. The KOOS was translated and validated for Dutch patients with osteoarthritis.[12]

IKDC Subjective Knee Form

The IKDC Subjective Knee Form (IKDC-knee) is developed by Irrgang et al.[21] The purpose of this questionnaire is to evaluate the symptoms and limitations caused by knee injuries during daily activities and sports. We divided the 18 questions into two subscales: pain (2) and function (16). Therefore, the score was calculated as a total overall score and a total score per subscale. The total overall score was calculated with the following formula: IKDC-knee total score = ((total rough score – 18) / 87) * 100. The total function score was calculated with the following formula: IKDC-knee total function score = ((total rough function score – 16) / 67) * 100

The total pain score was calculated with the following formula: IKDC-knee total pain score = ((total rough pain score – 2) / 20) * 100. The Dutch version of the IKDC Subjective Knee Form is validated in patients with a variety of knee-related problems.[18]

IKDC Current Health Assessment Form

The International Knee Documentation Committee (IKDC) Current Health Assessment Form (IKDC-health) is the Short-Form 36 (SF-36) and contains 36 questions. It measures health on eight multi-item dimensions: physical function, social function, physical problems, emotional problems, mental health, vitality, pain, general health perception and health change. In this study, the total overall score was used and was calculated with the following formula: IKDC-health = ((total rough score – 35) / 110) * 100. The total score was defined as a QoL score. The percentage of normal score was used, with 0% represents the worst possible score and 100% represents the best possible score. The SF-36 has shown to be reliable and valid in the Dutch general population.[1]

For all total scores the percentage of normal score was used, with 0% represents the worst possible score and 100% represents the best possible score. Missing values were calculated according to the scoring instructions of the questionnaire.

Anchor questions

In this study two different anchor questions were asked. The first anchor question was asked to find out, to what extent the patient could remember their answers on the previous questionnaires. The patients filled in a self-reported 3-Likert scale containing the following answers: I can remember every answer, I can partly remember every answer, I cannot remember any answer. The second anchor question was used to find out if the patient's complaints had been improved or worsened since completing the first questionnaires. We used a self-reported 7-Likert scale containing the following answers: completely recovered, much improved, slightly improved, unchanged, slightly worse, much worse, and worse than ever.

Validity

A questionnaire is valid if it measures the construct it is supposed to measure. Validity is divided into several domains: construct validity, content validity and criterion validity.[27,28] Because the Dutch version of the WOMET is the first meniscal pathology-specific health-related quality-of-life instrument, there is no golden standard for the criterion validity. Therefore, for the validation of the Dutch version of the WOMET only the construct and content validity were determined.

Construct validity

Construct validity refers to the degree to which the scores of a health related questionnaire are consistent with hypotheses based on the assumption that the questionnaire validly measures the construct to be measured.[27,28] The following measures were used to set up the hypotheses: Numeric Rating Scale (NRS) for pain, IKDC-knee subscale pain and function, KOOS subscales symptoms, pain, ADL, S&R and QoL and IKDC-health.

Correlation was classified in: very high correlation (0.90 to 1.00), high correlation (0.70 to 0.90), moderate correlation (0.50 to 0.70), low correlation (0.30 to 0.50) and negligible correlation (0.00 to 0.30).[20]

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Nine hypotheses were drawn up. WOMET subscale pain has at least a moderate positive correlation with KOOS and IKDC-knee pain subscales and at least a moderate negative correlation with the NRS for pain. WOMET subscale function has at least a moderate positive correlation with KOOS subscales symptoms, ADL and S&R, and with IKDC-knee subscale function. WOMET subscale QoL has at least a moderate positive correlation with KOOS subscale QoL and at least a low positive correlation with the IKDC-health. The IKDC-knee was specifically designed to assess overall knee problems and the KOOS to measure post traumatic osteoarthritis. Therefore, we predicted that the correlation between the WOMET and the IKDC-knee would be slightly stronger (r = 0.7) compared to the correlation between the WOMET and the KOOS (r = 0.5). Next to that, the IKDC-health was used to measure the overall conditions of the patient. That is why, we predicted a weaker (r = 0.4) correlation between the WOMET and the IKDC-health.

Content validity

Content validity examines the degree to which the content of a health related questionnaire is an adequate reflection of the construct to be measured.[27,28] For validation of the Dutch version of the WOMET, the floor and ceiling effects were calculated to determine the validity of its content. The floor and ceiling effect give insight of the variance in scores, that will not be measured anymore above or below a certain level. If many patients have the minimal or maximal score the question might be less relevant and patients cannot improve or deteriorate over time. Floor (minimal score) and ceiling (maximal score) effects at baseline were evaluated, because they could influence the content validity and responsiveness.[40] The floor and ceiling effects at baseline (T0 and T1 together) were determined for the overall WOMET score, for the three subscales of the WOMET and for the sixteen questions separately. The floor and ceiling effect was assessed by calculating the percentage of patients with a minimum or maximum score and was consideredacceptable if less than 30% of the patients had a minimum or maximum score.

Reliability

A questionnaire is reliable when a patient gets the same score on repeated admissions of the measurement. For reliability of the Dutch WOMET test-retest reliability and measurement error was calculated.

Internal Consistency

Internal consistency was determined in 86 patients for the overall WOMET score and for the three domains. Good internal consistency exists when Cronbach's alpha is >0.7.[41]

Test-retest reliability

The test-retest reliability, is the proportion of the total variance in the measurements which is due to 'true' differences between patients over time.[27,28] To asses test-retest reliability, first, patients with no significant change in QoL scores between T0 and T1 were selected. This was tested with the comparison of the KOOS subscale QoL and the IKDC-health. Second, the Intraclass Correlation Coefficient (ICC) was used to determine test-retest reliability in the selected patients. The 95% limits of agreement for the differences for the overall WOMET were determined as well.

Measurement error

Measurement error is the systematic and random error of a patient's score that is not attributed to true changes in the construct to be measured.[27,28] The measurement error was expressed by the Standard Error of the Measurement (SEM).[27] The precision of the WOMET was expressed in Standard Error of Measurement (SEM), which was be calculated by repeated measures in one participant: $SEM = SD_{baseline} * \sqrt{(1 - \text{Cronbach } \alpha)}$.[25,42] After calculating the SEM, it was used to determine the SDC: $SDC = 1.96 \times \sqrt{2} \times SEM$. For our study, we use the standard deviation (SD) of the WOMET score at T0 and the Cronbach's alpha. The smallest detectable change (SDC) represents the within-person change due to real change in one individual and without the measurement error.[3,13] A low SDC reflects to no real change and represents a high reliability.

Responsiveness

The responsiveness is the ability of a questionnaire to detect changes over time in the construct to be measured.[27,28] Because of lack of a gold standard, the second best option was to compare changes on the WOMET with changes on other questionnaires or subscales that measure slightly different constructs.[28] This was assessed by testing eight predefined hypotheses about the expected direction and magnitude of the correlation coefficients between the change scores of the questionnaires. To evaluate the responsiveness the changes on the WOMET scores (T0 versus T2) and subscales were compared with the other subscales. The following eight hypothesis, similar to the hypotheses for the construct validity, were drawn up. Changes on the WOMET subscale pain has at least a moderate positive correlation with changes on the KOOS subscale pain and at least a high positive correlation with changes on the IKDC-knee subscale pain . Changes on the WOMET subscale function has at least a moderate positive correlation with changes on the KOOS subscales symptoms, ADL and S&R, and at least a high positive correlation with changes on the IKDC-knee subscale function. Changes on the WOMET subscale QoL has at least a moderate positive with changes on the KOOS subscale QoL and at least a moderate positive correlation with changes on the IKDC-health. We considered the responsiveness of the WOMET to be good if at least 75% of the hypotheses were confirmed.[40]

Interpretability

Interpretability is the degree to which one can assign qualitative meaning to an instrument's quantitative scores or change in scores.[28] According to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines it is important to determine the minimal important change (MIC).[28] The MIC is defined as the smallest measured change score that patients perceive to be important. An instrument is useful if the SDC is smaller than the MIC.[15] The change scores on the questionnaires were calculated by subtracting each patient's T2 score from the T0 (baseline) score, and were then used to determine MIC using an anchor-based mean change score technique.[9] The anchor scores were used to categorize patients into seven subgroups, varying from completely recovered to worse than ever. Change scores were calculated in each of the seven subgroups. The MIC was defined as the mean change score in the subcategory of patients who were "slightly improved" according to the anchor scores.[14]

Statistical Analysis

All statistical analysis were performed with the use of SPSS (version 22.0). The questionnaire scores at T0, T1 and T2 were checked for normality with the one-sample Kolmogorov-Smirnov test. The hypotheses of the construct validity were tested at T0, T1 and T2 with the Pearson's correlation coefficient. The paired sample t-test (for normal distribution) or the Wilcoxon signed-rank test (for ordinal distribution) was used for the comparison of the KOOS subscale QoL and the IKDC-health between T0 and T1. After that, the test-retest reliability was calculated with the ICC using a two way random model. The Pearson's correlation coefficient was used to make a comparison between the change scores on the

WOMET subscale and the KOOS subscale, the IKDC-health and the IKDC-knee subscale. All reported p values were two-tailed with an α of 0.05 indicating significance.

RESULTS

Forward and backward translation of the WOMET revealed no problems or language difficulties. A total of 296 consecutive patients with meniscal pathology were eligible for this study. After first exclusion, 152 patients started to fill in questionnaires. A total of 86 patients completed all questionnaires at the three time moments. Reasons for exclusion are shown in Figure 1. The demographic data of all 86 patients included in the study is noted in Table 1. Median time (interquartile range (IQR)) of the first time interval (T0-T1) and second time interval (T0-T2) was 16 (13 – 22) days and 105 (91 - 209) days, respectively. The mean scores of the questionnaires at T0, T1 and T2 are noted in Table 2. Just one of the patients (1.2%) could remember every answer to the previous questionnaires on T1, while two patients (2.3%) did on T2. Most of the patients partly remembered their answers to previous questionnaires on T1 and T2, 79.8% and 58.1%, respectively. The rest of the patients could not remember any of their previous given answers.

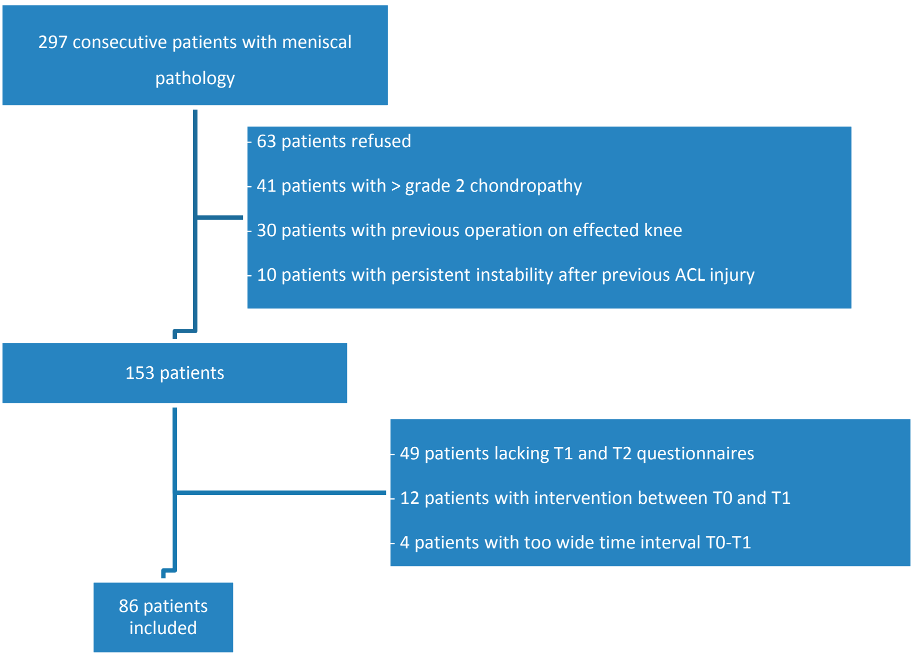

Figure 1. Flow chart of inclusion.

Table 2. Mean and SD of questionnaires at T0, T1, T2

WOMET	T0	T1	ICC	T2
Total score	40.8 (15.8)	43.6 (17.7)	0.78	63.0 (23.8)
Function	46.4 (17.4)	48.6 (18.5)	0.73	67.7 (22.5)
Pain	32.1 (18.5)	34.9 (19.6)	0.77	59.8 (27. 6)
QoL	34.8 (19.1)	38.1 (22.5)	0.75	55.3 (29.3)
KOOS	T0	T1		T2
Symptoms	60.5 (16.6)	62.0 (19.1)	0.72	75.0 (17.3)
Pain	48.9 (19.0)	52.9 (20.1)	0.82	71.8 (21.1)
ADL	57.1 (20.3)	60.1 (21.4)	0.81	76.8 (22.2)
S&R	23.4 (20.6)	28.5 (22.2)	0.73	48.8 (30.3)
QoL	35.7 (15.9)	37.5 (16.3)	0.64	54.3 (23.6)
IKDC-health	T0	T1		T2
Total score	62.6 (14.9)	63.1 (15.4)	0.85	70.3 (16.8)
IKDC-knee	T0	T1		T2
Total score	42.6 (13.8)	45.8 (15.3)	0.75	61.5 (19.5)
Function	46.0 (14.1)	44.8 (14.0)	0.71	61.7 (18. 6)
Pain	31.5 (18.8)	38.1 (21.2)	0.78	60.3 (26.9)

ICC = intraclass correlation coefficient. QoL = quality of life, ADL = activity in daily living, S&R = sports and recreation.

Validity

Construct validity

The WOMET subscales shows good correlation with the NRS pain score, IKDC Subjective Knee Form subscale pain and function, all the KOOS subscales, and with the IKDC Current Health Assessment (Table 3). As predicted, the correlation between the WOMET subscales and the IKDC Subjective Knee Form subscales were generally stronger compared to the correlation between the WOMET subscales and the KOOS subscales. Next to that, the weakest correlation was between the WOMET and the IKDC Current Health Assessment. All hypotheses were confirmed.

Content validity

For the total WOMET score there was no floor and ceiling effect. WOMET subscale pain, function and quality of life showed acceptable floor and ceiling effect as well. Next to that, every question of the WOMET was analysed for floor and ceiling effects. An acceptable but high floor effect was found for question four, about ‘numbness’, and for question seven, about ‘swelling’, 25.6% and 27.9% respectively.

Table 3. Content validity. Correlations between WOMET subscales (pain, function and quality of life) and IKDC-knee, IKDC-health and KOOS subscales at T0, T1 and T2.

	WOMET Pain		
	T0	T1	T2
NRS			
Pain	-0.61*	-0.72*	-0.83*
IKDC knee			
Pain	0.66*	0.78*	0.86*
KOOS			
Pain	0.52*	0.73*	0.81*
	WOMET Function		
IKDC-knee	T0	T1	T2
Function	0.68*	0.78*	0.77*
KOOS	T0	T1	T2
Symptoms	0.69*	0.78*	0.80*
ADL	0.62*	0.75*	0.83*
S&R	0.59*	0.61*	0.71*
	WOMET QoL		
KOOS	T0	T1	T2
QoL	0.64*	0.70*	0.79*
IKDC-health	T0	T1	T2
	0.50*	0.51*	0.66*

ADL = activity in daily living, S&R = sports and recreation, QoL = quality of life.
*: significant (<0.05)

Reliability

Internal consistency

Internal consistency of the overall WOMET score was good (Cronbach's alpha = 0.88).

Test-retest reliability

There was no significant difference between the KOOS subscale QoL and IKDC Current Health Assessment at T0 and T1. Therefore, all patients were used to measure the test-retest reliability. The test-retest reliability of the overall WOMET score and the three domains were all found to be good (Table 2). The 95% limits of agreement for the differences for the overall WOMET score are shown in Figure 2.

Measurement error

SEM and SDC for the overall WOMET score was 5.5 and 15.4 respectively.

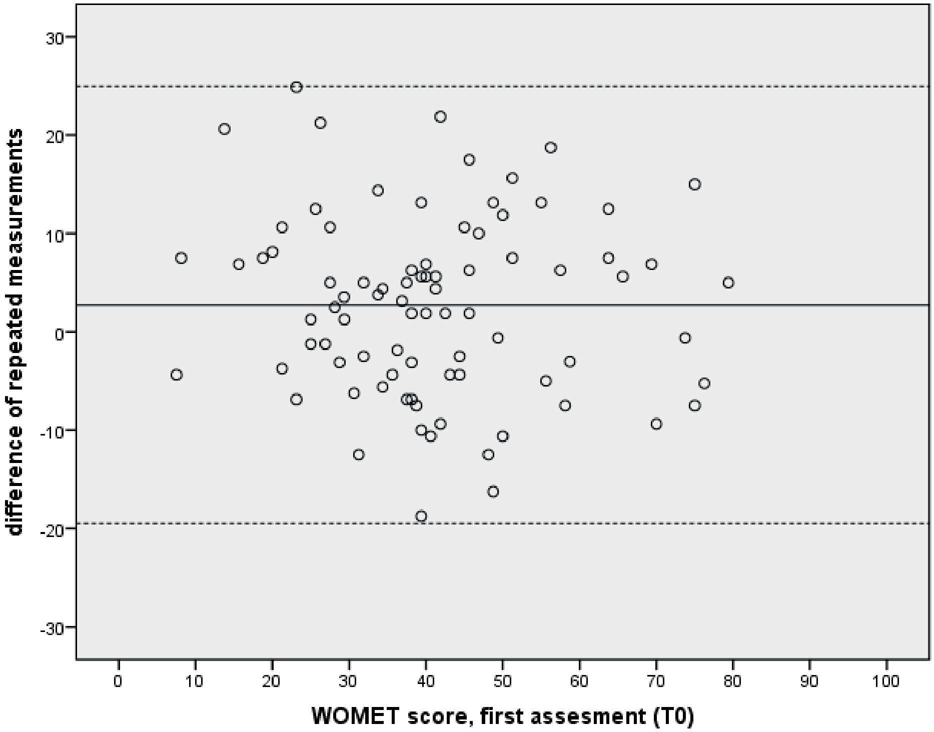

Figure 2. Scatter plot illustrating test-retest reliability, difference in overall WOMET score for each patient (n=85) between T0 and T1.

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Responsiveness

The results of the responsiveness analyses is shown in Table 4. The changes on the WOMET subscales showed good correlation with the IKDC Subjective Knee Form subscales pain and function, all KOOS subscales, and with the IKDC Current Health Assessment (Table 4). Seven out of eight hypotheses (88%) were confirmed.

Interpretability

The MIC for the overall WOMET score was 14.7 (Table 5).

DISCUSSION

This study showed that the Dutch version of the WOMET has good construct validity, content validity, test-retest reliability and responsiveness for measuring meniscal pathology-specific health-related quality of life in patients with traumatic or degenerative meniscal tears treated conservatively or operatively.

Table 4. Responsiveness. Mean changes in subscales of WOMET, IKDC-knee, KOOS and IKDC-health between T0 and T2. Correlation between changes on the WOMET subscales and the subscales of KOOS, IKDC-knee and the IKDC-health.

	Mean change (SD)	Correlation (Predefined correlation)
WOMET pain	27.7 (28.1)	
IKDC-knee pain*	28.8 (25.0)	0.78 (0.7)
KOOS Pain*	22.8 (19.4)	0.62 (0.5)
WOMET function	21.3 (22.5)	
IKDC-knee function#	15.6 (17.4)	0.66 (0.7)
KOOS Symptoms#	14.6 (17.3)	0.65 (0.5)
KOOS ADL#	19.7 (19.6)	0.66 (0.5)
KOOS S&R#	25.6 (26.3)	0.64 (0.5)
WOMET QoL	20.5 (25.7)	
KOOS QoL$	18.6 (23.7)	0.80 (0.5)
IKDC-health$	7.7 (11.9)	0.51 (0.4)
Hypotheses confirmed		7/8 (88%)

ADL = activity in daily living, S&R = sports and recreation, QoL = quality of life.
* = correlation with WOMET pain, # = correlation with WOMET function, $ =correlation with WOMET QoL.

Table 5. Interpretability. Mean change score for overall WOMET according to the anchor question on improvement. The 'slightly improved' group was used to determine the minimal important change.

	n	Δ overall WOMET (SD)
Completely improved	11	46.5 (17.3)
Much improved	32	33.7 (14.9)
Slightly improved	**22**	**14.7 (15.2)**
Unchanged	10	4.9 (12.8)
Slightly worse	8	-0.5 (14.3)
Much worse	2	-32.8 (19.0)
Worse than ever	0	N/A

Δ = mean change, SD = standard deviation. N/A = not applicable.

Sihvonen et al.[36] determined criterion validity using the Lysholm knee score. In our opinion Lysholm knee score is not suitable to use as a golden standard. Lysholm knee score was validated for patients with meniscal injury, but determination of quality of life deficits was not assessed.[5] So, in absence of a gold standard for evaluation meniscal pathology-specific health-related quality of life, construct validity was determined. Similar to the findings of Kirkley et al.[23] and Sihvonen et al.[36] we found good construct validity. All WOMET subscales showed good correlation with the subscales of the other questionnaires leading to confirmation of all our hypotheses. As we predicted the weakest correlation was found with IKDC-health, this is comparable to other WOMET validation studies.[6,36]

This confirms that the IKDC-Health measures additional aspects of the physical health and provides more comprehensive, but less specific, information about the patients' overall health compared to condition-specific questionnaires.[22]

The overall WOMET score, the three subscales of the WOMET score and all the sixteen questions separately had acceptable floor and ceiling effects (<30%). However, for the questions about 'numbness' and 'swelling' quite high floor effects were found. This was similar to the findings published by Sihvonen et al.[36] and Celik et al.[6] We agree with Celik et al, that 'numbness' is one of the rare symptoms of meniscal pathology, which can be an explanation for the high floor effect of this item. Compared to 'numbness', 'swelling' is a less rare symptom, but more often found in patients with isolated meniscal tears in combination with osteoarthritis.[36] Our study population consisted of patients with isolated meniscal tears without radiological signs of osteoarthritis, which may be a reason for the high floor effect of the question about 'swelling'. Taken together, these findings suggests that questions about 'numbness' and 'swelling' are less relevant for evaluation of patients with isolated, traumatic or degenerative meniscal tears without osteoarthritis.

In determining reliability, we found a high ICC (0.78), which equals the original study[23] and was comparable to the Turkish and Finnish validation studies.[6,36] In addition we determined measurement error in terms of SEM and SDC. This SDC means that if you want to determine a treatment effect, you need to find a difference of at least 15.4 points in an individual patient to make sure that the difference is not due to random error. We also found acceptable internal consistency (Cronbach's alfa = 0.88) for the overall WOMET score, which was similar to previous studies (α= 0.92 for the original WOMET, α=0.91 for the Finnish WOMET and α= 0.89 for the Turkish WOMET).[6,23,36] This means that all items of the WOMET reflect the same phenomenon.

As mentioned earlier, because of lack of a gold standard, the second best option to define responsiveness was to compare changes on the WOMET with changes on other questionnaires or subscales that measure slightly different constructs.[28] Our good responsiveness could not be compared with previous studies, in which responsiveness was only expressed by a calculated standardized response mean.[23,26]

To the best of our knowledge, there is no previous data on MIC for the WOMET score. We are the first who determined the MIC of the WOMET, which is a strength of this study. A score increased with 14.7 points on the WOMET score was considered clinically relevant. An instrument is more useful if the SDC is smaller than the MIC.[15] In our study, the SDC that was slightly larger than the MIC. This means that if an individual patient has a change score as large as the MIC, we cannot be 95% sure that this change is not due to measurement error. However, as the differences between the SDC and the MIC were rather small, we think that the WOMET is suitable for use in clinical practice and research.

Another strength of this study was that the participants were representative of patients with meniscal injury. Our study population consisted of young and old patients with different meniscal injury and meniscal treatment; acute and chronic meniscal injury, traumatic and degenerative meniscal injury, treated operatively (partial meniscectomy and meniscal repair) or conservatively.

Compared to the original WOMET instead of VAS, NRS was used on recommendation of the focus group patients. For our patient population the NRS appeared to be easier to understand and answer, shorter to complete and preferable above VAS, also reported previously.[2] Another distinction made compared to the original WOMET was the distribution of questions in the different domains or subscales. We divided the questions in the subscales: pain, function and quality of life, according to the International Classification of Functioning, Disability and Health (ICF).[44]

There are some limitations of this study. Firstly, time-interval between T0 and T1 was relatively long. Test-retest time-interval of two weeks is considered appropriate for the evaluation of PROMs instruments.[38] Secondly, we had to exclude 67 patients because of a too wide time interval, incomplete amount of questionnaires or an intervention which was started in the first time interval. A more strict control on returning questionnaires would probably had increased patient inclusion, at least to have more data to analyse test-retest reliability. Thirdly, defining hypotheses remains arbitrary and there is no consensus about the number of hypotheses which should be confirmed.

CONCLUSION

The Dutch version of the WOMET seems valid and reliable. It can be used as a disease specific tool to evaluate health related quality of life of Dutch patients with meniscal pathology.

ACKNOWLEDGEMENT

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Appendix: Nederlandse WOMET vragenlijst (Dutch version of the WOMET questionnaire)

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APPENDIX

WOMET vragenlijst

Instructie:

De vragenlijst bestaat uit 16 vragen. De vragen gaan over de gevolgen van meniscusproblemen en hebben betrekking op fysieke problemen, emotie en het algemeen dagelijks functioneren. U kunt bij iedere vraag uw antwoord weergeven op een schaal van 0 tot 10. Hierbij geeft u aan geen last te hebben bij 0, en heel erg veel last te hebben bij 10.

1. Hoeveel last heeft u van het gevoel dat u door uw knie zakt of dat uw knie instabiel is?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

2. Hoeveel last heeft u van pijn of irritatie in uw knie na activiteit?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

3. Hoeveel last heeft u van het verlies aan beweeglijkheid van uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

4. Hoeveel last heeft u van een verminderd gevoel in of rondom uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

5. Hoeveel last heeft u van stijfheid van uw knie als u ‘s morgens opstaat of als u opstaat nadat u lang gezeten heeft?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

6. Hoeveel last heeft u van zwakte in uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

7. Hoeveel last heeft u van zwelling van uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

8. Hoeveel last heeft u van pijnscheuten in uw knie nadat u deze heeft belast?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

9. Hoeveel last heeft u van kraken, knakken of het gevoel iets te voelen wegschieten in uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal geen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg veel

10. Hoe bang bent u uw knie weer te blesseren als u opnieuw gaat sporten of werken?

	0	1	2	3	4	5	6	7	8	9	10	
totaal niet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg

11. Hoeveel wordt u beperkt in uw huidige activiteiten ten opzichte van de activiteiten van voor uw blessure?

	0	1	2	3	4	5	6	7	8	9	10	
totaal niet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg

12. In hoeverre kunt u door uw knie minder goed uw sport beoefenen en/of uw werk doen? (als ze allebei slechter gaan, scoor de slechtste van de twee)

	0	1	2	3	4	5	6	7	8	9	10	
totaal niet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg

13. Hoeveel last heeft u met hurken?

	0	1	2	3	4	5	6	7	8	9	10	
totaal niet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg

14. Hoe vaak denkt u aan uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal niet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	altijd

15. Hoe bezorgd bent u over hoe het verder zal gaan met uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal niet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg

16. In hoeverre voelt u zich gefrustreerd of ontmoedigd vanwege uw knie?

	0	1	2	3	4	5	6	7	8	9	10	
totaal niet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	heel erg

9

Summary and general discussion

SUMMARY AND GENERAL DISCUSSION

Meniscal tears were amongst the most frequently encountered injuries of the musculoskeletal system which required surgery in the past.[35] Nowadays, meniscal lesions are less operated, since we know that at long term, patients who had knee arthroscopy and meniscal surgery versus those who had conservative management strategies have comparable results with respect to pain and function.[6] Even more, physiotherapy as an intervention strategy is a good alternative to surgery for patients with nonobstructive meniscal tears.[48]

For that matter, it is essential that any treatment decision is weighted more and more carefully. High value care as well as value added care to the patient, based on evidence based decision of the clinician and well-informed decision by the patient, is a central theme in health care. Should we perform a test (e.g. an MRI) or procedure (e.g. an arthroscopic meniscectomy) or should we refrain from these? All reasonable questions. Answering these questions, together with a patient, hopefully leads to better care, at least in understanding better favorable, but also worse outcome. However, leaving the decision on diagnostic tests or interventions (both surgical as well as conservative) to the patient or to the general practitioner will also create an overuse of diagnostics like MRI's, more operations, more complications and more health costs without an improvement in health outcomes.[51]

Nevertheless, meniscal tears are still often treated by arthroscopic meniscectomy; i.e., partial removal of the meniscus, which is one of most common surgical procedures, with an estimated number of 27500 procedures per year in the Netherlands.[37] With advancing age, an increase in the number of meniscectomies is observed, mainly on the medial side.[32] Although arthroscopic partial meniscectomy generally reduces pain and restores knee function immediately post-surgery, the patients are more prone to develop osteoarthritis in the long term.[13,18,20] From a biomechanical perspective this makes sense, since both menisci have important biomechanical functions (loadbearing, shock absorption, joint stability, joint lubrication, and proprioception) within the knee joint, and that these functions are to be maintained as much as possible, because the risk of osteoarthritis after meniscectomy correlates with the amount of meniscal tissue resected.[3,29] For that reason preservation of meniscal tissue, even injured tissue is mainstay since the last decades, whenever possible. The latter holds even more for the younger patient, in whom the risk of failure of a meniscal repair outweighs advantages of an early predictable outcome, against long term degenerative changes with worse outcome after partial meniscectomy. However, one must realize that the meniscus tear itself is possibly the greatest causal factor in the onset of osteoarthritis.[12] Another causal factor is that some patient phenotypes (i.e. cartilage genotype might be more prone to injury than other cartilage) are more associated with OA development.[21] The great variability in knee phenotyping (coronal tibial and femoral alignment), seen in both osteoarthritic[19] and non-osteoarthritic[33] knees, as well as pre-existing cartilage damage and physical activity are other contributing risk factors to the development of knee OA.[9]

The purpose of this thesis was to provide an overview of meniscal function, effects of meniscal deficiency on patients quality of life as well as at the knee as such and (historical) treatment options for meniscal lesions. In **Chapter 2** the functions of the menisci (load bearing, shock absorption, joint stability, joint lubrication, and proprioception) and the effect of the lack of well-functioning menisci are explained. Insights into the treatment of meniscal tears over time, including meniscal allograft transplantation, are discussed. For that matter, we evaluated the clinical results of patients with an arthroscopic meniscal repair, and determined the reparability of these tears based on Magnetic Resonance Imaging score. A patient reported outcome (PRO) evaluation instrument was validated for the Dutch population, with meniscal pathology.

In addition the clinical impact (patient reported outcomes (PRO), radiological Dual-energy X-ray absorptiometry (DXA)) of meniscal allograft transplantation was evaluated at long-term follow-up in different cohort of patients with open and arthroscopically assisted meniscal allograft transplantation (MAT).

Meniscal repair

Meniscus repair is recommended for tears occurring at the external third of the meniscus since it is the only completely vascularized region ('red zone') and thus may heal successfully.[5] Historically, arthroscopically based criteria (tear length, distance from tear to meniscosynovial junction, tear location and minimal meniscal damage) were considered important parameters to predict meniscal reparability on Magnetic Resonance imaging (MRI).[27] Unfortunately, these MRI parameters do not predict reparability of longitudinal meniscal tears. Other factors than these MRI criteria such as a surgeon's experience and daily practice and surgical skills are covariates in predicting success of the reparability of an injured meniscus. This was later on, also concluded by others.[15,31] Furthermore, patient's age is an important covariate as well, the younger the patient, the more likely his or hers meniscus will be surgically repaired. Although subjective items as patient's activity and expectation level will influence the surgeon's decision to perform surgery. Concomitant ACL injury, osteochondral lesions, and presence of medial meniscal tear increase the likelihood of meniscal repair.[31]

Chapter 3 describes the results from an observational study to determine intra- and interobserver agreement on meniscal reparability for longitudinal, peripheral meniscal tears based on MRI among both orthopaedic surgeons and musculoskeletal radiologists. We conclude that tear length and rim width are the only two measurements with moderate to good agreement. However, these measurements do not predict reparability of a longitudinal meniscal tear on MRI images. Based on our findings and others', a new scoring system for prediction of the success rate of meniscal repair using MRI is developed and evaluated. This scoring system is based on both clinical (patients age and chronicity of meniscal tear) and radiological (tear zone, tear pattern, grade of chondropathy) characteristics and predicts meniscal reparability good to excellent for medial tears (sensitivity 90.9%, specificity 93.2%) and moderate to good for lateral meniscal repairs (sensitivity 69.2%, specificity 78.8%).[25] However, the validity of using meniscal tear pattern (e.g. flap tears, longitudinal tears) as a predictive factor remains controversial. Next to the these MRI parameters, chronicity of meniscal tear (i.e. how long does the meniscal tear exists?) is a, often very controversial, parameter in the decision making about meniscal reparability.

In **chapter 4** we evaluated the failure rates and clinical outcome of arthroscopic meniscal repair in relation to chronicity of injury. Two hundred and thirty eight meniscal repairs were performed in 234 patients. Anterior cruciate ligament (ACL) was reconstructed in almost all ACL deficient knees. The time interval between moment of injury and moment of meniscal repair was divided into acute (<2 weeks), subacute (>2 weeks - <12 weeks) and chronic (>12 weeks). At a median follow-up of almost 3,5 years 55 medial and 10 lateral meniscal repairs failed (overall failure rate 27%). We have found a significant higher failure rate for medial meniscal repair ($p < 0.05$) and ACL deficient knees without ACL reconstruction. No significant difference was found for any interval between trauma and repair. It was shown that the time interval between trauma and arthroscopic meniscal repair has no influence on the failure rate. Survival of meniscal repair is more dependent on factors like type of meniscal lesion, patient's age and knee stability.[17] A shift in indication for meniscal repair in the last decades is seen, where radial tears[34], horizontal tears[40] and even complex or degenerative tears[14] are sutured. Suturing a meniscal tear which is more central to the red-red zone[7] and suture a meniscal lesion which is in a non-vascularized zone (i.e. salvage suture techniques)[2] will have different outcome and should therefore be evaluated separately. New suture devices were developed.[4] All these factors may contribute to the survival rate of the meniscal repair, sometimes for the better, sometimes for the worse. Basically, it's all about the indication.

Meniscal allograft transplantation

When meniscal repair is not possible, conservative treatment has failed or mechanical problems did not resolve, partial resection of the meniscus is an option, occasionally even (sub)total meniscectomy has to be performed. Before signs of degeneration of the knee occur or progress, patients with a history of (sub)total meniscectomy, can suffer from pain localised to the meniscus-deficient knee compartment (most often medial). In these cases, meniscal allograft transplantation (MAT) is a viable option for these patients. This can result in pain relief and improvement of function at long and short term follow-up.[26,47,52] The basic principle underlying MAT is to restore joint anatomy and to relocate an implant that will serve and perform in a similar fashion as the original one. To avoid or postpone the necessity of total knee replacement, it is crucial to timely treat patients with post-meniscectomy syndrome or in the first stage of development of osteoarthritis.[11] We were one of the first to show the long term success of MAT in still one of the largest cohorts of patients with open MAT with one of the longest average follow-up (≈14 years).

In **Chapter 5**, long-term clinical outcome of meniscal allograft transplantation was evaluated. Sixty-three meniscal allografts were transplanted with an open procedure in 57 patients. Clinical outcome and failure rate of 40 lateral and 23 medial meniscal allografts were evaluated at a mean follow-up of 13.8 years ± 2.8 years. After this long-term follow-up period we found an overall failure rate of 29% (8 medial and 10 lateral allografts failed). A significant improvement in overall mean Lysholm score was seen at long-term follow-up compared to baseline. Long-term and preoperative Lysholm scores were not significantly different in the subgroups; medial allografts, female patients and left treated knees. A significant difference between short- and long-term Lysholm scores was found for all subgroups. Significant differences for KOOS and IKDC scores were only present between male and female patients. No significant differences in Lysholm scores were seen between post-transplanted survivors and post-transplanted non-survivors who received a total knee arthroplasty. We concluded that meniscal allograft transplantation is a beneficial procedure. Good improvements in clinical function and pain relief have previously been shown at short-term follow-up in this population. Despite the deterioration over time in function scores, there is still improvement in level of functioning at long-term follow-up, although not at a high level. Thus, meniscal allograft transplantation is a good option for the treatment of degenerative arthritis of the symptomatic, post-meniscectomized knee. Meniscal allograft transplantation can be used to postpone total knee arthroplasty in young(er) patients.

Besides its proven effect on pain relief and function improvement, ideally, MAT should delay, or better prevent, the development of knee osteoarthritis. Since the first meniscal allograft transplantation (MAT) in 1984,[30] many papers are published in literature regarding different aspects of MAT: indications and contraindications, preoperative graft sizing, methods of graft preservation, surgical techniques, fixation of the allograft, relevance of associated chondral and ligamentous damage, concomitant procedures, histologic evaluation, clinical and radiographic outcomes, and rehabilitation. Despite all the research on indications and contraindications, surgical techniques, histologic evaluation, clinical and radiographic outcomes of MAT, a chondroprotective effect, as shown in sheep,[22] remains still unclear in humans.[38,43] This is due to lack of standardised evaluation methods and lack of high-quality studies. Nonetheless, MAT seems to provide good clinical results at the short and medium term, with improvement in knee function and acceptable complication/failure rates.[38]

In **Chapter 6**, we performed a study on bone mineral density (BMD) changes after MAT to gain more insight in the potential chondroprotective effect of MAT. Twenty-six consecutive patients underwent a MAT. BMD was measured using Dual-energy X-ray Absorptiometry (DXA) scan preoperative and 6 months, 1 and 2 years postoperative. BMD was measured in six regions of interest (ROIs) of tibia and femur (medial, central, lateral) in both treated and healthy contralateral knees.

During 2 years follow-up BMD levels of MAT knees did not significantly change in almost all ROIs. BMD was significant higher in nearly all ROIs in MAT knees at almost all follow-up moments compared to healthy contra-lateral knees. In the healthy contralateral knees BMD slightly, but not statistically, decreased in the first year postoperative, where after BMD normalized to baseline values at 2 years follow-up. BMD levels in all ROIs did not significantly differ between the patients with or without chondropathy at baseline and at 2 years follow-up. Based on our findings we concluded that MAT did not show a significant influence on BMD in the first 2 years postoperative. Longer follow-up is necessary to prove the potential chondroprotective effect of MAT using BMD measurements.

Measuring outcome after surgical treatment is of utmost importance to determine the success of treatment and to improve patient care. Measurement of health-related quality of life scores of patients with meniscal problems and their successive treatment modalities with validated questionnaires is important. The Western Ontario Meniscal Evaluation Tool (WOMET) is the first meniscal pathology-specific health-related quality of life instrument. In **Chapter 8,** we validated the Dutch version of the WOMET. After translation into Dutch it proved to be a valid and reliable patient reported outcome (PRO). Construct validity, content validity, internal consistency, test-retest reliability smallest detectable change (SDC) and minimal important change (MIC) were analysed. With good correlation with all other used questionnaires and confirmation of all hypotheses made, the Dutch WOMET showed good construct validity. Floor and ceiling effects were absent and there was an excellent internal consistency and good test-retest reliability. The Dutch WOMET was found responsive to change. The smallest detectable change and minimal important change determined: 15.4 and 14.7, respectively.

It can be used as a disease specific tool to evaluate health related quality of life of Dutch patients with meniscal pathology. Despite several cross-cultural adaptations, translations and validations for different languages, and the greater impact on health-related quality of life for patients with meniscal tears of the WOMET when compared with, people are reserved in using it.[39] In contrast, the WOMAC and the KOOS and other knee scoring systems (i.e. Lysholm, IKDC) are nonspecific for meniscal pathology. Thus, the WOMET should be used for the evaluation of knee function and quality-of-life impairment of patients with meniscal problems.

Once having goods PROMs, it would be interested to know if PRO is related to a patient's satisfaction and/or expectation. It is know that patients having a total knee arthroplasty (TKA), can show good progression in PRO, but who are not satisfied after their TKA or their expectations were not met. This was never investigated for MAT.

In **Chapter 7** we evaluated PRO, survival of the meniscal allograft and their association with prior interventions to the knee in 109 consecutive patients who underwent an arthroscopic MAT between 1999 and 2017 in a single-surgeon series.

Overall mean allograft survival was 16.1 year (95%CI: 14.8 to 17.5 year). Patient age at baseline was associated with MAT survival: hazard ratio 1.19 per increasing person year (95%CI: 1.04 to 1.36, p=0.009). At 4.5 years (IQR, 2 – 9) of follow-up all KOOS score were still improved. Age below 35 years, simultaneous anterior cruciate ligament reconstruction and number of knee surgeries before MAT were associated with lower KOOS scores. Expectations of MAT and overall satisfaction after MAT were not associated with preoperative patient characteristics nor with the number nor kind of preoperative interventions. We conclude that meniscal allograft transplantation has a good overall survival with a clinical relevant improvement. Both meniscal allograft survival and patient reported outcome were lower in patients younger than 35 years, and both were associated with preoperative characteristics or procedural characteristics. Interestingly, all patients reported improved postoperative satisfaction and met expectation after MAT. The latter was, independent of the preoperative history of knee interventions.

FUTURE PERSPECTIVES

Meniscal Repair

Magnetic Resonance Imaging

Advanced imaging techniques such as delayed gadolinium enhanced MRI of cartilage (dGEMRIC MRI) allow visualization of the molecular structure of the articular cartilage. dGEMRIC values correlate well with the histological evidence of cartilage degeneration.[41] When this technique is applied to meniscal tissue one has called an application designated gadolinium enhanced MRI of meniscus (dGEMRIM). In healthy subjects it is shown that the contrast medium distributes also into the meniscus after intravenous injection. Using dGEMRIM can differentiate between pathological and healthy meniscal tissue.[42] Combination dGEMRIM and dGEMRIC could be used to examine meniscal reparability, meniscal allograft ingrowth and cartilage conditions after meniscal surgery in future studies. The most favorable clinical indication for knee examinations at 7 T currently appears to be cartilage imaging. Sodium MRI at 7 T has many potential clinical applications, however no studies on meniscal injuries are performed yet and studies on cartilage imaging need to be further investigated.[10]

Fluorescence guided meniscal surgery

Near-infrared (NIR) fluorescence imaging has already been successful for various indications.[49] Fluorescence-guided imaging of the vascular supply to the meniscus could be a next topic. Some aspects where NIR imaging in meniscal surgery can be used for are the determination of meniscal tear reparability or evaluation of meniscal allograft ingrowth. Future studies using new imaging methodologies could guide us if meniscal repair or meniscal allograft transplantation would be an advance in vivo.

These new imaging techniques should be added to a clinical algorithm, to determine which patient benefits from an arthroscopic meniscal repair or arthroscopic partial meniscectomy. A more complex algorithm in future may use machine learning techniques, using an iterative data input process for outcome using confounders like knee phenotype, patient cartilage genotype, pre-existing cartilage damage and physical activity for each treated patient in a regional cohort. Thus the most optimal choice of treatment for a specific patient might be developed.

Meniscal Allograft Transplantation

Despite the increase in the amount of published studies about meniscal allograft transplantation, the chondroprotective effect of meniscal allograft transplantation is still not clearly demonstrated. An in-vitro study by Kim et al.[24] demonstrated that joint contact pressures in meniscectomized knees were significantly higher than pressure after MAT. Similarly, McDermott et al. showed that joint contact pressures after MAT are close to the ones in the intact knee, after being significantly risen in knees with medial meniscectomy,[28] which might provide some indirect evidence. However, several studies show the increasing risk of meniscectomy on the development or progression of osteoarthritis of the knee.[3,29]

Significant decreases in cartilage degeneration after MAT compared to meniscectomy and sham procedures was shown in sheep,[22,46] but not in humans.

Recently, preliminary in-vivo kinematic evaluation after MAT was published.[54] However, old techniques with plain X-rays were used in a study population of only two patients. Combined magnetic resonance (MR) and dual orthogonal fluoroscopic imaging techniques are developed for in vivo functional activity animation and already often used to analyze ACL deficient knees, and the effect of ACLR and lateral extra-articular reconstruction (LER).[23,50] This in vivo simulation techniques could give more insight on the biomechanical effect of meniscal allograft transplantation and might add evidence to its chondroprotective effect. Same technique can be used to observe biomechanical changes after meniscal repair, for which already demonstrated by cadaveric studies restoration of knee biomechanics occurs after meniscal lesion repair.[1,45]

Meniscal allograft alternatives

Due to the limited supply of suitable allografts and its further restriction by the size matching criteria formulated to optimize the chance of successful allograft functioning and survival, research on alternatives (meniscus regeneration strategies) should continue. The physicochemical requirements of an ideal scaffolds are easy processability to desired shapes, adequate mechanical strength, porous (large surface to volume ratio), biodegradable, and biocompatible, so that it can provide an adequate environment for cellular proliferation and extracellular matrix synthesis, all this is a big challenge in an approach to mimic a native meniscus. Total meniscus implants and scaffolds (natural, synthetic, or composite polymers) are developed,[36] however only short term data is presented or only animal studies were performed.[53] Different meniscus regeneration strategies are developed. Advanced techniques like bioreactors, formation of scaffold-free and composite scaffold constructs, and functionalization using growth factors ensure the possibility to reconstruct an anatomically correct and functional meniscus like tissue from cartilage cells.[36] The first 3D printed scaffolds reinforced with carbon nanofibers for human meniscal tissue engineering are produced. These nanocomposite scaffolds seem to be beneficial in terms of enhanced cellular activity over only polymer scaffolds.[16] However, the success in pre-clinical trials is limited so far, considering the partial or total meniscus regeneration, that future studies are still needed to develop the ideal meniscal replacement, till then, meniscal allograft transplantation seems the best option.

The development of osteoarthritis is multifactorial. Several susceptibility genes, involved in enchondral ossification, leading to loss and mineralization of articular cartilage, are considered to contribute in the underlying mechanisms of this disease.[8,44] Once reactivated or upregulated, these genes may contribute to the process of AO. Upregulation of these genes is associated with AO development and can be measured. Considering hypothetically, downregulation of these genes might be seen in patients having a potential chondroprotective operation like a meniscal repair compared to patients having a meniscectomy, or in patients before and after a meniscal allograft transplantation.

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Summary in Dutch
(Nederlandse samenvatting)

NEDERLANDSE SAMENVATTING

Een scheur in de meniscus behoorde tot voor kort tot een van de meest operatief behandelde letsels van het steun- en bewegingsapparaat. Sinds we weten dat patiënten die een kijkoperatie van de knie ondergaan in verband met een gescheurde meniscus in vergelijking met de patiënten die conservatief worden behandeld, geen belangrijke voordelen hebben op de lange termijn, wordt er tegenwoordig steeds minder geopereerd aan een meniscusscheur. Daarnaast is fysiotherapie een goed alternatief voor operatieve behandeling als behandeling voor patiënten met een meniscusscheur die geen slotklachten geeft. Desondanks, worden meniscusscheuren nog vaak behandeld door middel van een artroscopische partiële meniscectomie. Een dergelijke (partiële) meniscectomie leidt over het algemeen op korte termijn tot pijnverlichting en functieherstel, echter op de lange termijn is er een grotere kans op het ontwikkelen van artrose van de knie door het verlies van functie van de meniscus en daarmee het verlies aan gewrichtskraakbeen. Hierbij moet men zich realiseren dat de meniscusscheur zelf een belangrijke risicofactor is voor de ontwikkeling van artrose van de knie.

Het doel van dit proefschrift was om een overzicht te geven van de meniscusfuncties, effecten van meniscus deficiëntie op de kwaliteit van leven van patiënten en op de knie als zodanig en van de (historische) behandelopties voor meniscusscheuren. In **Hoofdstuk 2** worden de functies van de menisci en het effect van het ontbreken van goed functionerende menisci beschreven. Er wordt een overzicht gegeven van de behandelingen over de tijd, inclusief meniscustransplantatie.

Wanneer een meniscus is gescheurd, is de aanbeveling deze te repareren wanneer mogelijk, om zo de functie van de meniscus te herstellen. Vanuit historisch perspectief werden op artroscopie gebaseerde eigenschappen van een scheur (lengte van de scheur, afstand van de scheur tot aan het kapsel, locatie van de scheur en status van het meniscus weefsel) belangrijk geacht om de hechtbaarheid van een meniscus op MRI beelden te kunnen voorspellen. In **Hoofdstuk 3** worden de resultaten beschreven van een observationele studie naar de intra- en interbeoordelaarsbetrouwbaarheid van de hechtbaarheid van longitudinale, perifere meniscusscheuren op MRI bij zowel orthopedisch chirurgen als musculoskeletale radiologen. De uitkomsten lieten zien dat de lengte van de meniscusscheur en breedte van de perifere rim de enige twee metingen zijn met een matige tot goede overeenstemming. Deze metingen voorspellen echter niet de hechtbaarheid van een longitudinale meniscusscheur op MRI. Gebaseerd op deze bevindingen en op de bevindingen van anderen is een nieuw score systeem ontwikkeld om de hechtbaarheid van een meniscusscheur te kunnen beoordelen. Hierbij worden klinische en radiologische karakteristieken gebruikt, echter het gebruik van het type meniscusscheur als voorspellende parameter blijft hierin controversieel. Een ander vaak controversiële parameter met betrekking tot het hechten van meniscusscheuren is de leeftijd van een scheur (m.a.w. hoe lang bestaat de scheur al?).

In **Hoofdstuk 4** werd de klinische uitkomst van artroscopisch meniscushechtingen geëvalueerd in relatie tot de bestaansduur (leeftijd) van de meniscusscheur. Bij 234 patiënten werden 238 meniscushechtingen uitgevoerd. De voorste kruisband (VKB) werd gereconstrueerd in bijna alle VKB-deficiënte knieën. Het tijdsinterval tussen het moment van letsel en het moment van de meniscushechting werd verdeeld in acuut (<2 weken), subacuut (> 2 weken- <12 weken) en chronisch (> 12 weken). Bij een mediane follow-up van bijna 3,5 jaar waren 55 mediale en 10 laterale meniscushechtingen (totaal faalpercentage 27%) gefaald. Een significant hoger percentage mediale meniscushechtingen faalden (p <0,05) en in VKB-deficiënte knieën zonder VKB-reconstructie faalden significant meer meniscushechtingen. Er werd geen significant verschil gevonden voor elk tijdsinterval tussen het moment van het oplopen van de meniscusscheur en het moment van de meniscushechting. Hiermee werd aangetoond dat de leeftijd van de scheur geen invloed heeft op het falen van de meniscushechting.

Wanneer het hechten van een meniscusscheur niet mogelijk is, en hiermee het herstel van meniscusfunctie niet kan worden bereikt, of wanneer deze behandeling heeft gefaald, dan is partiële meniscectomie een optie. In sommige gevallen moet zelfs een (sub) totale meniscectomie worden uitgevoerd. Hierdoor is er functieverlies van de meniscus en evenredig met de hoeveelheid verwijderd meniscusweefsel, neemt de kans op het ontwikkelen van gonartrose toe. Voordat tekenen van degeneratie van de knie optreden of verergeren, kunnen patiënten met een status na een (sub)totale meniscectomie last hebben van pijn gelokaliseerd in het meniscus-deficiënte kniecompartiment (meestal mediaal). In deze gevallen is een meniscus transplantatie een geschikte optie. In **Hoofdstuk 5** werd de klinische uitkomst van meniscustransplantatie op de lange termijn geëvalueerd. Drieënzestig meniscustransplantaten werden getransplanteerd via een open procedure bij 57 patiënten. De klinische uitkomst van 40 laterale en 23 mediale meniscustransplantaten werden geëvalueerd na een gemiddelde follow-up van 13,8 jaar ± 2,8 jaar. Na deze follow-up periode werd een totaal faalpercentage van 29% gevonden (8 mediale en 10 laterale meniscustransplantaten faalden). Een significante verbetering van de Lysholm score werd gezien bij follow-up na 13.8 jaar in vergelijking met preoperatief. Langetermijn- en preoperatieve Lysholm scores waren niet significant verschillend in de subgroepen; mediale meniscustransplantaten, vrouwelijke patiënten en links behandelde knieën. Voor alle subgroepen werd een significant verschil gevonden tussen Lysholm scores op korte en lange termijn. Significante verschillen voor KOOS- en IKDC scores waren alleen aanwezig tussen mannelijke en vrouwelijke patiënten. Er werden geen significante verschillen in Lysholm scores gezien tussen patiënten met hun meniscustransplantaat nog in situ en patiënten die na hun meniscustransplantatie een totale knieprothese kregen. Ondanks de verslechtering van de functiescores in de loop van de tijd, was er nog steeds verbetering in het niveau van functioneren bij langdurige follow-up, echter niet op een hoog niveau. De resultaten lieten zien dat meniscustransplantatie een procedure is met gunstige uitkomsten (pijnverlichting en functieverbetering) en daarmee goede optie is voor de behandeling van patiënten met een symptomatisch meniscus-deficiënt kniecompartiment. Het uitvoeren van een meniscustransplantatie kan knieprothesiologie bij jonge(re) patiënten uit te stellen.

Naast het bewezen effect op pijnverlichting en functieverbetering, zou een meniscustransplantatie idealiter de ontwikkeling van knieartrose moeten vertragen of beter voorkomen. In de literatuur is veel gepubliceerd over meniscustransplantaties, echter een kraakbeen protectief effect, zoals aangetoond bij schapen, blijft bij mensen (nog) uit. Dit komt mede door het ontbreken van gestandaardiseerde evaluatiemethoden en het ontbreken van kwalitatief hoogwaardige onderzoeken.

In **Hoofdstuk 6** werd een studie uitgevoerd naar veranderingen in botmineraaldichtheid (BMD) na meniscustransplantatie om meer inzicht te krijgen in het potentiële kraakbeen protectieve effect van een meniscustransplantatie. Zesentwintig opeenvolgende patiënten ondergingen een meniscustransplantatie. BMD werd gemeten met behulp van Dual-energy X-ray Absorptiometry (DEXA) scan peroperatief en 6 maanden, 1 en 2 jaar postoperatief. BMD werd gemeten in zes interessegebieden (ROI's) van tibia en femur (mediaal, centraal, lateraal) in zowel behandelde als gezonde contralaterale knieën. Gedurende 2 jaar follow-up veranderden de BMD-niveaus van MAT-knieën niet significant in bijna alle ROI's. BMD was significant hoger in bijna alle ROI's in MAT-knieën op bijna alle follow-upmomenten in vergelijking met gezonde contralaterale knieën. In de gezonde contralaterale knieën daalde de BMD licht, maar niet statistisch significant, in het eerste jaar postoperatief, waarna de BMD genormaliseerd naar de uitgangswaarden na 2 jaar follow-up. BMD-niveaus in alle ROI's verschilden niet significant tussen de patiënten met of zonder chondropathie bij aanvang en na 2 jaar follow-up. Op basis van onze bevindingen concludeerden we dat meniscustransplantatie geen significante invloed had op BMD in de eerste 2 jaar na de operatie. Langere follow-up is nodig om het potentiële kraakbeen protectieve effect van MAT te bewijzen met behulp van botdichtheidsmetingen.

Het meten van de uitkomst na een chirurgische behandeling is van het grootste belang om het succes van de behandeling te bepalen en de patiëntenzorg te verbeteren. Meting van gezondheid gerelateerde kwaliteit van leven scores van patiënten met meniscusproblemen en hun opeenvolgende behandelmodaliteiten met gevalideerde vragenlijsten is belangrijk. De Western Ontario Meniscal Evaluation Tool (WOMET) is het eerste meniscuspathologie-specifieke gezondheid gerelateerde kwaliteit van leven-instrument. In **Hoofdstuk 8** hebben we de Nederlandse versie van de WOMET gevalideerd. Na vertaling in het Nederlands bleek het een valide en betrouwbare patiënt gerapporteerde uitkomstmaat te zijn. Constructvaliditeit, inhoudsvaliditeit, interne consistentie, test-hertest betrouwbaarheid, minimaal detecteerbare verschil en minimaal klinisch relevant verschil werden geanalyseerd. Met een goede correlatie met alle andere gebruikte vragenlijsten en bevestiging van alle hypothesen, vertoonde de Nederlandse WOMET een goede constructvaliditeit. Vloer- en plafondeffecten waren afwezig en er was een uitstekende interne consistentie en een goede test-hertest betrouwbaarheid. Het minimaal detecteerbare verschil en minimaal klinisch relevant verschil werden bepaald: respectievelijk 15,4 en 14,7. De Nederlandse versie van de WOMET kan worden gebruikt als een ziekte specifiek instrument om gezondheid gerelateerde kwaliteit van leven van Nederlandse patiënten met meniscuspathologie te evalueren.

Met het hebben van een valide en betrouwbare patiënt gerapporteerde uitkomstmaat zou het interessant zijn om te weten of de door de patiënt gerapporteerde uitkomst verband houdt met de tevredenheid en/of verwachting van een patiënt. In **Hoofdstuk 7** werden de patiënt gerapporteerde uitkomsten, de overleving van het meniscus transplantaat en hun associatie met eerdere interventies aan de knie geëvalueerd bij 109 opeenvolgende patienten die een artroscopische meniscus transplantatie ondergingen door eenzelfde chirurg in de periode 1999-2017. De totale gemiddelde overleving van het transplantaat was 16,1 jaar (95% I: 14,8 tot 17,5 jaar). De leeftijd van de patiënt op baseline was geassocieerd met de overleving van het meniscus: hazard ratio 1,19 per toenemend persoonsjaar (95% CI: 1,04 tot 1,36, p = 0,009). Na 4,5 jaar (IQR, 2 - 9) follow-up waren alle KOOS-scores nog steeds verbeterd. Leeftijd onder de 35 jaar, gelijktijdige reconstructie van de voorste kruisband en het aantal knieoperaties vóór meniscustransplantatie waren geassocieerd met lagere KOOS-scores. Verwachtingen van de meniscustransplantatie en de algehele tevredenheid na meniscustransplantatie waren niet geassocieerd met preoperatieve patiëntkenmerken, noch met het aantal of soort preoperatieve interventies. Op basis van de resultaten werd geconcludeerd dat meniscustransplantatie een goede algehele overleving heeft met een klinisch relevante verbetering. Zowel de overleving van de meniscustransplantatie als de door de patiënt gerapporteerde uitkomst waren lager bij patiënten jonger dan 35 jaar en beide waren geassocieerd met preoperatieve kenmerken of procedurele kenmerken. Interessant genoeg meldden alle patiënten verbeterde postoperatieve tevredenheid en voldeden ze aan de verwachting na meniscustransplantatie. Dit laatste was onafhankelijk van de preoperatieve interventies aan de knie.

Appendices

Publications related to this thesis

- van der Wal RJP, BJW Thomassen, ERA van Arkel. Long-term clinical outcome of open meniscal allograft transplantation. Am J Sports Med. 2009 Nov;37(11):2134-2139.
- van der Wal RJP, BJW Thomassen, JWA Swen, ERA van Arkel. Time interval between trauma and arthroscopic meniscal repair has no influence on clinical survival. J Knee Surg. 2016 Jul;29(5):436-442.
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CURRICULUM VITAE

Robert van der Wal was born on the 20th of January 1982 in Vlaardingen, the Netherlands. He graduated from secondary school (christelijke scholengemeenschap Aquamarijn, Vlaardingen) in 2000, where after he started to study Biomedical Sciences at the University of Leiden. In 2001 he started Medical School at the same university. During his internships he started his research on meniscal allograft transplantation under supervision of dr. Ewoud R.A. van Arkel. After obtaining his medical degree in 2007 he started working as an intern at the Department of General Surgery of the Medical Center Haaglanden (MCH) in The Hague (supervisor Alexander J.C. de Mol van Otterloo, MD, PhD). He was trained at the Department of General Surgery Albert Schweitzer Hospital Dordrecht (supervisors Rob J. Oostenbroek, MD, PhD and Peter W. Plaisier, MD, PhD), the Department of Orthopaedic Surgery and Trauma of MCH (supervisor Ewoud R.A. van Arkel, MD, PhD) and the Department of Orthopaedic Surgery Leiden University Medical Center (supervisor prof. Rob G.H.H. Nelissen, MD, PhD). The author received a study grant from the Research Fund of Medical Center Haaglanden (Wetenschapsbeurs 2014) to work on his research project after finishing his training in June 2015. During this period he was able to spend three months full time on this thesis. Since the first of October 2015 he works an Orthopaedic Surgeon at the Department of Orthopaedic Surgery at Leiden University Medical Center with special interest in orthopaedic oncology, complex joint reconstructions (in particular prosthetic joint infections) and trauma.

Robert lives in Wateringen with his lovely wife Marion and his three beautiful children: Mees, Gijs and Saar.

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