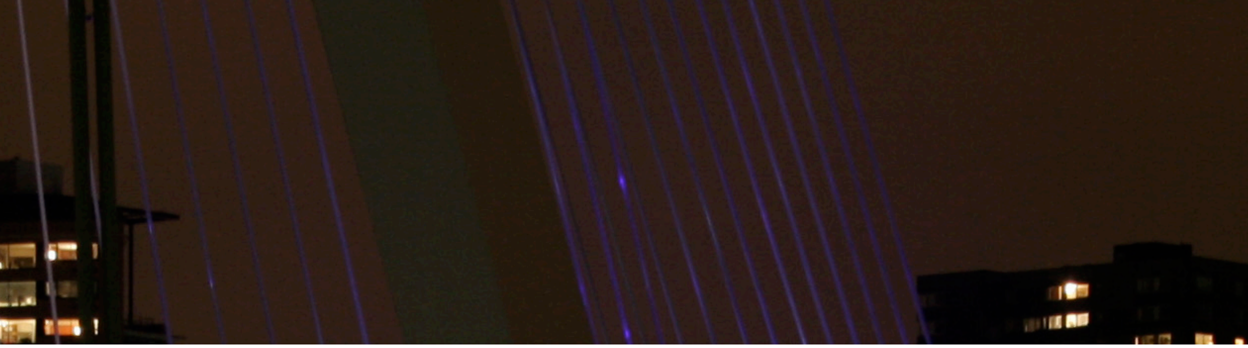
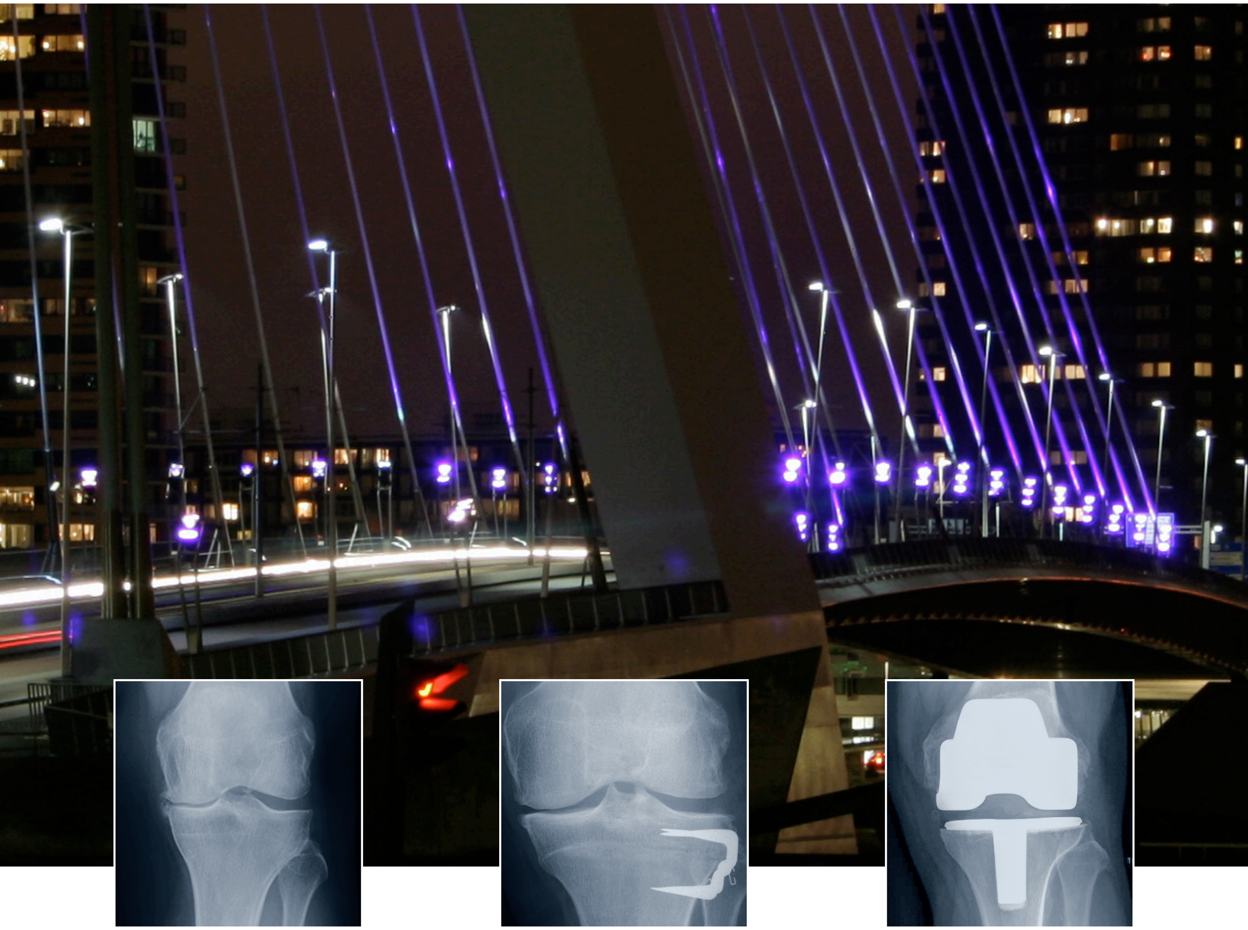


Treatment of Symptomatic Varus Osteoarthritis of the Knee



T.M. van Raaij

Treatment of Symptomatic Varus Osteoarthritis of the Knee

T.M. van Raaij

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Treatment of Symptomatic Varus Osteoarthritis of the Knee

Behandeling van symptomatische mediale gonartrose

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de
rector magnificus

Prof.dr. H.G. Schmidt

en volgens besluit van het College voor Promoties.

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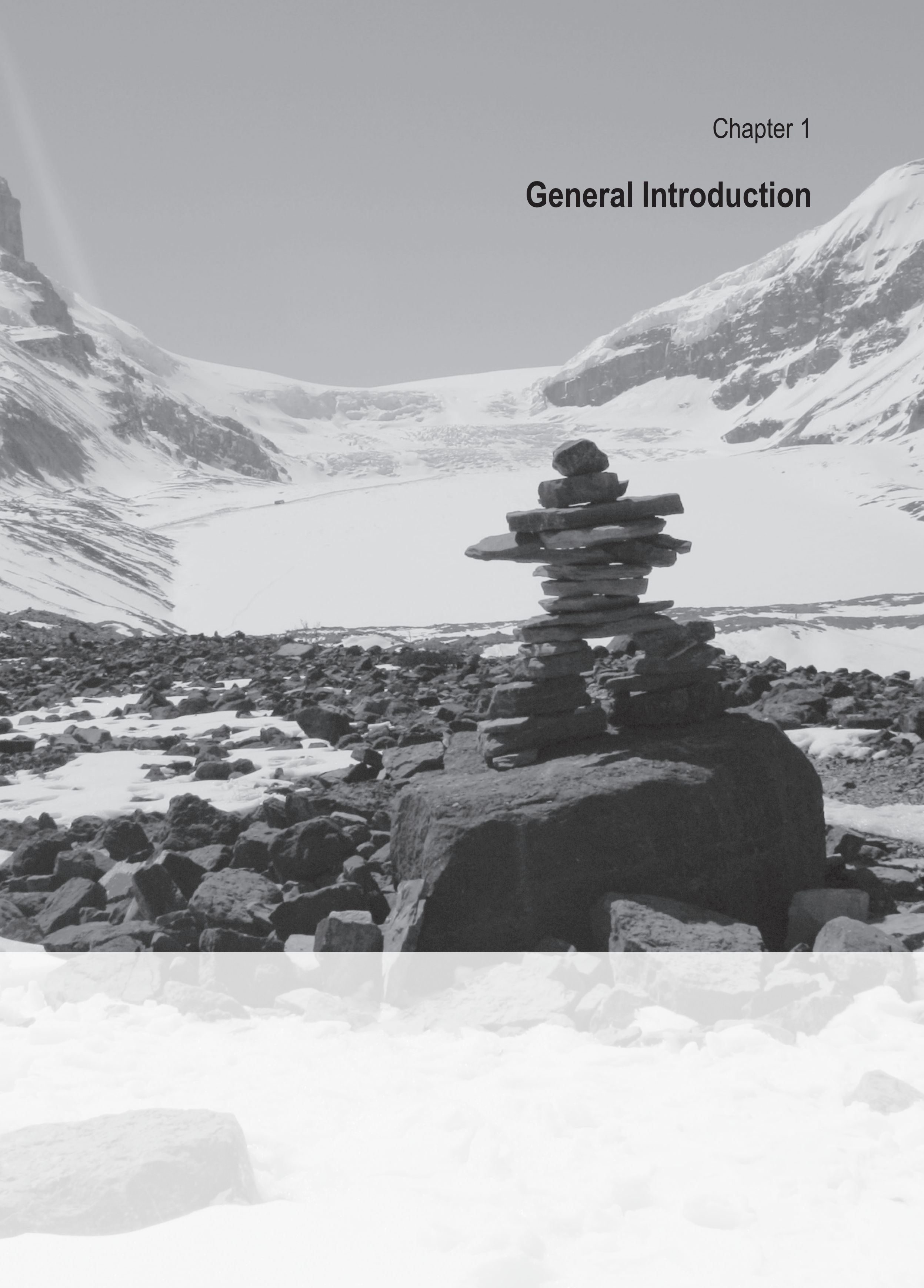
Contents

Chapter 1

General Introduction



Osteoarthritis (OA) is the 6th leading cause of Years Lost to Disability (YLD) at global level, accounting for 3% of total global YLDs. [1] Knee OA is the most common joint disorder [2], and in the Netherlands approximately 17% of the population aged 45 years and over suffer from knee OA. [3] It causes considerable pain and immobility, affects independence and psychosocial functioning, and in addition leads to financial losses. [4,5] Many patients present with unicompartmental disease, and the medial compartment is almost 10 times more frequently involved than the lateral compartment. [6] This thesis investigates both the non-operative and surgical treatment outcomes in active patients with symptomatic medial OA of the knee. The aim is to clarify indications for identified treatment modalities as controversy exists on how patient and/or intervention related factors affect the outcome of this disease. Furthermore, clearer indications will lead to better care, which may not only benefit the individual patient but also society as a whole because of expected savings in health care expenses and reduction of productivity losses.

Patients with OA of the medial compartment often have varus malalignment; the mechanical axis and load bearing passes through the medial compartment. Some report that malalignment may even have an impact on the development and progression of knee OA. [7,8] Although many consider whole leg radiographs in standing position (mechanical axis measurement) as the gold standard to determine knee alignment, in clinical practice, knee alignment is often assessed on shorter anterior-posterior knee radiographs (anatomic axis measurement) to cut expenses and cumbersome procedures. Significant correlation between mechanical and anatomic axis angles has been reported. [9,10] Some suggest using anatomic axis measurement in research and clinical settings. [9,11] In ***Chapter 2*** we compare two different methods of anatomic axis assessment in a group of patients with known mechanical varus alignment, and determine whether or not anatomic axis measurement on standard short knee views can be used in clinical settings.

The initial treatment of symptomatic medial unicompartmental knee OA is non-operative, consisting of patient education (weight reduction), medication and if needed physical therapy. Other specific non-operative interventions may have some additional beneficial effects. A recent multicenter randomized controlled trial (RCT) showed significant effect of bracing compared to no bracing in patients with medial compartmental OA of the knee regarding knee function score. However, many patients did not adhere to long-term bracing. [12] Biomechanical laboratory studies on the gait of a small number of patients have shown that lateral-wedged insoles as well as valgus knee bracing significantly reduce the adduction moment about the knee and the estimated medial compartment load. [13] In ***Chapter 3*** we present a prospective RCT in which we investigate the effectiveness of a lateral-wedged sole compared to bracing in patients with symptomatic medial compartmental OA and varus malalignment.

When non-operative treatment fails high tibial valgus osteotomy (HTO) is an accepted treatment of medial unicompartmental OA of the knee with varus alignment, especially in younger active patients. [14] The main goal of the correction osteotomy is to transfer the load bearing from the pathologic to the normal compartment of the knee. ***Chapter 4*** includes a substantive amendment of a systematic Cochrane review in which we summarize the current knowledge on the effectiveness and safety of an osteotomy for treating OA of the knee.

A successful outcome of the osteotomy relies on proper patient selection, and achievement and maintenance of adequate operative correction. [15-17] In ***Chapter 5*** we investigate the relation between success of HTO at long-term follow-up and potential preoperative patient risk factors (age, sex, body mass index, grade of OA, and preoperative varus deformity). Failure of the osteotomy is defined as conversion to a total knee arthroplasty (TKA). Achievement of an even distribution of mechanical load across the knee joint by obtaining an ideal lower-extremity mechanical axis alignment, may be influenced by preoperative axial alignment parameters. In ***Chapter 6*** we use a historic cohort of patients to analyze the influence of different sources of knee varus deformity on osteotomy failure. Loss of operative correction may also threaten the success of osteotomy. In both lateral closing wedge and medial opening wedge osteotomy the opposite cortex of the tibia is usually not osteotomized leaving 1 cm bone intact as a fulcrum. However, a fracture of this cortex may lead to loss of correction. ***Chapter 7*** presents the analysis of opposite cortical fracture in a cohort of patients who were included in a prospective level I study on two different techniques of HTO. [18]

Unicompartmental OA symptom progression may occur and some patients require knee replacement. Success of primary TKA in knee OA is well established, and about 85% of patients are satisfied with the surgical outcome. [19] Therefore, when considering osteotomy in the early treatment of symptomatic medial compartmental OA, subsequent TKA should not be compromised, and results should not deteriorate more rapidly than after primary TKA alone. [20] In ***Chapter 8*** we present a case control study to assess the influence of HTO on results and complications of total knee replacement. In the aim to prevent cohort disparity we match for diagnosis, time of follow-up, body weight and significant risk factors for failure of TKA to select an ideal comparison group. Although RCTs are considered the ideal and highest level of evidence in making decisions about the care of individual patients, numerous "good" surgical practices have evolved into "standard of care" without being randomized against placebo or ineffective treatment options. [21] This probably explains why no RCT has been conducted on the effect of TKA with previous HTO or not, and the highest practicable level of evidence is a review of nonrandomized studies. [22] In ***Chapter 9*** we systematically collect the best available scientific evidence from clinical studies examining TKA after HTO, which may help facilitate the decision making on osteotomy.

Chapter 10 of this thesis discusses the methods, results and implications of our studies, followed by recommendations for future research.

Chapter 11 and ***12*** present an English and Dutch summary of the work in this thesis.

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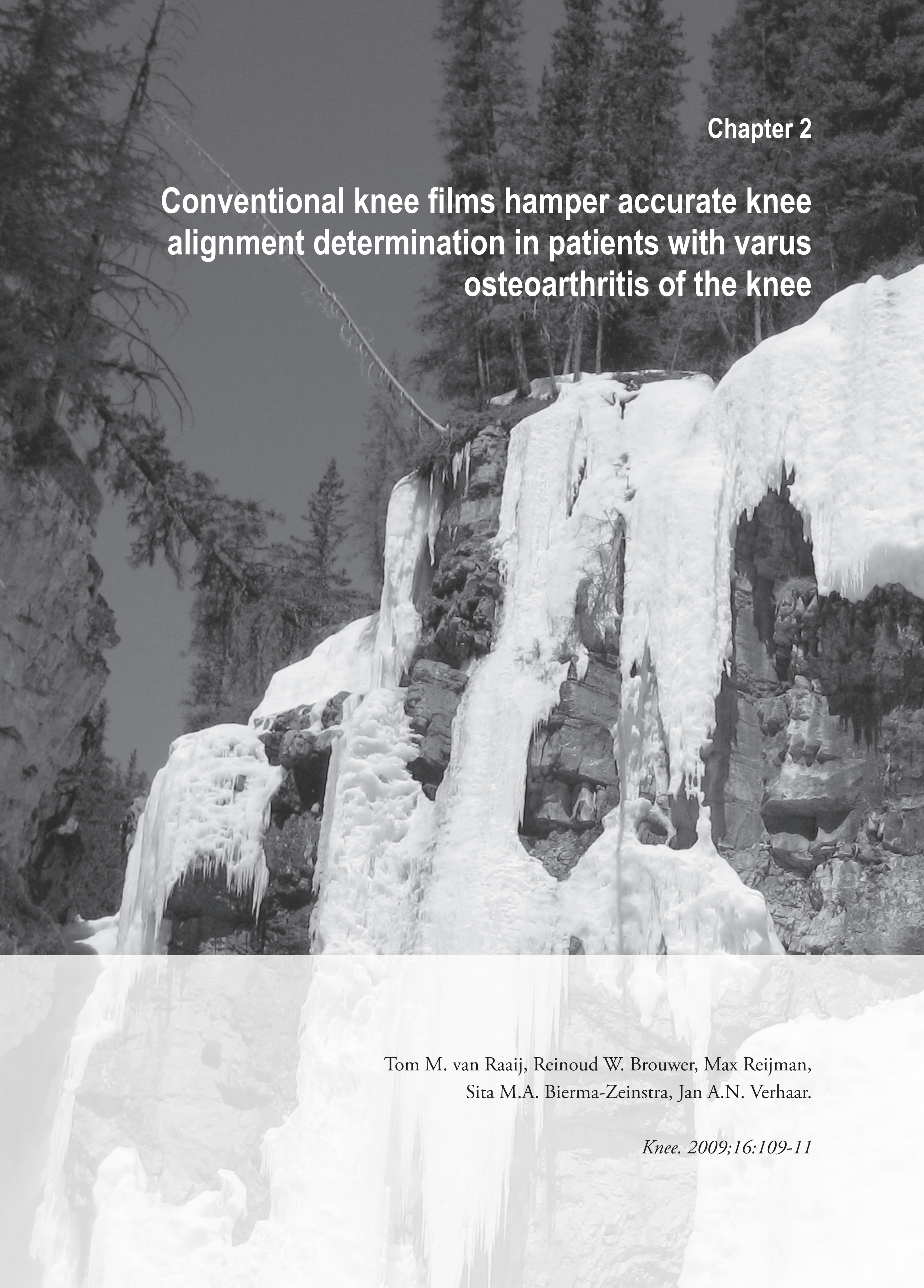


Chapter 2

Conventional knee films hamper accurate knee alignment determination in patients with varus osteoarthritis of the knee

Tom M. van Raaij, Reinoud W. Brouwer, Max Reijman,
Sita M.A. Bierma-Zeinstra, Jan A.N. Verhaar.

Knee. 2009;16:109-11

Abstract
Surgical therapeutic procedures such as knee osteotomy and knee replacement depend on proper knee alignment assessment. The aim of this study was to evaluate if femorotibial (FT) measurement on short knee films may be used in clinical settings. The study population comprised 68 patients with symptomatic medial compartmental knee osteoarthritis. We measured the FT angle with the use of mid-diaphyseal lines (FTa), and the knee joint centre (FTb) to determine anatomical knee alignment on a short knee image. Then, the accuracy of alignment was compared to the gold standard Hip-Knee-Ankle (HKA) angle on a full-limb view. FTa angle assessment correlated well (r = 0.65) with the HKA angle. However, this method showed poor inter-observer agreement (ICC = 0.37). Three percent of patients were incorrectly classified as having valgus alignment. Good intra- and inter-observer agreements were observed for FTb angle measurement (ICC = 0.89 and 0.79; respectively). But correlation between HKA and FTb angles was low (r = 0.34). Fifteen percent of patients were incorrectly classified as having valgus alignment. Short knee images cannot substitute whole leg views when accurate assessment of knee alignment is essential.

Keywords: knee; alignment; radiography; femorotibial angle

Introduction
Accurate determination of limb alignment is essential in adequate planning for knee surgical procedures such as osteotomy and arthroplasty. Full-limb films made in standing position to assess the HKA angle, are considered the gold standard, and allow reproducible measurement of the mechanical axis of the whole lower extremity [1]. However, these films may cause radiation to the pelvic organs, require special equipment, and generate extra costs [2]. In general practice, therefore, the FT angle is often employed on short knee films as to decide on the corrective angle for knee deformity or to define the entry point for intramedullary femoral alignment in total knee replacement. FT angle measurement is supposed to allow defining the anatomical axis in the knee, and significant correlation between mechanical and anatomical axis angles has been reported [3,4]. Many, however, determine the FT angle by using the knee joint centre point, which is only a valid point in mechanical axis measurement [5]. The angle formed between the mid-diaphyseal femur and tibia lines will represent the anatomical axis of the knee in the frontal plane more precisely. This study was designed to compare these two different methods of FT angle measurement, and to determine whether or not FT measurement on standard short knee films can replace whole leg views for assessment of knee alignment in everyday practice.

Patients and Methods

Seventy-four consecutive patients with symptomatic medial compartmental knee osteoarthritis, enrolled in a randomised controlled trial (ISRCTN92527149) that studied the effect of a lateral-wedged insole compared to a brace, were evaluated. Six patients were lost to follow-up or refused a whole leg radiograph (WLR). The study comprised 68 patients; Table 1 presents the study population characteristics.

Table 1: Baseline characteristics of the study population

		N = 68
Age, [years], mean (SD)		55 (6)
Gender, % female		53
BMI (kg/m2), mean (SD)		29 (4)
OA medial (grade), %		
	1	40
	2	18
	3	41
	4	1
Fixed flexion knee deformity (°), %		
	0	69
	5 - 10	27
	> 10	4

A digitalized WLR was made in standing anteroposterior (AP) position, while the patient stood on the affected leg with the knee in full extension. The AP projection was ensured during lateral fluoroscopic control by superimposing the dorsal aspect of the femoral condyles. The tube was set perpendicular to this lateral view and was moved from the proximal end to the distal end so that a WLR was obtained. The HKA angle was defined as the angle between a line of the centre of the femoral head to the top of the femoral notch, and a second line from the centre of the ankle to the centre of the tibial spines (Figure 1) [6]. When the HKA angle deviated in varus direction (> 0°), knee alignment was defined as varus. Both FT angles were assessed on a conventional knee image obtained by blinding the WLR 10 cm above and below the knee joint line. The FTa angle was defined as the angle between the femoral mid-diaphyseal line, and the tibial mid-diaphyseal line (Figure 2) [5]. The FTb angle was defined as the angle between the line from the midpoint of the femoral diaphysis through the top of the femoral notch and the mid-diaphyseal line of the tibia (Figure 2) [6]. An FTa angle more than -5° and an FTb angle more than -2° were considered to represent knee varus angulation [7,8].

Two observers (TR and RB) measured all described angles to assess inter-observer reproducibility. The radiographs were re-measured by TR at least 2 weeks later, without knowledge of the results of the first readings to assess intra-observer reproducibility. Both observers are orthopaedic surgeons and experienced with reviewing WLR.

The SPSS program statistical software version 10.1 (SPSS Inc., Chicago, Illinois) was used for statistical analysis. The intra- and inter-observer reproducibility was assessed by two-way mixed effect model, consistency definition, and expressed as intra-class correlation coefficients (ICC) that vary from 0 (no agreement at all) to 1 (total agreement). To determine the relationship between FT and HKA angles, Pearson's correlations were calculated. A p-value of 0.05 was considered to be statistically significant. The local Ethics Committee approved the protocol, and all patients gave their written informed consent

Figure 1: Mechanical lower limb axis assessment using HKA angle measurement according to Moreland

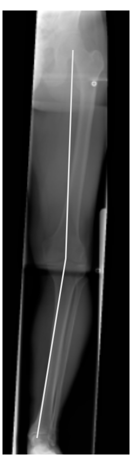
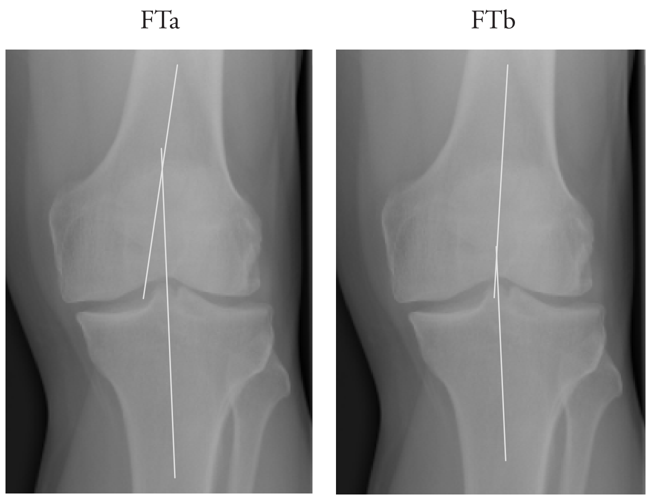


Figure 2: Anatomical lower limb axis assessment using femur and tibia mid-diaphyseal lines (FTa angle), and the knee joint center as a landmark (FTb angle).



Results

The mean HKA angle for the study group was 6.9° (SD 3.7°) of varus alignment. The FTa and FTb angles were respectively 0.2° (SD 3.5°) and 1.2° (SD 3.1°). The intra-and inter-observer reproducibility were excellent for HKA (0.99 and 0.96), and good for FTb angle (0.89 and 0.79). However, assessment of the FTa angle showed good intra-observer (0.77), but poor inter-observer agreement (0.37). The FTa angle correlated significantly with the HKA angle ($r = 0.65$, $p < 0.0001$), but correlation between the HKA angle and the FTb angle was low ($r = 0.34$, $p = 0.005$). All included patients had varus knee alignment with an HKA angle greater than 0°. Knee alignment assessment with the use of FTa measurement, showed 2 out of the 68 patients with an angle less than -5°; indicating that 3% of patients were incorrectly classified as having valgus alignment. Fifty-eight patients had an FTb angle of more than -2°, which meant that 15% of patients were classified as having no varus alignment.

Discussion

Although the knee joint centre is commonly regarded as a landmark for FT angle measurement, Moreland et al. demonstrated that the femoral anatomical axis does not pass through the centre of the knee joint [6]. Due to physiological valgus in the femur, the femoral anatomical axis converges distally with the mechanical axis, and intersects the knee joint line generally medial to the knee joint centre [9]. We evaluated the FT angle with the use of mid-diaphyseal lines (FTa), and the knee joint centre (FTb) on a standardized WLR. This allowed us to compare alternative alignment measurements without different radiological acquisition protocols. Different protocols, as well as knee function impairment may lead to large changes in projected angles [10]. In our study 96% of patients had less than 10 degrees of flexion deformity (Table 1). Earlier, a radiological cadaver study had shown that fixed flexion deformities of 30 degrees or less hardly influence accurate measurement of knee alignment on a WLR when there is no rotation at the knee joint [11]. We ensured 100% AP projection by superimposing the femoral condyles under lateral fluoroscopic control.

Issa et al. demonstrated in 146 individuals with knee osteoarthritis that the HKA angle determined on full-limb radiograph correlated well ($r = 0.86$) with the FT angle measured on a different, fluoroscopically controlled semi full-limb knee image [2]. In comparison with the aforementioned study we used a short knee image to measure FT angle, and this may represent a conventional knee radiograph more closely. With this image, high intra- and inter-observer reliability for FTb angle determination was achieved. However, FTb angle assessment with the use of the knee joint centre as a landmark, showed low correlation with the gold standard HKA angle ($r = 0.34$). The FTa angle had a far higher correlation ($r = 0.65$) with mechanical limb alignment, but poor inter-observer reproducibility with unacceptable low agreement between the 2 observers. These measurements may even be less accurate in everyday practice. Especially when one considers that fluoroscopic control to ensure adequate projection is not standard practice, and this may lead to unacceptable variations in projected angles. Values for varus knee alignment using the angle formed by the femur and tibia have been reported in normal populations, and are arbitrary. We used 2 cut-offs formulated in literature [7,8]. Varus knee alignment was misinterpreted in 3% of our cases when measuring the FTa angle. Fifteen percent of our patients were misdiagnosed as having no varus malalignment when the FTb angle on short knee images was assessed. Surgical therapeutic procedures such as knee osteotomy and knee replacement highly depend on proper knee alignment determination, and our findings suggest that clinical outcomes may be in jeopardy when short films are used.

In summary we found evidence that the frequently employed FT determination with the aid of the knee joint centre had poor relationship with the mechanical lower limb axis on conventional knee images, and should not be used in everyday practice. Knee anatomical axis measurement using the mid-diaphyseal lines of the femur and tibia correlated well with mechanical limb alignment, and may be helpful in defining the accurate entry point for intramedullary alignment guides when whole leg views are not readily available [9]. However, this method showed poor inter-observer agreement. Substitute short films, therefore, may cause inaccuracy, which is undesirable in patients undergoing corrective or replacement knee surgery.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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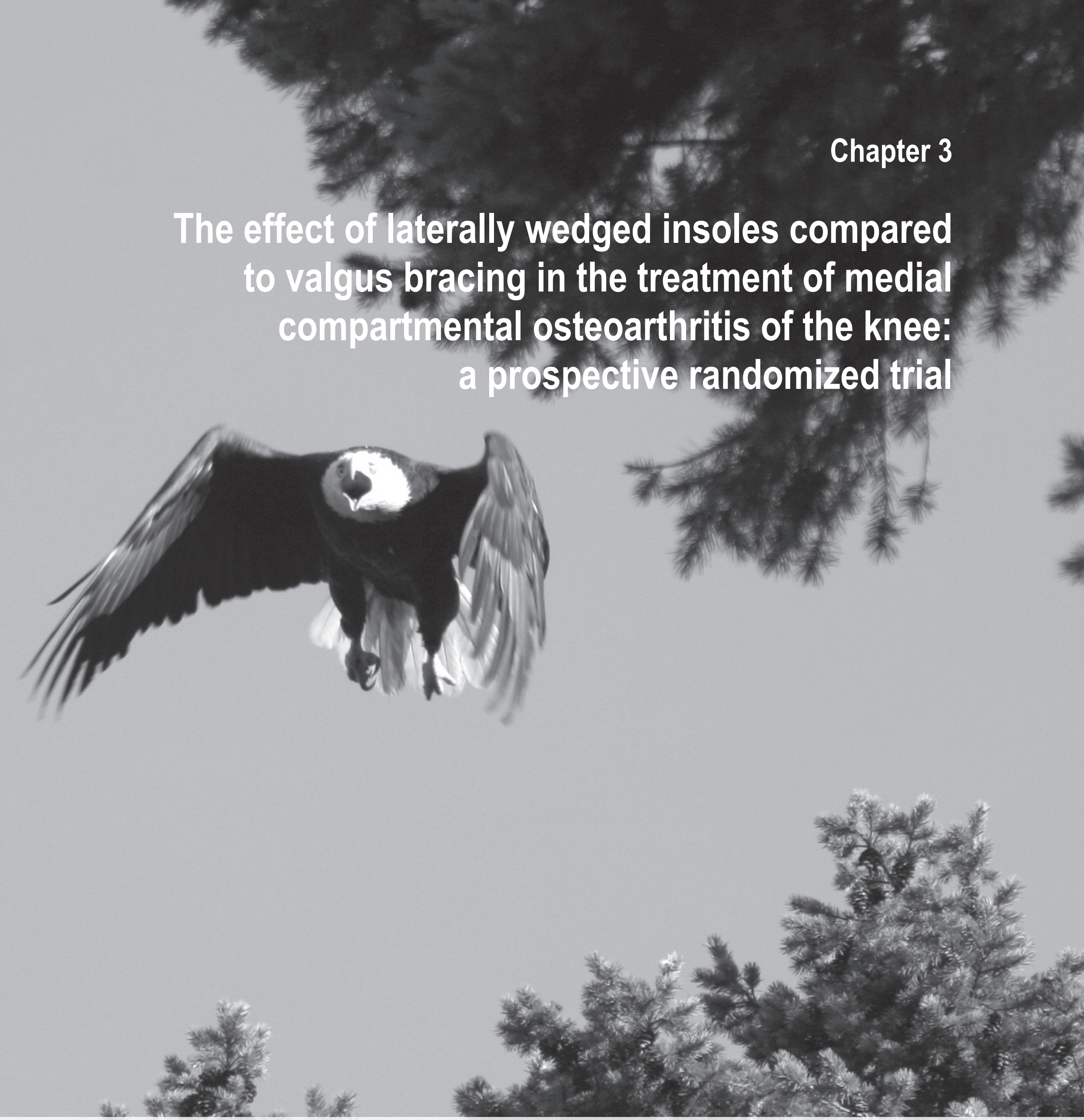

Chapter 3

The effect of laterally wedged insoles compared to valgus bracing in the treatment of medial compartmental osteoarthritis of the knee: a prospective randomized trial

Tom M. van Raaij, Max Reijman, Reinoud W. Brouwer,
Sita M.A. Bierma-Zeinstra, Jan A.N. Verhaar

CORR. 2009: accepted for publication

Abstract
Knee braces as well as foot orthoses may have beneficial effects in the treatment of knee osteoarthritis. A prospective randomized controlled clinical trial was conducted at a university medical center to compare both interventions head-tot-head. In 91 patients with symptomatic medial compartmental knee osteoarthritis, a 10-millimeter laterally wedged insole (index group, n = 45) was compared to a valgus brace (control group, n = 46). The follow-up was 6 months. Primary outcome measure was pain severity with VAS. Secondary outcome measures were knee function score with WOMAC, varus alignment, and compliance. Additionally, we compared the percentage responders according to the OMERACT-OARSI criteria for both groups. No significant differences in pain and functional outcomes were detected between both groups. Both interventions had no effect on knee varus malalignment. Patients in the insole group complied significantly (P = 0.015) better to their intervention. According to the OMERACT-OARSI criteria, about one sixth of our patients responded to the allocated intervention. Subgroup analysis showed a better effect for the insole in patients with mild medial OA. Our results suggest that a laterally wedged insole may be an alternative to valgus bracing in the non-invasive treatment of medial knee OA.

Level of Evidence: Level II, therapeutic study. See the guidelines online for a complete description of level of evidence.

Introduction
Knee osteoarthritis (OA) is one of the most common joint disorders, and causes considerable pain and immobility [10]. Many patients present with predominant medial compartmental knee OA [8]. The initial treatment is non-operative, and consists of patient education, weight reduction, physical therapy and if needed medication. Drugs use rarely relieves the symptoms entirely, and mainly acts as a palliative agent. Other rehabilitative interventions are based on altering knee biomechanics, which may have an impact on the development and progression of knee OA [3,24]. Especially in selected patients with OA of the medial compartment, significant improvements in pain, function, and loading forces have been seen with valgus unloader knee braces [22]. A randomized controlled trial (RCT) also showed that knee bracing compared to no brace has a significant effect on knee function improvement in knee OA patients with varus malalignment [7]. Many patients in this study, however, did not adhere to brace treatment, mainly because of skin irritation and bad fit. This may prevent good outcomes in the long run. Like knee bracing, laterally wedged insoles probably unload the diseased compartment, and correction of varus malalignment has been described [15,27]. A cross-over study showed no effect of wedged soles in an elderly population with advanced stages of OA [1]. Earlier, a significant improvement of symptoms had been shown for patients with mild to moderate OA treated with laterally wedged insoles [26]. Others

noticed a similar effect while observing a decreased nonsteroidal anti-inflammatory drugs intake when foot orthoses were used in the treatment of knee OA [18]. A Cochrane review concluded that there is some evidence that foot orthoses have additional beneficial effects in the treatment of symptomatic knee OA [6]. Laterally wedged soles may represent a huge potential in the treatment of symptomatic knee OA because they are safe and generate fewer costs than knee bracing. Furthermore foot orthoses are easy to apply, and good adherence to the intervention has been noticed [1,26]. We designed a RCT to study the effect of a laterally wedged insole compared to valgus bracing in patients with symptomatic medial compartmental knee OA.

Method

Study design

A prospective open-label parallel RCT (trial registration number: ISRCTN92527149) was conducted at the orthopedic outpatient department of a university medical center. The local Ethics Committee approved the protocol, and the patients gave their written informed consent. The data were collected and analyzed in compliance with the procedures and policies set forth by the Helsinki Declaration. Patients with symptomatic medial compartmental knee OA were included. We diagnosed the OA as medial when pain and tenderness in combination with osteoarthritic signs according to the Kellgren-Lawrence (K-L) score Grade 1 or higher, were located over the medial tibiofemoral compartment of the knee [11]. The radiological score was measured on digitalized standard short posteroanterior radiographs in standing position. Patients with symptoms not related to medial compartmental OA, younger than 35 years of age, an insufficient command of the Dutch language, or no varus malalignment were excluded. The degree of knee alignment was assessed by the hip-knee-ankle (HKA) angle, and measured on a digitalized whole leg radiograph (WLR) in standing position. Earlier we reported high intra- and interobserver agreement of the measurement of the HKA angle by the use of this technique [5]. The HKA angle was defined as the angle between two prolonged lines: one line of the center of the femur head to the top of the femoral notch, and a second line from the center of the ankle to the center of the tibial spines. A positive value represented varus direction, and patients with an HKA angle ≤ 0º were not eligible to be included in the study.

Participants were randomized according to a computer-generated procedure (block randomization, with variable size of the blocks); the randomization codes were held by an independent observer (MR). One investigator (TMR) enrolled the participants. The participants were randomly allocated to their groups after informed consent had been obtained, and all baseline measurements were completed. Participants were assigned to either an intervention group comprising a shoe inserted leather sole with a lateral-wedge cork elevation of 10 millimeters (mm) along the entire length of the foot (Figure 1), or to a control group comprising a knee brace. The shoe-inserted sole was custom made and fitted by a specialized orthopedic shoe technician.

Figure 1. Image of left foot showing the leather sole and a laterally wedged cork elevation of 10 mm (6º wedge).

The valgus knee brace was commercially available for right/left leg in four sizes (MOS Genu®, Bauerfeind, Germany), and consisted of a thigh shell and a calf shell connected by coated aluminum hinges on the medial and lateral sides (Figure 2). A specialized orthopedic technician applied the brace. The degree of valgisation depended on the degree of malalignment and the acceptance of the patient.

Figure 2. Image of left knee showing the MOS Genu® knee brace.

Participants were instructed to wear their intervention as much as tolerated, and they were asked to register the number of hours per week that they wore their intervention. At baseline age, gender, Body Mass Index (BMI), severity of radiologic OA, varus alignment, analgesic use during the previous month, Visual Analogue Scale (VAS) for pain severity during the previous week, and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score during the previous week were scored [2]. At 6 months one non-blinded investigator (TMR), trained as an orthopedic surgeon, assessed the follow-up measurements including standardized questionnaires, physical examination, analgesic use, and the number of hours per week that the participants had worn the intervention during the previous month.

Power analysis

The sample size calculation was based on the baseline mean score for pain (VAS, 0 - 10) of 6.0 and standard deviation (SD) of 2.2 in the study of Brouwer et al. who included patients according to similar criteria. We estimated that 1-point difference in VAS between both groups would represent a clinical relevant difference being 15% of the baseline score. To detect such a difference with two-sided testing ($\alpha = 0.05$ and power of 80%) we needed 40 patients in each group. With the assumption of 15% rate of loss of follow-up we included 92 patients.

Outcome measures

The primary outcome was pain severity with VAS (range 0 – 10; a lower score represents less pain). Secondary outcome measures were knee function using the WOMAC subscale (range 0 – 100; a higher score represents better outcome), varus alignment correction in the frontal plane using the HKA angle, and compliance to the intervention. Compliant patients were defined as those patients wearing the intervention more than 42 hours a week (7 days times 6 hours, which resembles 75% of working day). Responders to the intervention were defined as having an improvement of ≥ 20% compared to the baseline score for pain (VAS) and function (WOMAC function subscale score) [17].

Statistical analysis

The SPSS program statistical software version 15.0 (SPSS Inc., Chicago, Illinois) was used for statistical analysis. First, we established whether the variables had a normal distribution using the normality Shapiro-Wilk test. Based on these analyses, the results are presented as means and standard deviations. The primary analysis will be 'by intention to treat' in that all participants properly randomized will be included in the analysis even if they did not receive the intervention they were allocated to receive. A secondary analysis will be limited to participants who received (or were compliant to) the treatment to which they were randomized (per protocol analysis). A linear regression analysis, with the percentage responders after 6 months of follow-up as dependent variable and intervention as independent variable, was used to study whether patients with symptomatic medial compartmental knee OA will benefit more from additional foot orthoses than bracing. The analyses were adjusted

for gender (unbalanced covariate).
Subgroup analysis was performed for patients with mild OA (K-L grade < 2) versus mild / moderate (K-L grade ≥2) because it has been suggested that laterally wedged insoles are more effective in early medial compartment knee OA [16]. A p-value of 0.05 was considered to be statistically significant. The effect size was calculated as the difference in mean outcomes of the insole group and brace group, divided by the standard deviation of the outcome in the brace group [23].

Results
Between January 2006 and September 2007, 92 consecutive patients were randomized. One patient with medial compartment OA and clinical varus alignment was excluded because of valgus alignment assessed on the WLR, resulting in a total sample of 91 patients. Table 1 presents the baseline characteristics. There were 45 patients in the insole group and 46 patients in the bracing group; 4 patients in the insole group and 4 patients in the bracing group were lost to follow-up. Four patients in the insole group, and 6 patients in the bracing group changed their initial treatment during the 6 months follow-up period. Changes included surgery and non-operative treatment. The main reason was no effect of treatment (4 out of 4 patients in the insole group, and 3 out of 6 patients in the brace group). Other reasons were bad fit, reduction of symptoms, and increased crepitus at the knee. Figure 3 summarizes the study course.
Table 2 presents the primary and secondary outcomes. Compared to baseline the pain severity and WOMAC function scores improved in both groups. After 6 months no significant differences between the insole group and the bracing group were noted for VAS (.09; 95% CI: -1.13; 0.95; effect size 0.04) and WOMAC function scores (1.33; 95% CI: -6.62; 9.28, effect size 0.07). According to the HKA angle, the varus alignment for the insole group was 6.9° (SD 3.6°) at baseline compared to 6.9° (SD 4.1°) when wearing the intervention. The mean HKA angle for the bracing group was 7.0° (SD 3.6°) without the brace compared to 6.7° (SD 3.2°) when wearing the brace; these differences were not significant. At 6 months 71% of patients in the insole group complied with the intervention, which was significantly (p = 0.015) higher compared to 45% for the brace group. The laterally wedged insole was worn significantly (p = 0.006) longer hours during the week with a mean of 57.8 (SD 28.8) hours in comparison with a mean of 38.8 (SD 32.2) hours for the knee brace.
Both the intention-to-treat and per-protocol analyses showed no significant differences in percentages of responders (improvement of ≥ 20% compared to the baseline scores for VAS and WOMAC function) between the insole and the brace groups; respectively 13% vs. 20%, and 14% vs. 18% (Table 3-A and B). Explorative subgroup analysis stratified for patients with mild OA (K-L grade 1) showed a borderline significant (p = 0.068) higher percentage of responders in the insole group compared to the brace group (46% versus 15% responder).

Adverse events

Skin irritation was the main complaint in the brace group (n = 10), and 2 patients developed small blisters that had no clinical consequences. Seven patients experienced a bad brace fit. Five patients had difficulty fitting the laterally wedged sole into different pieces of footwear. Two patients in the insole group were successfully treated non-operatively for ipsilateral trochanteric bursitis.

Table 1. Baseline characteristics of the total study population and separately for the two intervention groups.

	Study population (n = 91)	Insole group (n = 45)	Brace group (n = 46)
Age, [years], mean (SD)	54.7 (7.0)	54.4 (6.5)	54.9 (7.4)
Gender, % female	49	65	35
BMI (kg/m2), mean (SD)	29.2 (4.5)	29.4 (4.9)	29.0 (4.2)
OA medial (grade), %			
Grade 1	41	32	48
2	19	23	15
3	39	42	37
4	1	3	0
Analgesic use, %			
none	48	45	52
when needed	23	24	22
daily	29	31	26
Pain severity (VAS, 0 – 10)	5.6 (2.6)	5.7 (3.0)	5.6 (2.2)
Function(WOMAC, 0 – 100)	46.6 (18.4)	46.5 (± 18.9)	46.8 (± 18.2)
HKA angle* [°], mean (SD)	6.9 (3.6)	6.9 (3.6)	7.0 (3.6)

* positive angle represents varus alignment

Figure 3. Flowchart showing the study course

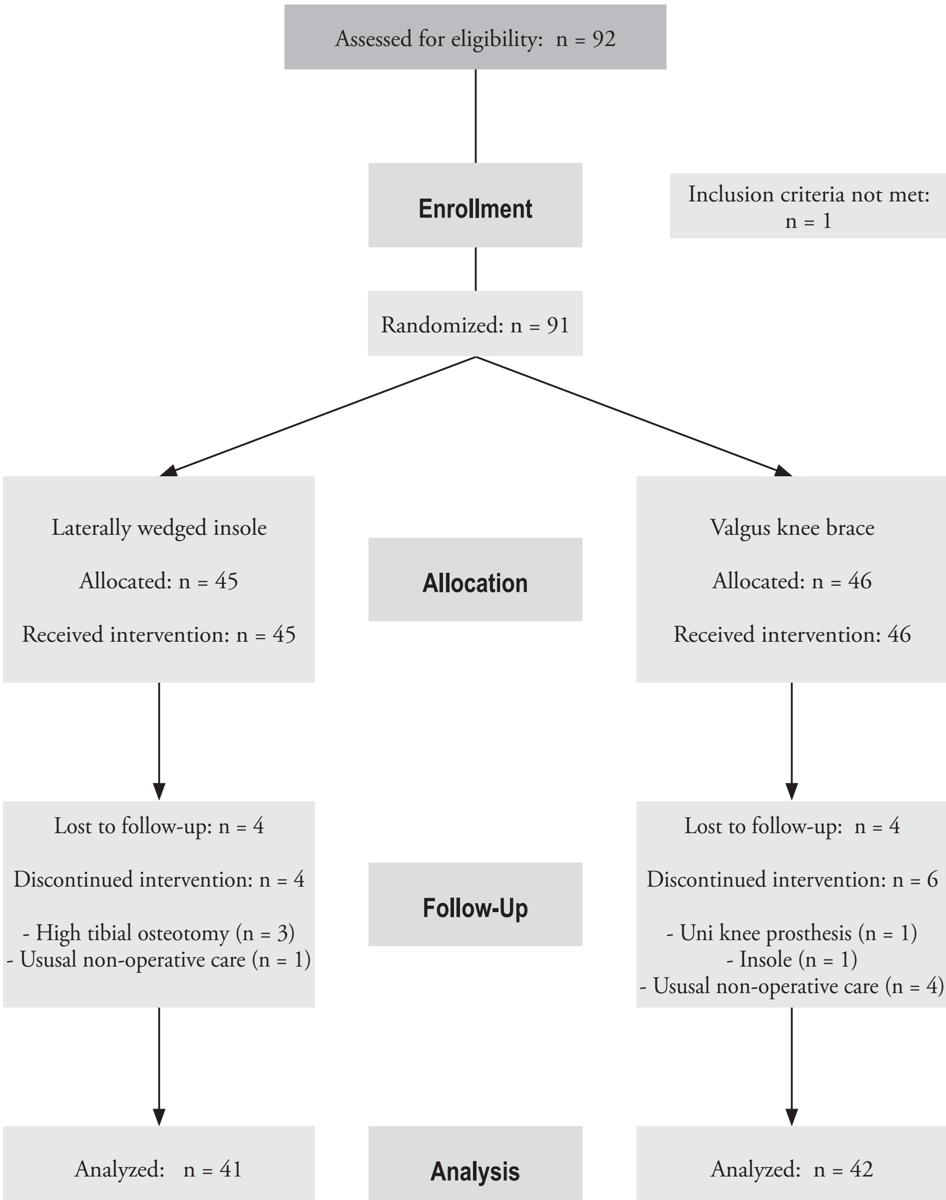

Table 2. Primary and secondary outcomes mean changes (SD) compared to baseline for the insole and brace groups with the mean differences between both groups after 6 months.

	Insole group (n = 41)†	Brace group (n = 42)††	Mean differences* (95% CI)	Effect size
Pain severity [VAS] (0 – 10)	- 1.1 (2.3)	- 1.0 (2.3)	.09 (-1.13; 0.95)	0.04
Function [WOMAC] (0 – 100)	4.9 (16.5)	3.5 (19.2)	1.33 (-6.62; 9.28)	0.07
HKA angle (°)	0 (.9)	- 0.3 (1.0)	-.22 (-.68; -.25)	.22
Intervention worn (hrs / week)	57.8 (28.8)	38.8 (32.2)	19.0 (-32.3; -5.7)	.59

† 4 patients lost to follow-up
†† 4 patients lost to follow-up
* corrected for gender, and use of pain medication at baseline and follow-up

Table 3-A. Proportion of responders in both groups after 6 months.*

	Insole group (n = 41)	Brace group (n = 42)
No response, %	60	67
Pain **or** function, %	27	13
Pain **and** function, %	13[1]	20[1]

* a responder was defined as having an improved score of ≥ 20% for pain and function compared to baseline score [16]
[1] P-value of .337

Table 3-B. Proportion of responders in both groups after 6 months (per-protocol analysis).*

	Insole group (n = 29)	Brace group (n = 19)
No response, %	62	65
Pain **or** function, %	24	17
Pain **and** function, %	14[1]	18[1]

* a responder was defined as having an improved score of ≥ 20% for pain and function compared to baseline score [16]
[1] P-value of .337

Discussion

Few good clinical studies have been published on orthoses or bracing in treatment of medial compartment knee OA. So far, no RCT has compared both interventions head-tot-head. Based on the results of this study we found no differences in effect for laterally wedged insoles compared to valgus knee bracing in the treatment of medial compartment knee OA after 6 months. The present study was limited that the assessor was also the caregiver as well as the one who informed the patient about the aims of the study. Although the kind of interventions did not allow blinding of patients, methodological strength would have been gained by blinding the assessor for the functional outcome measurement (clinical knee score), e.g. by using an independent assessor. Moreover this study was not powered to perform explorative subgroup analysis, and the results should be interpreted with caution.

Earlier Kirkley et al. described an improvement on the WOMAC pain scale of 9% in 41 patients treated with an unloader valgus brace, which was significantly better compared to a non-braced control group [14]. Brouwer et al. noted a significant better result after valgus bracing compared to non-bracing for knee function score (4 units improvement out of 100) in a group of 95 patients with medial knee OA [7]. A recent crossover RCT concluded that wedged shoe insoles were not efficacious in patients with medial knee OA [1]. They compared laterally wedged insoles to neutral insoles, which may act as shock absorber and relieve symptoms also [12]. In our study the laterally wedged insole improved pain with 1.1 units (out of 10) and function with 5 units (out of 100) from baseline. This was identical to brace therapy, although the compliance in the insole group was significantly ($p = 0.015$) higher. The optimal amount of time to wear an insole or brace during the day has not been determined yet. Some have suggested that proprioception plays a major role in the working mechanism of a brace [14]. Perhaps there is a threshold in time after which wearing the intervention does not contribute to the effectiveness. Another explanation might be that the insole failed to reduce varus malalignment. Lateral-wedge foot orthoses as well as bracing have been suggested to unload the diseased medial compartment and improve symptoms by providing valgus stress [15]. We used a 10 millimeters cork elevation, which represents a 6º lateral wedge, because more elevation is uncomfortable to wear [13]. Our analysis showed no significant reduction in varus malalignment with the use of a laterally wedged insole. Alignment only provides a static impression, and correction in the frontal plane may not affect clinical outcomes in the short term. Ramsey et al. demonstrated that when knees with medial compartment osteoarthritis are braced, neutral alignment performs as well as or better than valgus alignment [21]. Load distribution at the knee is determined mainly by the knee adduction moment [25]. Studies on the gait of small amount of patients have shown that insoles as well as knee bracing significantly reduce the adduction moment about the knee [15]. The improvement in knee pain we noticed in both groups may be attributed to the unloading of the diseased compartment during gait. Braces appear to provide greater reductions of knee load than insoles [9,19]. This may explain that although the laterally wedged insole was worn significantly ($p = 0.006$) longer during the day with a mean of 8 hours compared to 5.5 hours for the brace, it did not result in better clinical outcomes.

Changes in knee joint loading due to lateral shoe wedges and valgus bracing are small [25]. These small effects for both the insole and brace groups probably prevented us to observe significant differences between the two interventions. Our power permitted us to detect a 15% difference in pain reduction from baseline between both groups. In hindsight, this may have been to optimistic because a recent cross-over study failed to demonstrate changes more than 10% between a neutral and a laterally wedged insole [1]. Furthermore we found no significant differences in percentage of responders after 6 months follow-up for both interventions (insole group 13% versus brace group 20%). In accordance to the OMERACT-OARSI set of responder criteria we defined a responder as having an improved score of ≥ 20% for pain and function compared to baseline scores [17]. Pham et al. also found low percentages of responders for pain (27%) and function (29%) in patients treated with a laterally wedged insole after 12 months [18]. It may be too ambitious to expect ≥ 20% improvement in function. Especially when one bears in mind that established operative treatment like valgus producing high tibial osteotomy in adequately corrected patients, only achieved 12% improvement on a 100-points HSS scale 1-year postoperative [4].

Ogata et al. suggested earlier that laterally wedged insoles are most effective in patients with low grade OA [16]. Based on explorative subgroup analysis we found that almost half of our patients with medial OA K-L < grade 2 responded to the laterally wedged insole after 6 months. Few alternative treatments for patients with symptomatic mild knee OA do exist. Correction osteotomy in active patients has good results [20], but surgery can present complications. We found that a 10 mm laterally wedged insole was well tolerated, and had a borderline significant ($p = 0.068$) better response than valgus bracing in patients with K-L grade 1. Especially for patients who do not want to undergo surgery this may provide an alternative treatment option, which may be the focus of future research.

In summary, we found no differences in effectiveness of a 10 mm laterally wedged leather shoe inlay and a commercially available valgus unloader brace in the treatment of patients with symptomatic medial OA of the knee joint, despite a significant better compliance for the insole group. Both devices achieved no correction of knee varus malalignment in the frontal plane. According to the OMERACT-OARSI set of responder criteria for clinical trials in OA, about one sixth of our patients benefited from either the insole or brace intervention after 6 months follow-up.

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Conflict of interest

The authors declare that they have no conflict of interest. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. No funds were received in support of this study.

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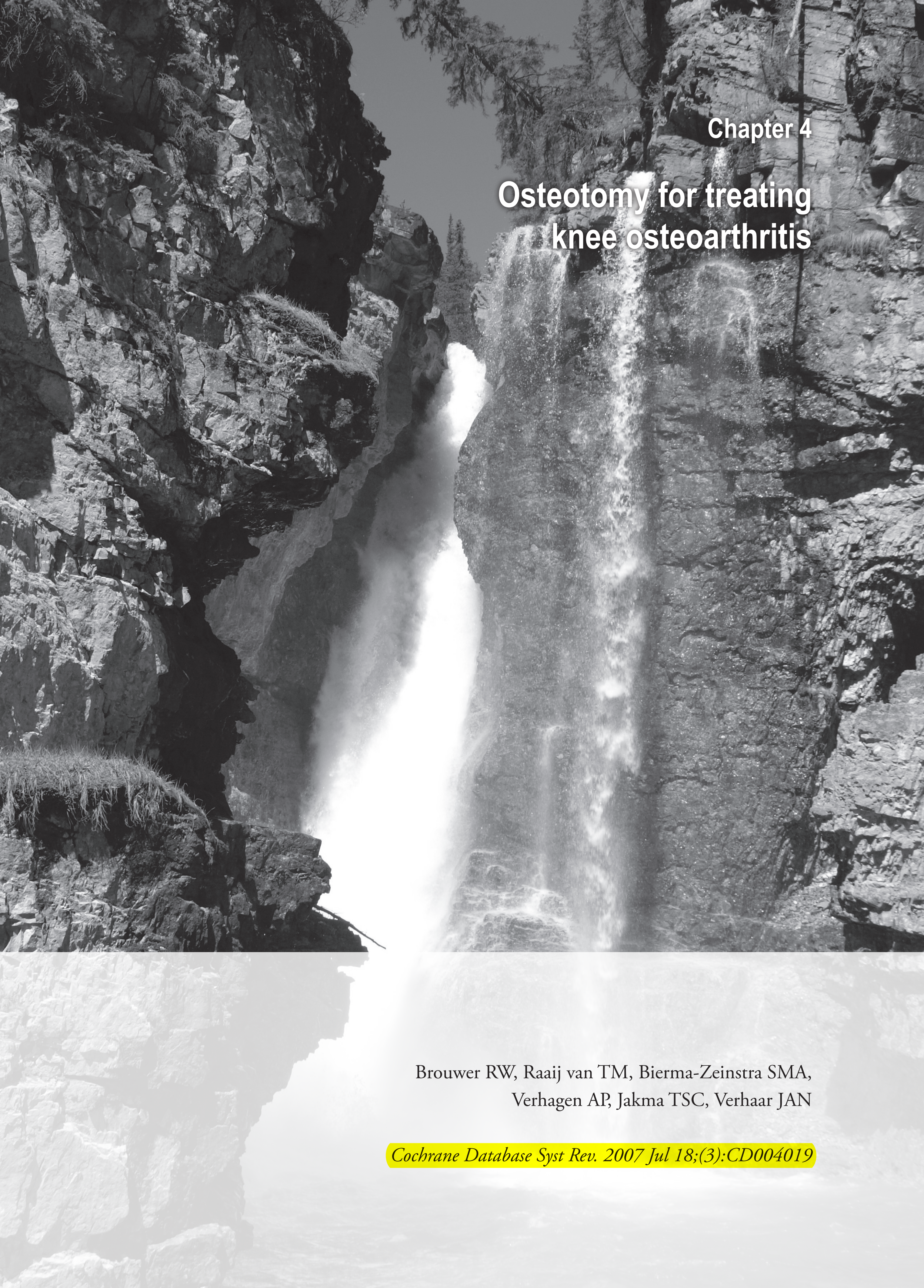

Chapter 4

Osteotomy for treating knee osteoarthritis

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Cochrane Database Syst Rev. 2007 Jul 18;(3):CD004019

Synopsis

This summary of a Cochrane review presents what we know from research about the effect of an osteotomy for osteoarthritis of the knee. The review shows that:

In people with osteoarthritis of the inside of the knee,
-an osteotomy can improve pain and function
-it is not known which techniques are better and which should be used
-some osteotomy techniques may lead to more complications
-it is not known whether an osteotomy (valgus high tibial osteotomy) is better than no surgery at all
But there is not enough evidence to be certain of these results.

What is osteoarthritis of the knee and what is an osteotomy?
Osteoarthritis (OA) is the most common form of arthritis that can affect the hands, hips, shoulders and knees. In OA, the cartilage that protects the ends of the bones breaks down and causes pain and swelling and can change the alignment of joints.

There are three main types of surgery for osteoarthritis of the knee: a total knee replacement (arthroplasty), partial knee replacement (minimally invasive), and an osteotomy. An osteotomy is surgery in which the bones are cut and reshaped. An osteotomy changes the position of the knee so that the bones bear on an area of the knee that is not diseased. By 'unloading' the bear to a better part of the knee, it is thought that an osteotomy may decrease pain, improve function, slow damage in the knee, and possibly delay the need for partial or total knee replacement surgery.

What are the effects of an osteotomy?
The studies included in this review did not compare an osteotomy to no surgery at all. All of the studies tested a 'valgus high tibial osteotomy' (HTO) for osteoarthritis on the inside of the knee.

All studies showed that people had less pain and improved function in the knee 2 months to 7½ years after any type of HTO.

Some of the studies compared HTO to HTO with another procedure such as using a tourniquet, abrasion and overcorrection. Some compared HTO to HTO plus electromagnetic stimulation, and a plaster cast to a hinged-cast brace after surgery. Improvements in pain and function may not be any different between these different techniques. But there is not enough evidence to be certain.

Some studies also compared HTO to a partial knee replacement, the benefits may not be different between these surgeries. But there is not enough evidence to be certain.

When comparing HTO techniques with each other, some techniques may lead to complications, such as pin-track infections or more revisions when a total knee replacement is done in the future. But there is not enough evidence to be certain.

Abstract

Background

Patients with unicompartmental osteoarthritis of the knee can be treated with a correction osteotomy. The goal of the correction osteotomy is to transfer the load bearing from the pathologic to the normal compartment of the knee. A successful outcome of the osteotomy relies on proper patient selection, stage of osteoarthritis, achievement and maintenance of adequate operative correction. This is an update of the original review published in Issue 1, 2005.

Objectives

To assess the effectiveness and safety of an osteotomy for treating osteoarthritis of the knee.

Search strategy

Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE (Current contents, Health STAR) up to October 2002 in the original review and in the update until May 2007. Reference lists of identified trials were screened.

Selection criteria

Randomised and controlled clinical trials comparing a high tibial osteotomy or a distal femoral osteotomy in patients with unicompartmental osteoarthritis of the medial or lateral compartment of the knee.

Data collection & analysis

Two review authors independently selected trials, extracted data and assessed trial quality. Due to heterogeneity of the studies, pooling of outcome measures was not possible.

Main results

Thirteen studies involving over 693 people were included; 11 studies were included in the first version and two studies and one longer follow-up study were included in this update. All studies concerned a valgus high tibial osteotomy (HTO) for medial compartment osteoarthritis of the knee. Six studies, in which two studies were included in this update,

compared two techniques of HTO. One study compared HTO alone versus HTO with additional treatment. Four studies compared within the same type of HTO, different peri-operative conditions (two studies) or two different types of post-operative treatment (two studies). Two studies, including the longer follow up, compared HTO with unicompartmental joint replacement. No study compared an osteotomy with conservative treatment.
Most studies showed improvement of the patient (less pain and improvement of function scores) after osteotomy surgery, but in the majority of the studies there was no significant difference with other operative treatment (other technique of HTO/ unicompartmental joint replacement). Overall, the methodological quality was low.

Reviewers' conclusions
Based on 13 studies, we conclude that there is 'silver' level evidence (www.cochranemsk.org) that valgus HTO improves knee function and reduces pain. There is no evidence whether an osteotomy is more effective than conservative treatment and the results so far do not justify a conclusion about effectiveness of specific surgical techniques.

Background
Osteoarthritis of the knee (gonarthrosis) is a common medical condition that is seen quite often in orthopaedic practice and causes pain and disability. The knee joint can be divided into three compartments:
(1) the medial compartment consisting of the medial femur condyle and medial tibial plateau;
(2) the lateral compartment consisting of the lateral femur condyle and lateral tibial plateau;
(3) the patellofemoral compartment.

Osteoarthritis of the entire knee is distinguished from osteoarthritis of one compartment (Grelsamer 1995), which is generally caused by a mechanical problem (Tetsworth 1994). The mechanical axis of a straight leg is a line passing from the centre of the hip, through the centre of the knee to the centre of the ankle (Phillips 1998). Patients with osteoarthritis of the medial compartment often have varus alignment, and the mechanical axis and load bearing pass through the medial compartment. Patients with osteoarthritis of the lateral compartment often have a valgus alignment, and the mechanical axis and load bearing pass through the lateral compartment. Malalignment increases risk and progression of knee osteoarthritis and predicts decline in physical function (Sharma 2001).

Patients with osteoarthritis not reacting to non-surgical therapy, can be treated with a correction osteotomy (Aglietti 2000; Coventry 1993; Edgerton 1993; Naudie 1999). The goal of the correction osteotomy is to transfer the mechanical axis and load bearing from the pathologic to the normal compartment. Patients with osteoarthritis of the medial compartment can be treated with a proximal tibia valgus osteotomy and patients with osteoarthritis of the lateral compartment with a distal femoral varus osteotomy or a proximal tibia varus osteotomy.

Literature suggests that a correction osteotomy for gonarthrosis of one compartment has good results, but there are different operation techniques and alternatives (Bouwmeester 2002; Broughton 1986; Stukenborg 2001). A successful outcome of the osteotomy relies on a proper patient selection, stage of arthrosis, achievement and maintenance of adequate operative correction (Berman 1991; Cameron 1997; Finkelstein 1996; Hernigou 1987; Mathews 1998; Naudie 1999; Rudan 1990). The osteotomy cannot stop the degenerative process and most of the patients will get a total knee arthroplasty. However, the osteotomy seems to delay the progress of deterioration.

Objectives

To assess the effectiveness and safety of an osteotomy to treat osteoarthritis of the knee.

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and controlled clinical trials (CCTs) investigating all types of osteotomy for treating osteoarthritis of the knee compared to other surgical and non-surgical treatment.

Types of participants

Adult patients (>18 years) with unicompartmental osteoarthritis of the medial or lateral compartment of the knee confirmed by radiographic or arthroscopic investigation.

Types of interventions

Types of interventions

All types of high tibial osteotomy and distal femoral osteotomy for patients with unicompartmental gonarthrosis including osteotomy versus conservative treatment, different techniques of osteotomy, and osteotomy versus other surgery.

Types of outcome measures

The primary measure of effectiveness is pain relief, as suggested by the third conference of Outcome Measures in Rheumatology (OMERACT) (Bellamy 1997):

The core OMERACT measure for hip, knee, and hand osteoarthritis include:
• pain;
• physical function;
• patient global assessment;
• joint imaging (for studies of one year and longer);
• health related quality of life measure;
• physician global assessment.

Secondary outcomes include:
• inflammation;
• stiffness;
• performance-based measures, tenderness, time to revision surgery, difficulties at revision
• surgery, number of flares, and biologic markers.

Safety and side effects
Number of people with side effects were measured whenever possible.
Safety was scored according to occurrence of complications postoperatively.
Side effects were scored according to anatomic changes after HTO, such as patellar descent and change of inclination angle of the tibial plateau, which possibly influence the results of total knee arthroplasty in the future.

Search strategy for identification of studies
We searched the Cochrane Central Register of Controlled Trials (CENTRAL). We also searched MEDLINE and EMBASE (Current contents, Health STAR) up until October 2002 in the original review and in the update until May 2007 in the update to identify all clinical trials concerning an osteotomy for gonarthrosis. MEDLINE searches for clinical trials were based on the Cochrane Collaboration strategy. No language restriction was applied.
In MEDLINE, the following search strategy was combined with all phases of the optimal trial search strategy (Robinson 2002) and was modified for uses in other databases:

1. osteoarthritis, knee
2. osteoarthritis
3. (osteoarthritis or osteoarthrosis or degenerative joint disease).tw.
4. 2 or 3
5. knee joint/ or knee.tw.
6. 4 and 5
7. 1 or 6

8. exp Osteotomy/
9. Osteotomy$.tw.
10. 8 or 9
11. 7 and 10
12. meta-analysis.pt,sh.
13. (meta-anal: or metaanal:).tw.
14. (quantitativ: review: or quantitativ: overview:).t.w.
15. (methodologic: review: or methodologic: overview:).tw.
16. (systematic: review: or systematic: overview) .tw.
17. review.pt. and medline.tw.
18. or/12-17
19. clinical trial.pt.
20. randomised controlled trial.pt.
21. tu.fs.
22. dt.fs.
23. random$.tw.
24. (double adj blind$).tw.
25. placebo$.tw.
26. or/ 19-25
27. 11 and 18
28. 11 and 26

Methods of the review

Selecting trials for inclusion

Two review authors (RB, TJ) selected the trials, initially based on title and abstract. The title, keywords and abstract were assessed to establish whether the study met the inclusion criteria regarding diagnosis, design and intervention. For each selected study, the full article was retrieved for final assessment. Next, two review authors (RB, TJ) independently performed a final selection of the trials to be included in the review, using a pre-tested standardized form. Disagreements on inclusion were resolved by discussion, and the final decision of a third review author (JV) was not necessary.

Methodology quality assessment

Two review authors (RB, SB) independently assessed the methodological quality of the included studies. They used the Delphi list (Verhagen 1998) and one additional question adapted from the criteria list for Methodological Quality Assessment (van Tulder 2003). Disagreements were resolved in a consensus meeting.

The nine questions from the Delphi list and the additional question with M are:

D1. Was a method of randomisation performed?
D2. Was the treatment allocation concealed?
D3. Were the groups similar at baseline regarding the most important prognostic indicators?
D4. Were the eligibility criteria specified?
D5. Was the outcome assessor blinded?
D6. Was the care provider blinded?
D7. Was the patient blinded?
D8. Were points estimates and measures of variability presented for the primary outcome measures?
D9. Did the analysis include an intention-to-treat analysis?
M. Was the surveillance active and of clinically appropriate duration?

The scores of the quality items of each study are presented in Additional Table 01. A score of 1 is given to each item with a 'yes' answer and a 0 score is given for a negative response.

Data extraction

Three review authors (RB, TJ, AV) independently extracted the data on the intervention, type of outcome measures, follow up, loss to follow up, and outcomes, using a pre-tested standardized form. The various outcome measures are presented separately.

Analysis

Methodology

The maximum number of points in assessing quality is 10 (Delphi list is 9 points). The measure of agreement between the two review authors (RB, SB) is presented as kappa.

Quantitative analysis

For dichotomous outcomes, we calculated relative risks (RR) with corresponding 95% confidence intervals. For continuous outcomes, standardised mean differences (SMD) with 95% confidence intervals were calculated. The RevMan 4.2 software (RevMan 2000) was used to analyze these data and the various outcomes are presented in Analyses graphs.
Pooling was not implemented, as trials were considered clinically heterogeneous concerning study population and intervention. Should this be possible in the future, results of comparable groups of trials will be pooled using a random-effects model and 95% confidence intervals.

For continuous outcomes both absolute and relative benefit were calculated. The absolute benefit is calculated as the improvement in the treatment group less the improvement in the control group, in the original units. The relative benefit (RPD) is calculated as the absolute benefit divided by the baseline mean of the control group. These results are described in the clinical relevance tables 02 - 36 (See Additional tables).

The analysis was set up to identify three study groups

A. Operative versus conservative treatment
B. Different operative treatments:
   1. different high tibial osteotomy techniques
   2. high tibial osteotomy versus unicompartmental joint replacement
   3. differences in perioperative conditions
C. Different treatment post surgery.

Qualitative analysis

Since the trial results are heterogeneous, an overall grading of evidence (Tugwell 2004) is used:

Platinum level

The Platinum ranking is given to evidence that meets the following criteria as reported.
Is a published systematic review that has at least two individual controlled trials each satisfying the following.
Sample sizes of at least 50 per group. If they do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
Blinding of patients and assessors for outcomes.
Handling of withdrawals > 80% follow up (imputations based on methods such as Last Observation Carried Forward (LOCF) acceptable).
Concealment of treatment allocation.

Gold level

The Gold ranking is given to evidence if at least one randomised clinical trial meets all of the following criteria for the major outcome(s) as reported.
Sample sizes of at least 50 per group. If they do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
Blinding of patients and assessors for outcomes.
Handling of withdrawals > 80% follow up (imputations based on methods such as Last Observation Carried Forward (LOCF) acceptable).
Concealment of treatment allocation.

Silver level
The Silver ranking is given to evidence if a randomised trial does not meet the above criteria. Silver ranking would also include evidence from at least one study of non-randomised cohorts who did and did not receive the therapy or evidence from at least one high quality case-control study. A randomised trial with a 'head-to-head' comparison of agents is considered Silver level ranking unless a reference is provided to a comparison of one of the agents to placebo showing at least a 20% relative difference.

Bronze level
The bronze ranking is given to evidence if there is at least one high quality case series without controls (including simple before/after studies in which the patient acts as their own control) or if it is derived from expert opinion based on clinical experience without reference to any of the foregoing (for example, argument from physiology, bench research or first principles).

Description of studies
From the search strategy the review authors (RB, TJ, TR) independently selected 14 abstracts. After reading the full articles, one trial (Odenbring 1992b) was excluded because the design was a post-hoc analysis. After checking the reference lists of publications we added one study (Myrnerts 1980).
One study (Weidenhielm 1993) published the one-year results in 1993 and the five-year follow up results in 2005 (Borjesson 2005 in Weidenhielm 1993).
The remaining 13 studies included, in which two studies (Brouwer 2005; Brouwer 2006) were included in the update, are described in detail in the 'Characteristics of included studies' table. All studies concerned a valgus high tibial osteotomy (HTO) for medial compartment osteoarthritis of the knee, but were quite heterogeneous.
The mean number of patients in the thirteen studies was 52 (range 30 to 88). The interventions were different techniques of HTO, HTO versus unicompartmental joint replacement, different per-operative conditions, and different types of postoperative treatment. Outcome measures were range of motion (ROM), walking distance, VAS, complications , Western Ontario-McMaster (WOMAC) osteoarthritis score, Hospital for Special Surgery (HSS) knee score, Lysholm score, Wallgren-Tegner score, Nottingham Health Profile (NHP) score , British Orthopaedic Association (BOA) knee score, Japanese Orthopaedic Association (JOA) knee score, quality of life (EuroQol), gait analysis, joint imaging, degree of osteoarthritis, leg alignment (Hip Knee Ankle (HKA)-angle, and Femoral Tibial Angle (FTA), change of patellar height and inclination angle of the tibial plateau.

Adili 2002 described a matched comparative analysis of two techniques: the osteotomy with the Ilizarov apparatus versus the Coventry-type closing wedge osteotomy. Inclusion criteria were varus alignment and symptomatic medial compartment osteoarthritis. Both groups consisted of 15 participants, but they were not randomised. The study included 20 men and 10 women. The mean age was 52 and the body mass index was 32.8. The mean degree of varus was three degrees (FTA). The follow up was different: 25.4 months in the Ilizarov group and 30.9 months in the Coventry group.

Akizuki 1997 described a RCT of 79 participants (88 knees). Forty five participants (51 knees) were treated by osteotomy with arthroscopic abrasion arthroplasty and 34 participants (37 knees) were treated by osteotomy alone. The inclusion criterion was medial compartment osteoarthritis. The study included 9 men and 70 women. The mean age was 64 years. The mean degree of varus was five degrees (FTA). The follow up was 4.8 years in the osteotomy with abrasion group and 3.5 years the osteotomy group.

Brouwer 2005 presented a RCT in which two techniques were evaluated: the opening wedge high tibial osteotomy versus the closing wedge high tibial osteotomy. The criteria for inclusion included osteoarthritis of the medial compartment with medial pain and varus malalignment of the mechanical axis measured on long- standing radiographs. The outcome measures were factors which may cause difficulties in conversion to total knee arthroplasty and were scored as side effects. Fifty one participants (33 men and 18 women) were randomised (opening HTO; n = 26/ closing HTO; n = 24). The mean-age was 50. The mean degree of varus was seven degrees (HKA-angle). The follow up was one year and one participant was lost.

Brouwer 2006 published a second RCT study comparing the opening wedge high tibial osteotomy versus the closing wedge high tibial osteotomy. The criteria for inclusion included osteoarthritis of the medial compartment with medial pain and varus malalignment of the mechanical axis measured on long- standing radiographs. Ninety two participants (59 men and 33 women) were randomised (opening HTO; n = 45/ closing HTO; n = 47). The mean-age was 50. The mean degree of varus was six degrees (HKA-angle). The outcome measures were accuracy of the operative correction, pain severity (VAS), knee function score (HSS) and walking distance. The follow up was one year. One participant was lost to follow up and for one participant the follow-up data were incomplete.

Magyar 1999a presented a RCT of two techniques: the hemicallotasis opening wedge osteotomy (HCO; 24 participants/25 knees) versus the closing wedge high tibial osteotomy (HTO; 22 participants/25 knees). Inclusion criteria were medial gonarthrosis and younger, active patients. The study included 32 men and 14 women. The mean age was 55 years. The mean degree of varus was nine degrees (HKA-angle). The follow up was two years. There were two drop outs (one in each group) for the NHP assessment.

Magyar 1999b published a second RCT study with radiostereometry (RSA). RSA is a method that uses tantalum markers in the bone to determine 3-dimensional changes in the osseous correction. This study is probably linked with the study Magyar 1999a, because the participants and interventions (HCO versus HTO) are identical. The inclusion criterion was medial gonarthrosis grade I-III. Thirty-three participants (22 men and 11 women) were studied: HCO 18 participants/19 knees; HTO 15 participants/16 knees with a baseline grade I-III. The mean age was 54 years and the mean body mass index was 29.5. The mean degree of varus was nine degrees (HKA-angle). The follow up was one year.

Mammi 1993 described a double-blind study of 40 participants. In this study, the HTO technique was the same but post-operatively participants were randomly assigned to the intervention group (long plaster cast with an electromagnetic field stimulation; n = 20) or the control group (a long plaster cast with a dummy stimulator; n = 20). The randomisation was according to their order of admission to the hospital. Inclusion criteria were maximum age of 80 years, good health, and requiring tibial reduction osteotomy. The study included 9 men and 31 women. The mean age was 62 years. The follow up was 60 days. There were two dropouts in the intervention group versus one dropout in the control group.

Motycka 2000 published a RCT of 65 patients to look at the side effects of HTO. He studied the incidence of thrombosis in HTO with (n = 37) and without (n = 28) the use of a tourniquet. A Dimer-test and phlebography were used to confirm the diagnosis. The inclusion criterion was varus osteoarthritis. The study included 30 men and 35 women. The mean age was 61 years. There was a follow up nine weeks. There was a dropout of 15 participants which caused the inequality in numbers in the groups.

In the RCT of Myrnerts 1980, the closing wedge HTO technique was the same, but the 77 participants were allocated at random to two groups: the normal correction group (n = 40) and the five degree overcorrection group (n = 37). The inclusion criterion was varus alignment. The study included 32 men and 45 women. The mean age was 61 years. All the participants had a follow up of one year and "most" were examined 24 months post-operatively.

Nakamura 2001 presented a RCT where 46 participants were randomly allocated to either a hemicallotasis opening wedge osteotomy (HCO; 23 participants/25 knees) or a dome osteotomy (DMO; 23 participants/25 knees). The inclusion criterion was medial osteoarthritis of the knee. This study included 9 men and 37 women. The mean age was 63 years. The mean degree of varus was two degrees (FTA). They studied changes of FTA, patella tendon length, inclination angle of tibial plateau and condylar offset at one year post-operative. The follow up was one year.

Odenbring 1992 published a RCT study with 32 participants randomised to either a cylinder plaster cast (n = 17) or a hinged cast-brace (n = 14) after HTO. Because of a complication, one patient in the brace group was excluded and not included in analysis. Inclusion criteria were stages I-III medial gonarthrosis. The follow up was one year.

Stukenborg 2001published a RCT of 60 participants. The study compared high tibial osteotomy (HTO; n = 32) with unicompartmental joint replacement (= unicompartmental knee arthroplasty UKA; n = 28). Inclusion criteria were medial unicompartmental OA, varus < 10 degrees, flexion contracture < 15 degrees, age > 60 years, ligament instability < grade II. This study included 25 men and 35 women. The mean age was 67 years. The mean degree of varus was nine degrees (HKA-angle). The follow up was 7.5 (6.6 to 10) years.
Weidenhielm 1993 published the one-year results of an ongoing RCT. This RCT has been started with 100 participants, but during the one-year follow up 41 participants were lost and were not included for the analysis. The reason for the big number of patients who were lost to follow up was not described. In 59 participants a HTO (n = 23) was compared with the UKA (n = 36). Inclusion criteria were medial OA grade I-II, 55 to 70 years old. This study included 28 men and 31 women. The mean age was 64 years. The mean body mass index was 28.5. The mean degree of varus was nine degree (HKA-angle). The five-year follow up results have been published in 2005 (Borjesson 2005 in Weidenhielm 1993). After the five-year follow up there were 40 participants left: HTO (n = 18) and UKA (n = 22).

Methodological quality of included studies
Further details on methodolgical quality of each study is available in 'Additional Table 01'.
In two studies, there was no randomisation performed (Adili 2002; Akizuki 1997).
In five studies, the randomisation procedure was adequate or concealed (Brouwer 2005; Brouwer 2006; Magyar 1999a; Magyar 1999b; Odenbring 1992).
In five studies the intervention groups were not similar at baseline regarding the most important prognostic indicators (Brouwer 2005; Brouwer 2006; Mammi 1993; Motycka 2000; Nakamura 2001).
In only six studies the eligibility criteria were specified (Adili 2002; Brouwer 2005; Brouwer 2006; Mammi 1993; Stukenborg 2001; Weidenhielm 1993).
In most of the trials the blinding procedures of the outcome assessors, treatment providers, and participants frequently scored 'no'.
In two studies, the outcome assessor was blinded (Magyar 1999a; Mammi 1993) and only in one of these studies, the care provider and the patient were also blinded (Mammi 1993).
With the exception of one study (Myrnerts 1980) points estimates and measures of variability were presented for the primary outcome measures.
Five studies did not include an intention-to-treat analysis (Adili 2002; Mammi 1993;

Motycka 2000; Myrnerts 1980; Weidenhielm 1993).
In all studies the surveillance was active and of clinically appropriate duration.
Overall the quality was low: Only one study presented adequate or concealed randomisation procedure and adequate blinding (Magyar 1999a).
The measure of agreement (kappa) between the two review authors (RB, SB) was 0.59. Disagreement occurred mainly because of reading errors and differences in interpretation of the methodology criteria list.

Results

All studies used different interventions or comparison treatments with a wide variety of outcome measures. Pooling of the results was not possible due to the heterogeneity of the studies. We have described the different comparisons and performed a best evidence synthesis and an overall grading of evidence based on these studies.
The results are also presented in the clinical relevance tables 02-36 (See Additional tables).

A. Osteotomy versus conservative treatment:
No studies found.

B1. Different techniques of a high tibial osteotomy:
Six trials compared two techniques of high tibial osteotomy (Adili 2002; Brouwer 2005; Brouwer 2006; Magyar 1999a; Magyar 1999b; Nakamura 2001).
In Adili 2002 the Ilizarov group showed significantly less (WOMAC) pain with a relative percentage difference (RPD) of 24.2% improvement. Ilizarov also showed better WOMAC stiffness (RPD 32.6%) and function (RPD 33.3%) as well as more patient satisfaction (Clinical relevance Table 02; Table 03; Table 04). The Ilizarov group had significantly more complications; especially pin-track infections: RR 1.88 (95% CI 1.15 to 2.92) (Graph 02.06)

In Brouwer 2005, the patellar height measured by the Insall Salvati (IS) (RPD 11.0%) and Blackburn Peel (BP) (RPD 13.3%) methods was significantly more decreased after an opening wedge high tibial osteotomy (HTO) compared with a closing wedge HTO. The angle of inclination of the tibial plateau measured by the Moore and Harvey method differed significantly (RPD 62.7%), increasing after opening wedge HTO and decreasing after closing wedge HTO.

In Brouwer 2006 the closing wedge HTO achieved significantly more accurate correction with less deviation after at follow up at one year (RPD 47.1%). The severity of pain (VAS), knee score (HSS) and walking distance improved in both groups, but the difference was not significant. Due to the pain there was significantly more hardware removal (plate/screws, staples) after the opening wedge HTO compared with the closing-wedge HTO.

In Magyar 1999a, there was a significant improvement in HSS, Lysholm, Wallgren-Tegner, NHP scores in both groups, but no significant difference between both groups. The hemicallotasis osteotomy (HCO) group had significantly more complications, especially pin-track infections. The hospital stay of the HCO group was significantly shorter. After one year follow up, the HTO-group showed significantly more loss of correction. The HCO-group had significantly more patients with optimal postoperative correction (HKA 182 to 186 degrees) after one year follow up; the two year follow-up results showed the same tendency, but the difference was not significant.

In Magyar 1999b the alignment (HKA-angle) was not significantly different one year postoperatively. The HCO group showed significantly less translation, which means a more stable fixation of the osteotomy.

In Nakamura 2001, similar to the Brouwer 2005 RCT, factors which may cause difficulties in conversion to total knee arthroplasty were measured and scored as side effects. The HCO group had significantly less decrease in patellar height measured by IS, less change in inclination angle of the tibial plateau measured by Moore and Harvey method and less increase of the tibial offset. The FTA was not significantly different. The outcomes were presented as mean with a range, but without a standard deviation or 95% confidence intervals. This prevented any form of statistical analysis.

Pooling of the results (complication after HTO) of the studies Adili 2002, Brouwer 2006 and Magyar 1999a was possible and showed less complications after a closing wedge HTO compared with another HTO technique (hemicallotasis and opening HTOs) with a pooled effect of RR 3.06 (95%CI 1.44 to 6.53) (Graph 02.06).

B2. High tibial osteotomy versus the unicompartmental joint replacement:
Two studies were found (Stukenborg 2001; Weidenhielm 1993).
The HTO in Stukenborg 2001showed better knee and function scores, but the differences were not significant. The range of motion (ROM) was 103 degrees (HTO) versus 117 degrees (UKA). The HTO group had more complications (nine versus two). The Kaplan-Meier survivorship after 5 and 10 years was not significantly different.
In Weidenhielm 1993 at one-year follow up and in Borjesson 2005 (Weidenhielm 1993) at five -year follow up, the BOA-score, pain during walking and the passive ROM and gait analysis tests improved after surgery in both groups (HTO and UKA), but there were no

differences between the groups. The BOA, pain during walking and the passive ROM scores after five-year follow up were presented as median and range. This prevented any form of statistical analysis. Only three months after surgery some gait analysis tests showed greater improvement after unicompartmental joint replacement, compared with HTO. This difference may be explained by the fact that to achieve consolidation of the osteotomy the patients were immobilized with a plaster cast from groin to ankle during six weeks postoperatively.
B3. Differences in per-operative conditions:
Three studies were found (Akizuki 1997; Motycka 2000; Myrnerts 1980).

Akizuki 1997 found there was no difference of the mean Japanese Orthopaedic Association (JOA) knee score at final follow up between the osteotomy with abrasion group and the osteotomy alone group. The one year post-operative FTA angle did not differ.

After 12 months in the Myrnerts 1980 RCT, there was no significant difference in pain reduction between the normal and an overcorrection group. However, the overcorrection group was significantly more satisfied with the results of the operation and reported significantly better walking ability. The ROM and complications were described for the whole group with percentages and no numbers. This prevented any form of statistical analysis.

Motycka 2000 found that the average incidence of thrombosis was 10.8% and occurred five times with the use of a tourniquet and one time without the use of a tourniquet, but the difference was not significant.
C. One technique of high tibial osteotomy with different types of post-operative treatment
Two studies were found (Mammi 1993; Odenbring 1992).

In Mammi 1993, the intervention group with a long plaster cast with electromagnetic field stimulation had significantly positive effect on the rate of union of the HTOs compared to the control group with a dummy stimulator.

After one year follow up in the Odenbring 1992 trial, there was significantly better range of motion in the hinged cast-brace group compared to the cylinder plaster cast group. There were neither significant differences in the other clinical results (degree of pain, Lysholm knee score) nor changes in knee alignment or progression of osteoarthritis.

Discussion
The purpose of this systematic review analysis was to assess the effectiveness and safety of an osteotomy for osteoarthritis of the knee. All the studies concerned valgus HTO for medial compartment osteoarthritis of the knee. Only thirteen studies were included in this updated review and no study compared an osteotomy with conservative treatment and no RCTs or

CCTs examined the effect of a varus osteotomy for lateral compartment osteoarthritis of the knee.

Unfortunately the methodological quality of the included studies was generally moderate: the randomisation procedure was frequently not described or insufficient. In the majority of the trials, the inclusion and exclusion criteria were briefly presented. The number of participants in most of the studies was too low to show significant differences. In most studies the blinding procedures were insufficient, although we realize that blinding is not always possible. Except for the study of Stukenborg 2001 the follow up of the trials was relatively short. Some studies did not provide full data on outcome measures, measures of variability (such as the standard deviation) were especially lacking (Magyar 1999b; Myrnerts 1980; Nakamura 2001), which makes quantitative analysis impossible. Due to the heterogeneity of the studies, pooling of the results was only possible for the complication rate after a closing wedge HTO compared with another HTO technique.

Although in most studies patients improved in knee function and had pain reduction after HTO, there were no studies which compared these results with conservative treatment.
There was only one study which showed a significant difference in WOMAC pain and function between different techniques (Adili 2002). Only one study showed that the closing wedge HTO achieves a significantly more accurate correction with less morbidity compared with the opening wedge technique (Brouwer 2006).
The safety of an osteotomy may be in question: the HTO technique with the external fixator (Adili 2002; Magyar 1999a) had a significantly higher infection rate (pin-track), but showed fewer side effects for revision to total knee arthroplasty in the future (Nakamura 2001). The opening wedge HTO showed more side effects or revision to total knee arthroplasty in the future compared with the closing wedge HTO (Brouwer 2005). Early mobilisation of the knee joint postoperative seems of imminent importance: the postoperative treatment with a cylinder plaster showed significantly less reduction of range of motion (Odenbring 1992).

Conclusions for each group

A. Osteotomy versus conservative treatment

No studies were found: there is no evidence to suggest that an HTO is more effective than conservative treatment.

B1. Different techniques of a high tibial osteotomy

According to the six studies, we conclude:
there is silver level evidence for significantly less pain and a better function on WOMAC scale after a HTO with Ilizarov compared with a closing wedge HTO;

- there is silver level evidence for no difference of FTA after HCO or dome osteotomy HTO;
- there is silver level evidence for more optimal 1-year postoperative correction after HCO compared with closing wedge HTO;
- there is silver level evidence for less side-effects influencing total knee arthroplasty in the future with HCO technique compared with the DMO;
- there is silver level evidence for less side-effects influencing total knee arthroplasty in the future with the closing wedge HTO compared with the opening-wedge HTO;
- there is silver level evidence for more short term complications after HTO with an external fixator compared with a closed wedge HTO;
- there is silver level evidence for significantly a more accurate correction after a closing-wedge HTO compared with a opening-wedge HTO;
- there is silver level evidence for less morbidity after the closing-wedge HTO compared with the opening-wedge HTO.

B2. High tibial osteotomy versus the unicompartmental joint replacement

According to these two studies, we conclude:

- there is silver level evidence for no significant difference in pain and function after HTO compared to UKA;
- there is silver level evidence that HTO causes more complications compared with UKA;
- there is silver level evidence for no difference in gait analysis between UKA and closed wedge HTO.

B3. Differences in peri-operative conditions

According to these three studies we conclude:

- there were no studies which measured pain as an outcome for this comparison;
- there is silver level evidence for no differences of JOA knee score and FTA after HTO without and HTO with abrasion arthroplasty;
- there is silver level evidence that there is no significant difference in incidence of thrombosis during HTO with or without a tourniquet;
- there is silver level evidence that HTO with five degrees overcorrection has better walking ability and more patient satisfaction compared with HTO with normal correction.

C. One technique of high tibial osteotomy with different types of post-operative treatment

According to these two studies we conclude:

there were no studies which measured pain as an outcome for this comparison;

- there is silver level evidence that electromagnetic field stimulation stimulates HTO healing;

- there is silver level evidence that a hinged cast-brace after HTO results in a better range of motion compared with a post-operative plaster cast.

Therefore, based on the results of 13 studies, we conclude that there is no evidence to indicate that an osteotomy is more effective than conservative treatment and the results so far do not allow us to draw any conclusion regarding the effectiveness of specific surgical techniques.

Reviewers' conclusions

Implications for practice

Based on the results of this review we conclude that valgus HTO improves knee function and reduces pain, but there are no significant differences between different techniques. There is limited evidence for the effectiveness of an osteotomy for treating medial compartment osteoarthritis when compared with unicompartmental joint replacement. It is unclear which technique of osteotomy we have to use, quite a number of complications were reported, and there is no evidence of whether an osteotomy is more effective than conservative therapy.

Implications for research

1. The methodological quality of future studies will be improved by a concealed randomisation.
2. New research should use outcome measures relevant to the patients, and adequate and responsive to the treatment under study. One general knee score makes pooling of the results possible. Follow up should be of sufficient length to assess long-term effects.
3. New research should provide full data on outcome measures, including the mean and standard deviation or 95% confidence intervals.
4. Therefore, large, high quality research is needed, focusing on appropriate allocation concealment, blinding and an adequate data presentation and analysis. The design and reporting of future trials should conform to the CONSORT-statement (Ross 1996).
5. Future research should examine the effect of treatments not only in pragmatic trials comparing various interventions with each other, but also in more explanatory trials comparing the intervention with conservative or no treatment control group.
6. Future research should focus on treating unicompartmental knee osteoarthritis because there are a broad variety of treatments available and most treatments are costly, and data on effectiveness are not available.

We conclude that performing randomised studies with high methodological quality concerning the effectiveness of osteotomy compared to other frequently performed treatments is both possible and necessary to provide strong evidence on the effectiveness of treatments in knee osteoarthritis.

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Potential conflict of interest

There is potential conflict of interest because two new included studies were conducted by the author of the systematic review.

Characteristics of included studies

Study	**Adili 2002**
Methods	CCT; no randomization Not blinded
Participants	Varus alignment and symptomatic medial compartment osteoarthritis
Intervention	I: high tibial osteotomy (HTO) using an Ilizarov apparatus (n=15) C: closed wedge HTO (n = 15) Follow up: I = 25.4 months C = 30.9 months
Outcomes	WOMAC scores FTA Patient satisfaction Complications
Notes	The follow up period was different No drop-outs mentioned
Allocation concealment	D – Not used

Study	**Akizuki 1997**
Methods	CCT; no randomisation: patients were assigned in both groups in turn Not blinded
Participants	Medial compartment osteoarthritis
Intervention	I: HTO with arthroscopic abrasion (n = 45) C: HTO alone (n = 34) Follow up: I = 4.8 years C = 3.5 years
Outcomes	JOA knee score FTA
Notes	The follow up period and the number of the patients were different. No drop-outs
Allocation concealment	D – Not used

Study	**Brouwer 2005**
Methods	RCT; computer blocked randomisation Not blinded
Participants malalignment	Osteoarthritis of the medial compartment and varus
Intervention	I: opening wedge HTO (n = 26) C: closing wedge HTO (n = 24) Follow up: 1 year
Outcomes	Patellar height Inclination of the tibial plateau
Notes	C: 1 drop-out
Allocation concealment	A – Adequate

Study	**Brouwer 2006**
Methods	RCT; computer blocked randomisation Not blinded
Participants	Osteoarthritis of the medial compartment with medial joint pain and varus malalignment
Intervention	I: opening wedge HTO (n = 45) C: closing wedge HTO (n = 47) Follow up: 1 year
Outcomes	Accuracy of postoperative correction VAS pain score HSS knee score Walking distance Complications
Notes	I: 1 drop-out C: 1 drop-out
Allocation concealment	A – Adequate

Study	**Magyar 1999a**
Methods	RCT; randomisation procedure was not described The follow-up examination was blinded
Participants	Medial gonarthrosis and younger active patients
Intervention	I: hemicallotasis open-wedge osteotomy (HCO/ n = 24) C: closing wedge HTO (n = 22) Follow up: 2 years
Outcomes	VAS score ROM HSS knee score Lysholm score Wallgren-Tegner activity score NHP score HKA-angle Hospital stay Complications
Notes	Only pre- and post analysis Only subgroup scores of the NHP were given. In our opinion the ROM of the HCO group on page 446 is not correct. Two drop-outs for the NHP assessment; one in each group.
Allocation concealment	B – Unclear

Study	**Magyar 1999b**
Methods	RCT; randomisation using numbered closed envelopes Not blinded
Participants	Medial gonarthrosis grade I-III
Intervention	I: HCO (n = 18) C: closing wedge HTO (n = 15) Follow up: 1 year
Outcomes	Radiostereometry (RSA) HKA-angle
Notes	RSA measurement is no outcome measurement in our protocol, but HTO was associated with more translation No drop-out
Allocation concealment	A – Adequate

Study	**Mammi 1993**
Methods	RCT; randomisation according to order of admission to the hospital Double blind
Participants	Maximum age of 80 years, good health, requiring tibial reduction osteotomy
Intervention	I: HTO with electrical stimulation (n = 18) C: HTO without electrical stimulation (n = 19) Follow up: 60 days
Outcomes	Rate of union (score 1t/m4)
Notes	I: 2 drop-outs. C: 1 drop-out.
Allocation concealment	C – Inadequate

Study	**Motycka 2000**
Methods	RCT; randomisation procedure was not described Not blinded
Participants	Varus osteoarthritis
Intervention	I: HTO with a tourniquet (n = 40) C: HTO without a tourniquet (n = 40) Follow up: 9 weeks
Outcomes	D-Dimer test and phlebography
Notes	I: 3 drop-outs C: 15 drop-outs
Allocation concealment	B – Unclear

Study	**Myrnerts 1980**
Methods	RCT; randomisation procedure was not clear Not blinded
Participants	Varus alignment
Intervention	I: HTO without an overcorrection (n = 40) C: HTO with 5 degrees overcorrection (n = 37) Follow up: 1 year
Outcomes	Pain on weightbearing Patient’s opinion

	HKA-angle
	Complications
Notes	The study reports percentages and no numbers
	No drop-out mentioned
Allocation concealment	B – Unclear

Study	**Nakamura 2001**
Methods	RCT; randomisation procedure was not described
Participants	Medial osteoarthritis of the knee
Intervention	I: HCO (n = 23)
	C:dome osteotomy (DMO; n = 23)
	Follow up: 12 months
Outcomes	FTA-angle
	Patellar height
	Inclination angle of tibial plateau
	Tibial condylar offset
Notes	No drop-out
Allocation concealment	B – Unclear

Study	**Odenbring 1992**
Methods	RCT; "randomization code was opened"
	Not blinded
Participants	Stages I-III medial gonarthrosis
Intervention	I: HTO with a hinged cast brace postoperative (n = 14)
	C: HTO with a cylinder plaster cast postoperative (n = 17)
Outcomes	ROM
	Pain free walking distance
	Pain at rest
	Degree of OA
	HKA-angle
	Lysholm-score
	Complications
Notes	One patient with a complication was excluded
Allocation concealment	B – Unclear

Study	**Stukenborg 2001**
Methods	RCT; patients were computer randomised Not blinded
Participants	Medial unicompartmental OA, varus < 10 degrees, flexion contracture < 15 degrees, age > 60 years, ligament instability < grade II
Intervention	I: HTO (n = 32) C: unicompartmental knee arthroplasty (UKA; n = 28). Follow up: 7.5 years
Outcomes	Knee score Functional score ROM HKA-angle Survivorship Complications
Notes	No drop-outs
Allocation concealment	A – Adequate

Study	**Weidenhielm 1993**
Methods	RCT; randomisation procedure was not described Not blinded
Participants	Medial OA grade I-II, 55-70 years old
Intervention	I: HTO (n = 23). C: UKA (n = 36). Follow up: 1 year I: HTO (n=18) C: UKA (n=22) Follow-up: 5 years
Outcomes	BOA knee score Pain during walking Passive ROM HKA-angle Gait analysis Survivorship
Notes	The 1- and 5- year results have been reported in two different publications.

	The original study started with 100 participants including 50 patients in each group. After one-year follow up there are 59 patients left. In the first publications the cause of this big number of loss has not been described. In the second publication including the 5-years results only 40 participants are left, because in the 5 years analysis “only patients with strictly unilateral osteoarthritis were included. Drop-outs: After 1-year follow up: 41 After 5- year follow up: 60
Allocation concealment	B – Unclear

Legend:
BOA - British Orthopaedic Association; FTA - Femoral Tibial Angle DMO - Dome osteotomy; ROM - Range of motion; JOA - Japanese Orthopaedic Association; VAS - Visual analogue score; WOMAC - Western Ontario-McMaster Osteoarthritis score ; HKA - Hip Knee Angle; UKA - unicompartmental joint replacement (=unicompartmental knee arthroplasty)

Characteristics of excluded studies

Study	**Reason for exclusion**
Odenbring 1992b	The study is a post-hoc analysis and not an RCT or CCT

Additional tables

Table 01. Methodological quality of included studies

Study	D1 D2	D3 D4	D5 D6	D7 D8	D9 M
Adili 2002	0 0	1 1	0 0	0 1	0 1
Akizuki 1997	0 0	1 0	0 0	0 1	1 1
Brouwer 2005	1 1	0 1	0 0	0 1	1 1
Brouwer 2006	1 1	0 1	0 0	0 1	1 1
Magyar 1999a	1 1	1 0	1 0	0 1	1 1
Magyar 1999b	1 1	1 0	0 0	0 1	1 1
Mammi 1993	1 0	0 1	1 1	1 1	0 1
Motycka 2000	1 0	0 0	0 0	0 1	0 1
Mymerts 1980	1 0	1 0	0 0	0 0	0 1
Nakamura 2001	1 0	0 0	0 0	0 1	1 1
Odenbring 1992	1 1	1 0	0 0	0 1	1 1
Stukenborg 2001	1 0	1 1	0 0	0 1	1 1
Weidenhielm 1993	1 0	1 1	0 0	0 1	0 1
% agreement	85% 77%	69% 69%	85% 85%	92% 85%	69% 92%
	D1: Randomisation	D3: Differences between baseline	D5: Blinding outcome assessor	D7: Blinding patient	D9: Intention to treat analysis
	D2: Allocation concealment	D4: Specification	D6: Blinding care provider	D8: Outcomes	M: appropriate follow-up
		inclusion criteria		including SD; 95%CI	

Table 02. Clinical relevance table; Adili 2002: WOMAC pain at 25.4/ 30.9 months

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Adili 2002	HTO (Ilizarov)	WOMAC pain (0-20)	15	12.3	5.5 (25.4 months)	-3.1 (I)	-24.2% (I)	Yes	Silver
	HTO (Coventry)		15	12.8	9.1 (30.9 months)				

Table 03. Clinical relevance table; Adili 2002: WOMAC stiffness at 25.4/ 30.9 months

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Adili 2002	HTO (Ilizarov)	WOMAC stiffness (0-8)	15	4.5	2.6 (25.4 months)	-1.4 (I)	-32.6% (I)	No	Silver
	HTO (Coventry)		15	4.3	3.8 (30.9 months)				

Table 04. Clinical relevance table; Adili 2002: WOMAC function at 25.4/ 30.9 months

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Adili 2002	HTO (Ilizarov)	WOMAC function (0-68)	15	39.0	19.0 (25.4 months)	-12.1 (I)	-33.3% (I)	Yes	Silver
	HTO (Coventry)		15	36.3	28.4 (30.9 months)				

Table 05. Clinical relevance table; Akizuki 1997: JOA-score at 4.8/ 3.5 years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Akizuki 1997	HTO with abrasion	JOA-score (0-100)	45	52.4	86.0 (4.8 years)	-3.1 (W)	-6.2% (W)	No	Silver
	HTO		34	49.8	86.5 (3.5 years)				

Table 06. Clinical relevance table; Brouwer 2005: Patellar height (IS) at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Brouwer 2005	HTO (opening wedge)	Patellar height	26	0.90	0.81	-0.10 (W)	-11.0% (W)	Yes	Silver
	HTO (closing wedge)	(Insall-Salvati, normal ratio 1.0))	24	0.91	0.92				

Table 07. Clinical relevance table; Brouwer 2005: Patellar height (BP) at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Brouwer 2005	HTO (opening wedge)	Patellar height	26	0.78	0.70	-0.10 (W)	-13,3% (W)	Yes	Silver
	HTO (closing wedge)	(Black-burne-Peel, normal ratio 0.8)	24	0.75	0.77				

Table 08. Clinical relevance table; Brouwer 2005: Inclination angle tibia at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Brouwer 2005	HTO (opening wedge)	Inclination angle tibia	26	9.50	11.87	6.14	62.7%	Yes	Silver
	HTO (closing wedge)	(Moore-Harvey; degrees)	24	9.79	6.02				

Table 09. Clinical relevance table; Brouwer 2006: HKA-angle at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Brouwer 2006	HTO (opening wedge)	HKA-angle (degrees)	45	5.7	-1.3	3.2 (W)	47.1% (W)	Yes	Silver
	HTO (closing wedge)	varus = +; valgus = -	47	6.8	-3.4				

Table 10. Clinical relevance table: Brouwer 2006: VAS pain score at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Brouwer 2006	HTO (opening wedge)	VAS pain score (0-10)	45	6.3	3.6	-0.4 (I)	-6.8% (I)	No	Silver
	HTO (closing wedge)	47	5.9	3.6					

Table 11. Clinical relevance table; Brouwer 2006: HSS knee score at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Brouwer 2006	HTO (opening wedge)	HSS knee score (0-100)	45	71.5	80.9	0.9 (I)	1.3% (I)	No	Silver
	HTO (closing wedge)	47	70.9	79.4					

Table 12. Clinical relevance table; Brouwer 2006: Walking distance at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Brouwer 2006	HTO (opening wedge)	Walking distance	45	3.1	5.3	0.5 (I)	17,2% (I)	No	Silver
	HTO (closing wedge)	(km)	47	2.9	4.6				

Table 13. Clinical relevance table; Magyar (1) 1999: ROM at two years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Magyar 1999a	HCO	ROM (degrees)	24	130	125	0	0%	No	Silver
	HTO	22	125	120					

Table 14. Clinical relevance table; Magyar (1) 1999: HSS knee score at two years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Magyar 1999a	HCO	HSS knee score	24	69	94	3(I)	4.5% (I)	No	Silver
	HTO	(0-100)	22	67	89				

Table 15. Clinical relevance table; Magyar (1) 1999: Lysholm score at two years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Magyar 1999a	HCO	Lysholm score	24	55	91	6 (I)	10.7% (I)	No	Silver
	HTO	(0-100)	22	56	86				

Table 16. Clinical relevance table; Magyar (1) 1999: Wallgren-Tegner score at two years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Magyar 1999a	HCO	Wallgren-Tegner score	24	7	10	2(I)	25,0%(I)	No	Silver
	HTO	(0-15)	22	8	9				

Table 17. Clinical relevance table Magyar (1) 1999: NHP-pain score at two years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Magyar 1999a	HCO	NHP pain (0-100)	24	63	8	-20 (I)	-46,5% (I)	No	Silver
	HTO	22	43	8					

Table 18. Clinical relevance table; Myrnerts 1980: Pain on weight-bearing at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Myrnerts 1980	HTO with over-corection	pain	37	100%	31	-14 (I)	-14,0% (I)	No	Silver
	HTO	on weight bearing	40	100%	45				

Table 19. Clinical relevance table; Nakamura 2001: Patellar height (IS) at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Nakamura 2001	HCO	Patellar height	23	0.94	0.93	0.11 (I)	11.9% (I)	Yes	Silver
	HTO	(Insall-Salvati ratio)	23	0.92	0.80				

Table 20. Clinical relevance table; Nakamura 2001: Inclination angle tibia at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Nakamura 2001	HCO	Inclination angle tibial plateau	23	10.9	10.1	5.1 (I)	48.1% (I)	Yes	Silver
	HTO	(degrees)	23	10.6	4.7				

Table 21. Clinical relevance table; Nakamura 2001: Tibial condylar offset at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Nakamura 2001	HCO	Tibial condylar offset (normal ratio 0.5)	23	0.50	0.56	-0.05 (I)	-10% (I)	Yes	Silver
	HTO		23	0.50	0.61				

Table 22. Clinical relevance table; Odenbring 1989: ROM at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Odenbring 1989	HTO with brace	ROM (degrees)	14	128	135	17 (I)	12.6% (I)	Yes	Silver
	HTO with plaster		17	135	125				

Table 23. Clinical relevance table; Odenbring 1989: Pain free walking at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Odenbring 1989	HTO with brace	Pain free walking	14	5.9	2.1	0.4(W)	6.6% (W)	No	Silver
	HTO with plaster	(Lysholm; score 1-7)	17	6.1	1.9				

Table 24. Clinical relevance table; Odenbring 1989: Pain at rest at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Odenbring 1989	HTO with brace	Pain at rest	14	1.7	1.1	0.4 (W)	19,0% (W)	No	Silver
	HTO with plaster	(Lysholm; score 1-3)	17	2.1	1.1				

Table 25. Clinical relevance table; Stukenborg 2001: Knee score at 7.5 years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Stukenborg 2001	HTO	knee score (0-100)	32	32	76	2 (I)	6.3% (I)	No	Silver
	UKA		28	32	74				

Table 26. Clinical relevance table; Stukenborg 2001: Function score at 7.5 years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Stukenborg 2001	HTO	function score	32	46	71	15 (I)	30.6% (I)	No	Silver
	UKA	(0-100)	28	59					

Table 27. Clinical relevance table; Weidenhielm 1993: BOA knee score at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Weidenhielm 1993	HTO	BOA knee score	23	30	38	1 (I)	3.3% (I)	No	Silver
	UKA	(0-39)	36	30	37				

Table 28. Clinical relevance table; Weidenhielm 1993: Pain during walking at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Weidenhielm 1993	HTO	Pain during walking	23	3.5	1.0	0.5 (W)	14.2% (W)	No	Silver
	UKA	(Borg: 0-10)		36	3.5	0.5			

Table 29. Clinical relevance table; Weidenhielm 1993: Passive ROM at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Weidenhielm 1993	HTO	Passive ROM	23	116	121	4(I)	3.4% (I)	No	Silver
	UKA	(degrees)	36	118	119				

Table 30. Clinical relevance table; Weidenhielm 1993: Free walking speed at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Weidenhielm 1993	HTO	Free walking speed	23	1.03	1.09	-0.1 (W)	-9.7% (W)		Silver
	UKA	(m/s)	36	1.03	1.19				

Table 31. Clinical relevance table; Weidenhielm 1993: Step frequency at one year

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Weidenhielm 1993	HTO	Step frequency	23	1.68	1.75	-0.06 (W)	-3.6% (W)	No	Silver
	UKA	(steps/s)	36	1.65	1.78				

Table 32. Clinical relevance table; Weidenhielm 1993: BOA knee score at five years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. significance	Quality of evidence
Weidenhielm 1993	HTO	BOA knee score	18	30	37	0	0	No	Silver
	UKA	(0-39)	22	30	37				

Table 33. Clinical relevance table; Weidenhielm 1993: Pain during walking at five years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Weidenhielm 1993	HTO	Pain during walking	18	3	0	0	0	No	Silver
	UKA	(Borg: 0-10)	22	3	0				

Table 34. Clinical relevance table; Weidenhielm 1993: Passive ROM at five years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Weidenhielm 1993	HTO	Passive ROM	18	116	119	1 (I)	0.9% (I)	No	Silver
	UKA	(degrees)	22	117	119				

Table 35. Clinical relevance table; Weidenhielm 1993: Free walking speed at five years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Weidenhielm 1993	HTO	Free walking speed	18	1.07	1.13	0.03 (I)	2.6% (I)	No	Silver
	UKA	(m/s)	22	1.16	1.19				

Table 36. Clinical relevance table; Weidenhielm 1993: Step frequency at five years

Study	Treatment group	Outcome (scale)	No. of patients	Baseline mean	End-of-study mean	Absolute benefit	Relative difference	Stat. signifi-cance	Quality of evidence
Weidenhielm 1993	HTO	Step frequency	18	1.68	1.76	-0.06 (W)	-3.6% (W)	No	Silver
	UKA	(steps/s)	22	1.66	1.80				

Analyses

Comparison 02. Closing wedge HTO versus other types of HTO

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pain			Standardised Mean Difference (Random) 95% CI	Totals not selected
02 Stiffness			Weighted Mean Difference (Random) 95% CI	Totals not selected
03 Function			Weighted Mean Difference (Random) 95% CI	Totals not selected
04 HSS score			Weighted Mean Difference (Random) 95% CI	Totals not selected
05 Walking distance (km)	1	92	Weighted Mean Difference (Random) 95% CI	1.24 [-0.41, 2.89]
06 Complications	3	174	Relative Risk (Random) 95% CI	3.06 [1.44, 6.53]
07 Patient Satisfaction			Relative Risk (Random) 95% CI	Totals not selected
08 Valgus angle (HKA-angle)	1	92	Weighted Mean Difference (Random) 95% CI	-2.30 [-3.90, -0.70]
09 Valgus angle (FTA)			Weighted Mean Difference (Random) 95% CI	Totals not selected
10 Patellar height (Insall Salvati ratio)	1	50	Weighted Mean Difference (Random) 95% CI	-0.11 [-0.21, -0.01]
11 Inclination of the tibial plateau (degrees)	1	50	Weighted Mean Difference (Random) 95% CI	5.85 [3.80, 7.90]

Comparison 03. Closing wedge HTO versus UKA

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
04 Survival (revision)			Relative Risk (Random) 95% CI	Totals not selected
05 Complications			Relative Risk (Random) 95% CI	Totals not selected
07 Patient opinion: improvement at 5 years			Relative Risk (Random) 95% CI	Totals not selected
10 Gait analysis: Free walking speed at 5 years			Weighted Mean Difference (Random) 95% CI	Totals not selected
11 Gait analysis: Step frequency at 5 years			Weighted Mean Difference (Random) 95% CI	Totals not selected

Comparison 04. Differences in peroperative conditions

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 JOA score			Weighted Mean Difference (Random) 95% CI	Totals not selected
02 Valgus angle (FTA)			Weighted Mean Difference (Random) 95% CI	Totals not selected
03 Complication (phlebography)			Relative Risk (Random) 95% CI	Totals not selected

Comparison 05. Differences in postoperative treatment

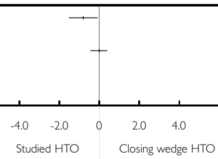
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Less than 50% consolidation			Relative Risk (Random) 95% CI	Totals not selected
02 More than 50% consolidation			Relative Risk (Random) 95% CI	Totals not selected
03 Complications			Relative Risk (Random) 95% CI	Totals not selected
04 Range of motion			Weighted Mean Difference (Random) 95% CI	Totals not selected
05 Painfree walking distance			Weighted Mean Difference (Random) 95% CI	Totals not selected
06 Pain at rest			Weighted Mean Difference (Random) 95% CI	Totals not selected
07 Degree of osteoartritis			Weighted Mean Difference (Random) 95% CI	Totals not selected
08 Valgus angle (HKA-angle)			Weighted Mean Difference (Random) 95% CI	Totals not selected

GRAPHS AND OTHER TABLES

Analysis 02.01. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 01 Pain

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 01 Pain

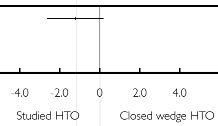
Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Standardised Mean Difference (Random) 95% CI	Standardised Mean Difference (Random) 95% CI
Adili 2002	17	5.50 (4.60)	15	9.10 (4.20)		-0.79 [-1.52, -0.07]
Brouwer 2006	45	3.60 (2.90)	47	3.60 (2.20)		0.00 [-0.41, 0.41]



Analysis 02.02. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 02 Stiffness

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 02 Stiffness

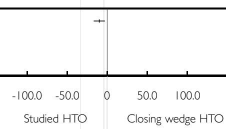
Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Adili 2002	17	2.60 (1.90)	15	3.80 (2.20)		-1.20 [-2.63, 0.23]



Analysis 02.03. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 03 Function

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 03 Function

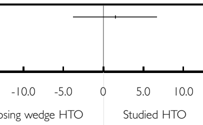
Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Adili 2002	17	19.00 (11.60)	15	28.40 (7.30)		-9.40 [-16.04, -2.76]



Analysis 02.04. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 04 HSS score

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 04 HSS score

Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Brouwer 2006	45	80.90 (13.50)	47	79.40 (12.00)		1.50 [-3.73, 6.73]

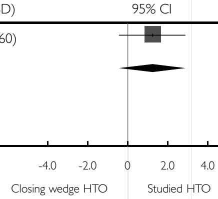


Analysis 02.05. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 05 Walking distance (km)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 05 Walking distance (km)

Study	Studued HTO N	Studued HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Brouwer 2006	45	5.30 (4.40)	47	4.06 (3.60)		100.0	1.24 [-0.41, 2.89]
Total (95% CI)	45		47			100.0	1.24 [-0.41, 2.89]

Test for heterogeneity: not applicable
Test for overall effect z=1.48 p=0.1

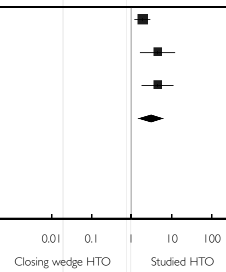


Analysis 02.06. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 06 Complications

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 06 Complications

Study	Studied HTO n/N	Closing wedge HTO n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Adili 2002	17/17	8/15		43.6	1.88 [1.17, 3.01]
Brouwer 2006	17/45	4/47		27.2	4.44 [1.62, 12.18]
Magyar 1999a	18/25	4/25		29.3	4.50 [1.77, 11.41]
Total (95% CI)	87	87		100.0	3.06 [1.44, 6.53]

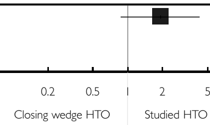
Total events: 52 (Studied HTO), 16 (Closing wedge HTO)
Test for heterogeneity chi-square=5.53 df=2 p=0.06 I^2 =63.8%
Test for overall effect z=2.90 p=0.004



Analysis 02.07. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 07 Patient Satisfaction

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 07 Patient Satisfaction

Study	Studied HTO n/N	Closing wedge HTO n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Adili 2002	11/17	5/15		1.94 [0.87, 4.31]

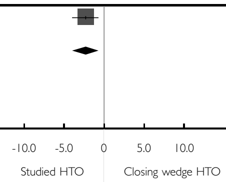


Analysis 02.08. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 08 Valgus angle (HKA-angle)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 08 Valgus angle (HKA-angle)

Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Brouwer 2006	45	1.30 (4.70)	47	3.60 (2.90)		100.0	-2.30 [-3.90, -0.70]
Total (95% CI)	45		47			100.0	-2.30 [-3.90, -0.70]

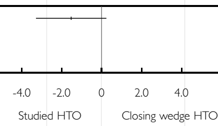
Test for heterogeneity: not applicable
Test for overall effect z=2.81 p=0.005



Analysis 02.09. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 09 Valgus angle (FTA)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 09 Valgus angle (FTA)

Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Adili 2002	17	7.90 (1.60)	15	9.40 (3.10)		-1.50 [-3.24, 0.24]

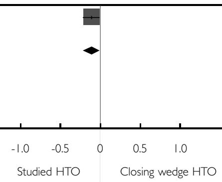


Analysis 02.10. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 10 Patellar height (Insall Salvati ratio)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 10 Patellar height (Insall Salvati ratio)

Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Brouwer 2006	26	0.81 (0.20)	24	0.92 (0.17)		100.0	-0.11 [-0.21, -0.01]
Total (95% CI)	26		24			100.0	-0.11 [-0.21, -0.01]

Test for heterogeneity: not applicable
Test for overall effect z=2.10 p=0.04

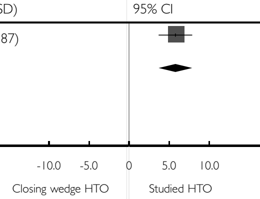


Analysis 02.11. Comparison 02 Closing wedge HTO versus other types of HTO, Outcome 11 Inclination of the tibial plateau (degrees)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 02 Closing wedge HTO versus other types of HTO
Outcome: 11 Inclination of the tibial plateau (degrees)

Study	Studied HTO N	Studied HTO Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Brouwer 2005	26	11.87 (3.50)	24	6.02 (3.87)		100.0	5.85 [3.80, 7.90]
Total (95% CI)	26		24			100.0	5.85 [3.80, 7.90]

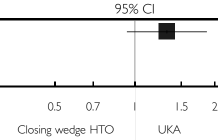
Test for heterogeneity: not applicable
Test for overall effect z=5.59 p<0.00001



Analysis 03.04. Comparison 03 Closing wedge HTO versus UKA, Outcome 04 Survival (revision)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 03 Closing wedge HTO versus UKA
Outcome: 04 Survival (revision)

Study	UKA n/N	Closing wedge HTO n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Stukenborg 2001	22/28	19/32		1.32 [0.94, 1.87]



Analysis 03.05. Comparison 03 Closing wedge HTO versus UKA, Outcome 05 Complications

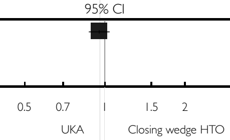
Review: Osteotomy for treating knee osteoarthritis
Comparison: 03 Closing wedge HTO versus UKA
Outcome: 05 Complications

Study	UKA n/N	Closing wedge HTO n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Stukenborg 2001	2/28	9/32		0.25 [0.06, 1.08]

Analysis 03.07. Comparison 03 Closing wedge HTO versus UKA, Outcome 07 Patient opinion: improvement at 5 years

Review: Osteotomy for treating knee osteoarthritis
Comparison: 03 Closing wedge HTO versus UKA
Outcome: 07 Patient opinion: improvement at 5 years

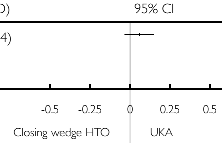
Study	UKA n/N	Closing wedge HTO n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Weidenhielm 1993	21/22	18/18		0.95 [0.87, 1.05]



Analysis 03.10. Comparison 03 Closing wedge HTO versus UKA, Outcome 10 Gait analysis: Free walking speed at 5 years

Review: Osteotomy for treating knee osteoarthritis
Comparison: 03 Closing wedge HTO versus UKA
Outcome: 10 Gait analysis: Free walking speed at 5 years

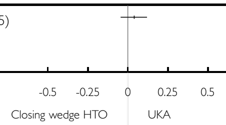
Study	UKA N	UKA Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Weidenhielm 1993	22	1.19 (0.15)	18	1.13 (0.14)		0.06 [-0.03, 0.15]



Analysis 03.11. Comparison 03 Closing wedge HTO versus UKA, Outcome 11 Gait analysis: Step frequency at 5 years

Review: Osteotomy for treating knee osteoarthritis
Comparison: 03 Closing wedge HTO versus UKA
Outcome: 11 Gait analysis: Step frequency at 5 years

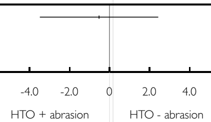
Study	UKA N	UKA Mean(SD)	Closing wedge HTO N	Closing wedge HTO Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Weidenhielm 1993	22	1.80 (0.11)	18	1.76 (0.15)		0.04 [-0.04, 0.12]



Analysis 04.01. Comparison 04 Differences in peroperative conditions, Outcome 01 JOA score

Review: Osteotomy for treating knee osteoarthritis
Comparison: 04 Differences in peroperative conditions
Outcome: 01 JOA score

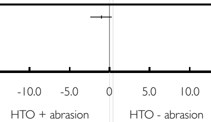
Study	HTO + abrasion N	HTO + abrasion Mean(SD)	HTO - abrasion N	HTO - abrasion Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Akizuki 1997	51	86.00 (7.20)	37	86.50 (6.80)		-0.50 [-3.45, 2.45]



Analysis 04.02. Comparison 04 Differences in peroperative conditions, Outcome 02 Valgus angle (FTA)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 04 Differences in peroperative conditions
Outcome: 02 Valgus angle (FTA)

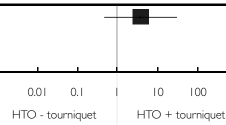
Study	HTO + abrasion N	HTO + abrasion Mean(SD)	HTO - abrasion N	HTO - abrasion Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Akizuki 1997	51	13.00 (2.90)	37	14.00 (3.30)		-1.00 [-2.33, 0.33]



Analysis 04.03. Comparison 04 Differences in peroperative conditions, Outcome 03 Complication (phlebography)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 04 Differences in peroperative conditions
Outcome: 03 Complication (phlebography)

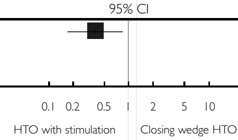
Study	HTO with tourniquet n/N	Closing wedge HTO n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Motycka 2000	5/37	1/28		3.78 [0.47, 30.60]



Analysis 05.01. Comparison 05 Differences in postoperative treatment, Outcome 01 Less than 50% consolidation

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 01 Less than 50% consolidation

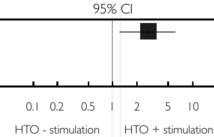
Study	HTO + stimulation n/N	HTO - stimulation n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Mammi 1993	5/18	14/19		0.38 [0.17, 0.83]



Analysis 05.02. Comparison 05 Differences in postoperative treatment, Outcome 02 More than 50% consolidation

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 02 More than 50% consolidation

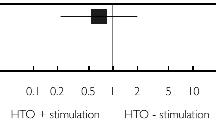
Study	HTO + stimulation n/N	HTO - stimulation n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Mammi 1993	13/18	5/19		2.74 [1.23, 6.14]



Analysis 05.03. Comparison 05 Differences in postoperative treatment, Outcome 03 Complications

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 03 Complications

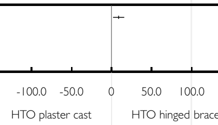
Study	HTO + stimulation n/N	HTO - stimulation n/N	Relative Risk (Random) 95% CI	Relative Risk (Random) 95% CI
Mammi 1993	4/20	6/20		0.67 [0.22, 2.01]



Analysis 05.04. Comparison 05 Differences in postoperative treatment, Outcome 04 Range of motion

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 04 Range of motion

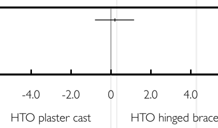
Study	HTO hinged brace N	HTO hinged brace Mean(SD)	HTO plaster cast N	HTO plaster cast Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Odenbring 1992	15	134.60 (9.50)	17	125.30 (11.40)		9.30 [2.06, 16.54]



Analysis 05.05. Comparison 05 Differences in postoperative treatment, Outcome 05 Painfree walking distance

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 05 Painfree walking distance

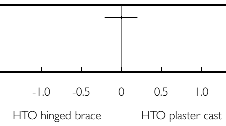
Study	HTO hinged brace N	HTO hinged brace Mean(SD)	HTO plaster cast N	HTO plaster cast Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Odenbring 1992	15	2.10 (1.60)	17	1.90 (1.20)		0.20 [-0.79, 1.19]



Analysis 05.06. Comparison 05 Differences in postoperative treatment, Outcome 06 Pain at rest

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 06 Pain at rest

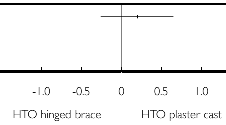
Study	HTO hinged brace N	HTO hinged brace Mean(SD)	HTO plaster cast N	HTO plaster cast Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Odenbring 1992	15	1.10 (0.30)	17	1.10 (0.30)		0.00 [-0.21, 0.21]



Analysis 05.07. Comparison 05 Differences in postoperative treatment, Outcome 07 Degree of osteoartritis

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 07 Degree of osteoartritis

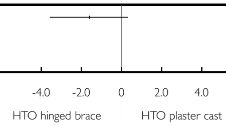
Study	HTO hinged brace N	HTO hinged brace Mean(SD)	HTO plaster cast N	HTO plaster cast Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Odenbring 1992	15	1.40 (0.60)	17	1.20 (0.70)		0.20 [-0.25, 0.65]



Analysis 05.08. Comparison 05 Differences in postoperative treatment, Outcome 08 Valgus angle (HKA-angle)

Review: Osteotomy for treating knee osteoarthritis
Comparison: 05 Differences in postoperative treatment
Outcome: 08 Valgus angle (HKA-angle)

Study	HTO hinged brace N	HTO hinged brace Mean(SD)	HTO plaster cast N	HTO plaster cast Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weighted Mean Difference (Random) 95% CI
Odenbring 1992	15	5.30 (1.80)	17	6.90 (3.60)		-1.60 [-3.54, 0.34]



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** Indicates the major publication for the study*

Chapter 5

Survival of closing wedge high tibial osteotomy: good outcome in men with low-grade osteoarthritis after 10 – 16 years

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Abstract

Background and purpose

High tibial valgus osteotomy (HTO) is a well accepted treatment of medial unicompartmental osteoarthritis of the knee with varus alignment in relatively young and active patients. Controversies about factors affecting survival of HTO still exist. We assessed preoperative risk factors for failure of closing wedge HTO at long-term follow-up.

Patients and methods

A cohort of 104 consecutive patients, mean age 49 (24 - 67) years, who had closing wedge HTO performed between January 1991 and December 1996, were retrospectively analyzed. A survival analysis was carried out according to the Kaplan-Meier method. Logistic regression analysis was used to assess the relation between failure of the osteotomy and known potential preoperative risk factors.

Results

The probability of survival for HTO was 75% (SD 4%) at 10 years with knee replacement as the end point. Female sex and grade ≥ 2 osteoarthritis were identified as preoperative risk factors for conversion to arthroplasty 10 years after HTO.

Interpretation

Our findings suggest that ideal candidates for corrective osteotomy are males with symptomatic medial compartmental osteoarthritis Ahlbäck grade 1, who 10 years after surgery have an almost 10 times lower probability of failure of HTO than women with more degenerative changes.

Introduction

High tibial valgus osteotomy (HTO) is a generally accepted treatment of medial unicompartmental osteoarthritis of the knee with varus alignment in active patients. Although successful osteotomy is effective in delaying the degenerative progress, results deteriorate over time and patients may require knee arthroplasty because of progression of symptoms (Virolainen et al. 2004).

Some studies report no clinical or radiographic difference in outcome for total knee arthroplasty (TKA) with or without a previous osteotomy (Staeheli et al. 1987, Meding et al. 2000) while others see substandard TKA outcome after HTO (Katz et al. 1987, Nizard et al. 1998). Patient selection may be one of the reasons for this disparity, as young heavy males with malalignment have a significantly higher prevalence of radiolucent lines and revision rate after TKA. Also technical difficulties have to be dealt with when performing a TKA after HTO, with greater risks of complications than a primary knee replacement without prior osteotomy (Parvizi et al. 2004). Therefore it is important to identify factors that predict a good HTO survival.

Controversies about factors affecting survival of HTO still exist. Some studies have shown that the success of HTO outcome may depend on the stage of osteoarthritis (Odenbring et al. 1990, Flecher et al. 2006). Other studies recognized preoperative tibiofemoral alignment, or more individual factors, such as age, sex and obesity to be predictors of patient dissatisfaction and conversion to arthroplasty (Coventry et al. 1993, Naudie et al. 1999, Huang et al. 2005).

The goal of the present study was to identify significant preoperative risk factors for failure of closing wedge HTO at long-term follow-up.

Patients and methods

We retrospectively analysed a cohort of 104 consecutive patients who had 108 closing wedge HTOs, performed between January 1991 and December 1996**.** Patients' records were reviewed, and patients or relatives of the patients who had died, were interviewed via telephone to obtain the postoperative status at the time of follow-up. Failure of the osteotomy was defined as conversion to a total knee arthroplasty. In 4 patients with staged bilateral procedures, only the first leg was included. 4 patients were lost to follow-up. 7 patients had died (10 – 11) years after the osteotomy, from an unrelated condition without their osteotomies being converted to a knee arthroplasty. The baseline characteristics for the 100 patients are shown in Table 1.

Table 1: Baseline characteristics of the 100 patients at the time of closing wedge osteotomy.

Age, mean (SD)		49 (11)
Men		61
BMI		
	Mean (SD)	27 (3.9)
	< 25 (no of pts)	37
	25 – 30	42
	> 30	21
Ahlbäck grading,		
	Grade 0 (no of pts)	5
	1	43
	2	44
	3	8
HKA angle (degrees)		
	Mean (SD)	6.5 (3.7)
	> 9° of varus, (no of pts)	30

The mean age at the time of surgery was 49 years (SD 11); there were 61 men. The average time of follow-up was 12 years (range 10-16 years). The grade of radiographical osteoarthritis was scored according to Ahlbäck (1968), and measured on standard short posteroanterior radiographs in standing position and the knee in full extension. The mechanical axis (Hip-Knee-Ankle angle; HKA) was measured on a whole leg radiograph (WLR) in standing position. The patient stood barefooted on the affected leg with the knee in full extension, while the contra-lateral flexed knee was supported by means of a small box. The anteroposterior projection was ensured during lateral fluoroscopic control by superimposing the dorsal aspect of the femoral condyles. The tube was set perpendicular to this lateral view and was moved from the proximal end to the distal end so that a WLR was obtained. Earlier we reported high intra- and interobserver agreement of the measurement of the HKA angle by the use of this technique (Brouwer et al. 2003). All patients had varus malalignment of the knee with a mean preoperative HKA angle of 6.5 degrees (SD 3.7) of varus.

A closing wedge technique through a transverse incision with the patient in supine position was performed in all patient. Standard antibiotic prophylaxis was used. The common peroneal nerve was exposed and protected. Subsequently the anterior part of the proximal fibular head (anterior part of the proximal tibia-fibular syndesmosis) was resected. We used a calibrated slotted wedge resection guide to remove the wedge size determined from the preoperative WLR, proximal to the patellar tendon insertion. The goal was to achieve a correction of 4 degrees in excess of physiological valgus. The osteotomy was fixated with 2 step staples. At the end of the procedure a fasciotomy of the anterior compartment was performed to prevent a compartment syndrome. After surgery a standard cylinder plaster cast was applied for 6 weeks, no standard anticoagulation was used. All patients were mobilized on the first postoperative day, and partial weight-bearing with the use of two crutches was allowed for 6 weeks.

Adverse events related to the surgical technique

1 patient was re-operated because of overcorrection (varus HTO), and another patient because of a symptomatic exostosis at the anterior site of the osteotomy. 3 patients had sensory peroneal neuropathy, but normal motor function. All osteotomies healed and no deep infections occured. The staples were removed in 47 patients because of local pain.

Statistics

The SPSS statistical software version 10.1 (SPSS Inc., Chicago, Illinois) was used for statistical analysis and a p-value of 0.05 was considered to be statistically significant. A survival analysis was carried out according to Kaplan and Meier. We investigated the relation between conversion of HTO to a TKA and known potential preoperative risk factors; respectively age (Naudie et al. 1999), sex (Aglietti et al. 2003), body mass index (BMI) (Matthews et al. 1988), preoperative Ahlbäck grading (Flecher et al. 2006) and preoperative HKA angle < 9 degrees of varus (Huang et al. 2005).

We calculated odds ratios, by logistic regression analysis, to estimate the relation between failure of the osteotomy and potential preoperative risk factors. We performed multivariate, stepwise (backward) logistic regression and entered variables with a p-value of ≤ 0.05 into the model.

Results

25 osteotomies were revised to a TKA at the 10-year follow-up. The average time between the osteotomy and TKA was 6 (SD 3) years. The probability of survival for a closing wedge HTO was 75% (SD 4%) at 10 years with knee replacement as the end point (Figure 1).

Using the logistic regression model, sex and osteoarthritis Ahlbäck's grade ≥ 2 were identified as preoperative risk factors for conversion to arthroplasty (p = 0.008 and p = 0.004) 10 years after HTO. There was a 4 times (95% CI; 1.4–11) higher chance of conversion to arthroplasty for women, and a 5 times (95% CI; 1.7–16) higher risk for knee replacement in patients with Ahlbäck's grade ≥ 2. If the preoperative grade of osteoarthritis was Ahlbäck ≥ 2, the probability of no failure at 10 years was 62%. In comparison with a probability of 90% for Ahlbäck Grade ≤ 1 (p < 0.004) (Figure 2). Age just failed to reach significance (p = 0.06) as a risk factor for failure. BMI and the preoperative HKA angle were not associated with HTO failure. Men with Ahlbäck grade 1 osteoarthritis at baseline had the lowest (6%) risk of failure. Women with Ahlbäck grade > 1 had high risk of failure (57%) (Figure 3).

Figure 1: Survival curve for 100 knees after HTO with TKA as the end point at 10-years follow-up.

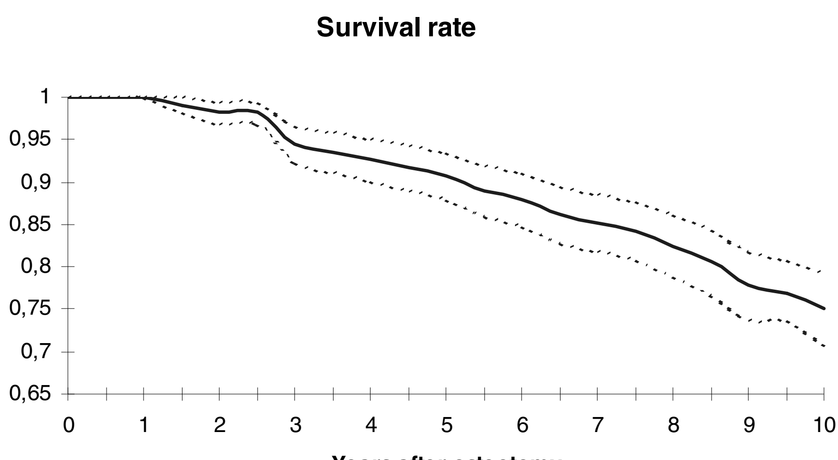


Figure 2: Survival curve for HTO with TKA as the end point according to Ahlbäck's classification.

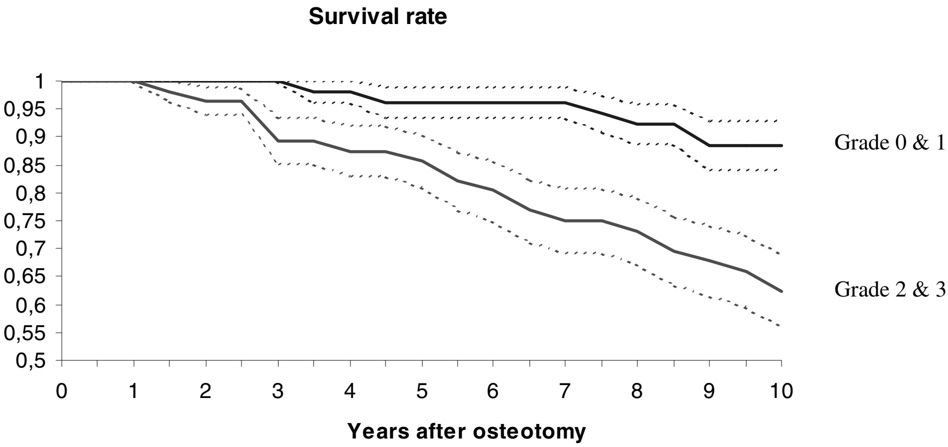
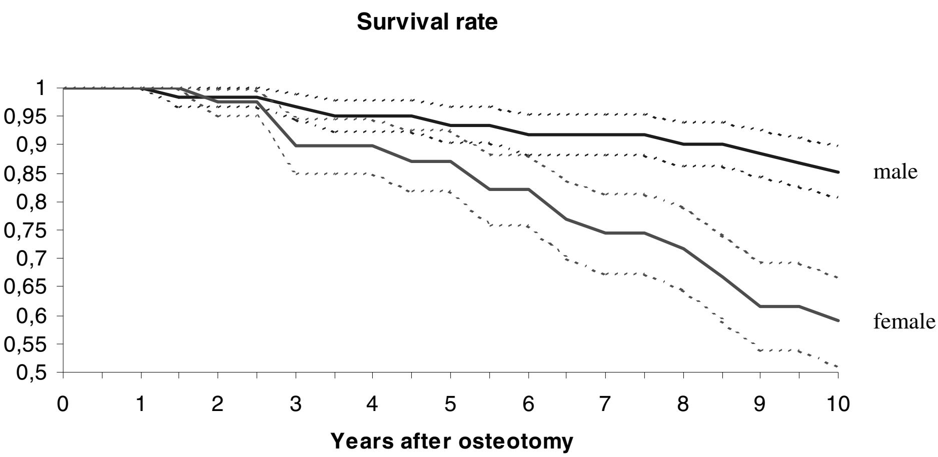


Figure 3: Survival curve for HTO with TKA as the end point according to sex.



Discussion

In our experience active patients, with radiographic or arthroscopic confirmed symptomatic unicompartmental medial osteoarthritis of the knee and varus malalignment, may be treated successfully with a correction osteotomy instead of arthroplasty. A Swedish Knee Arthroplasty Register study found that young age was associated with an increased risk of prosthetic revision. The cumulative revision rate for unicompartmental arthroplasty (UKA) was even higher than for TKA (Robertsson et al. 2001). One of the technical problems after removal of UKA will be loss of bone stock. This requires significantly more osseous reconstructions in total knee revision compared with revision TKA after HTO (Gill et al. 1995). However, we have restricted HTO to patients with knee motion more than 90 degrees and with less of 15 degrees of flexion contraction, without collateral laxity greater than the expected from the diminished joint space on physical examination, and with varus malalignment on a WLR not more than 15 degrees. Our findings in the present study, with 75% of patients at 10 years not requiring a TKA after HTO, compare well with other studies; with percentages ranging from 51% to 92% at 10 years (Coventry et al. 1993, Naudie et al. 1999, Sprenger et al. 2003, Flecher et al. 2006). Factors such as age, preoperative grade of osteoarthritis, sex, BMI, and preoperative angular deformity have been reported to influence HTO survivorship. We conducted this retrospective long-term follow-up study to determine the effect of these factors on HTO survival, and to further clarify osteotomy indications with the aim to improve our revision rate even more.

We used strict indications to perform osteotomy, but our study was not prospective. The HTO procedure was also performed and supervised by different surgeons over the given time period in a teaching hospital setting. On the other hand, this represents common orthopedic practice. Another limitation might be that failure of HTO was only defined as conversion to a TKA. No knee scores or radiographs were used to measure knee function or grade of radiographical osteoarthritis at the time of follow-up. However, delaying or perhaps even avoiding knee replacement is one of the main reasons to perform HTO. Therefore, it is useful to choose arthroplasty as end-point of HTO survival.

Previous studies reported young patients, less than 50 years of age, to be appropriate candidates for HTO (Naudie et al. 1999, Flecher et al. 2006). We did not find age to be a risk factor for failure. Other studies agree and have found no influence of age on survival rate (Odenbring et al 1990, Sprenger et al. 2003, Huang et al. 2005, Spahn et al. 2006). This disparity in findings may be due to different distribution in the study groups. Conversion of HTO to TKA is used as the end-point of HTO failure in almost all survival analyses. A younger population will then have a favourable result because, irrespective of the clinical outcome, patients younger than 55 years are generally not considered suitable candidates for knee replacement. This could be the reason why, in our study, age just failed to reach

significance in the multivariate model.
The Ahlbäck scoring system of knee osteoarthritis is widely used, and is considered a valuable tool in surgical decision-making. Recent reports show poor reproducibility and validity (Galli et al. 2003, Weidow et al. 2006). This might explain the existing controversy about the role of the severity of osteoarthritis on HTO survival. Huang et al. (2005) found no correlation between radiographical arthritic severity and clinical outcome. The authors attributed this to their strict indication for HTO; all knees had Ahlbäck grade 3 or less preoperatively. We found that the preoperative stage of osteoarthritis strongly correlated with osteotomy failure. Odenbring et al. (1990) also found that advanced stages of arthrosis increased the revison rate of osteotomy. Also Flecher et al. (2006) found that preoperative Ahlbäck grade 1 corresponded with a good outcome.

Although HTO with optimal correction gives pain relief, it does not seem to prevent the progression of medial arthrosis (Flecher et al. 2006). Radiographic progression of medial-compartment arthritis was observed by Stuart et al. (1990) in four fifths of patients 9 years after closing wedge HTO. A recent meta-analysis demonstrated sex differences in osteoarthritis prevalence and incidence, with females at a higher risk. Females also tended to have more severe knee osteoarthritis, particularly after menopausal age (Srikanth et al. 2005). Although some studies (Huang et al. 2005, Flecher et al. 2006) did not find sex to be an influencing factor, Aglietti et al. (2003) noted superior results for men in an analysis of 120 closing wedge HTOs at an average follow-up of 15 years. In our study women also had poorer results at 10-year follow-up. Being overweight has been recognized as a significant factor for predicting a poor outcome after HTO (Spahn et al. 2006). We found however, that BMI had a minor role in comparison to preoperative grade of osteoarthritis and sex.

Large preoperative tibiofemoral varus malalignment has been described as a predictor of HTO failure and patient dissatisfaction after HTO (Huang et al. 2005). In our opinion patients with a varus of more than 15 degrees are not suitable for closing wedge osteotomy. In our patients, probably due to the moderate mean preoperative 6.5 degrees (SD 3.7) of varus malalignment, we found no correlation between preoperative varus deformity and HTO failure. In a similar group of patients (average 6 degrees of preoperative varus) no influence of the preoperative angle was found on outcome after osteotomy either (Flecher et al. 2006).
In summary we found that sex and preoperative stage of osteoarthritis predict the survival of closing wedge HTO. Men with medial compartmental osteoarthritis Ahlbäck grade 1 had an almost 10 times lower probability of failure of HTO than women with higher grades of osteoarthritis.

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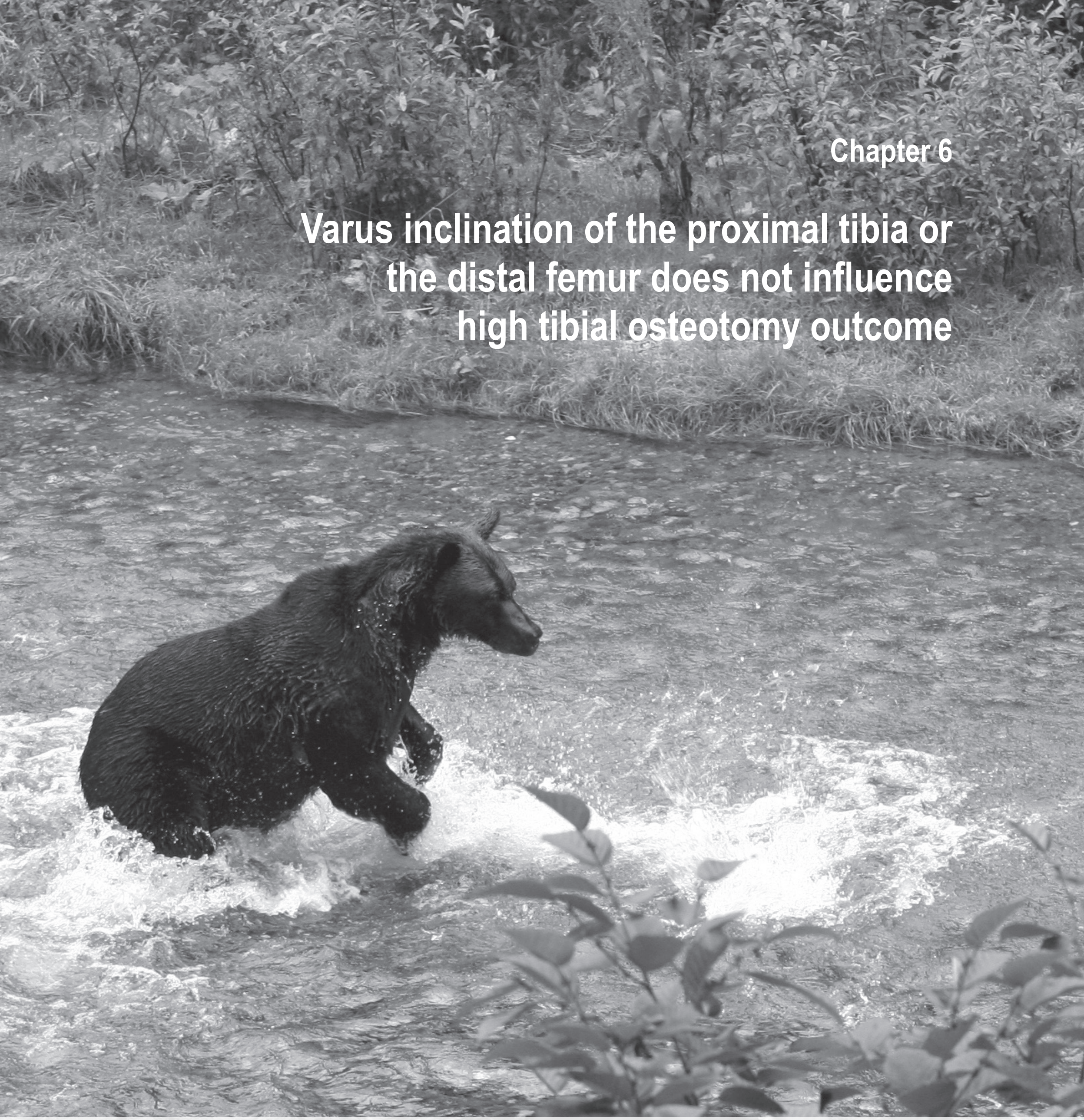
Chapter 6

Varus inclination of the proximal tibia or the distal femur does not influence high tibial osteotomy outcome



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Knee Surg Sports Traumatol Arthrosc. 2009;17:390-5.

Abstract
We have analysed retrospectively the influence of different sources of knee deformity on failure of closing wedge HTO. Preoperative frontal plane varus deformities of the lower extremity, distal femur and proximal tibia, and medial convergence of the knee joint line, were assessed on a standard whole leg radiograph in 76 patients. Using the logistic regression model, the probability of survival for HTO was 77% (SD 4%) at 10-years follow-up. Varus deformity of the lower extremity (< 175°), and medial convergence of the knee joint line (> 3°) were identified as preoperative risk factors for conversion to arthroplasty (p = 0.03 and p = 0.006). We found no evidence that varus inclination of the proximal tibia or distal femur influences long-term survival of HTO.

Key words: proximal tibia; osteotomy; varus; inclination; failure

Introduction
High tibial valgus osteotomy (HTO) is a well accepted treatment of medial unicompartmental osteoarthritis of the knee with varus alignment in active patients. Results, however, seem to deteriorate in time, and this group of patients may ultimately require knee replacement [16]. One of the key factors for long-term HTO success is the achievement of an even distribution of the mechanical load of the knee joint by obtaining an ideal lower-extremity mechanical axis alignment. This may be influenced by preoperative axial alignment parameters such as the tibiofemoral angle, which has been found to predict conversion to arthroplasty and patient dissatisfaction [5]. Also preoperative varus deformity of the distal femur has been observed to be associated with varus recurrence and poor results seven years after HTO [15]. On the other hand, patients with specific anatomical conditions such as congenital bowing of the proximal tibia have been reported to benefit more from a valgus correction osteotomy than patients with varus of the proximal tibia caused by degenerative changes [1]. The Lyon knee school postulated that valgus correction of a constitutional tibia varus deformity restores tibia alignment in a curative way, and thus creates a more physiological knee load distribution [7]. Therefore, Bonnin and Chambat suggested measuring the "tibial bone varus angle" according to Lévigne to help differentiate between a bony deformity of the proximal tibia and secondary bony erosion, with a worse prognosis [1,7].
The objective of the present study was to analyze the influence of different sources of knee varus deformity on failure of closing wedge HTO at 10-year follow-up. Failure was defined as conversion to total knee arthroplasty (TKA), because avoiding knee replacement is one of the main reasons to perform HTO. First we determined preoperative axial alignment parameters in a group of patients who underwent closing wedge HTO because of symptomatic medial unicompartmental knee osteoarthritis. Then we investigated the relation between failure of HTO and different sources of knee varus deformity in the frontal plane.

Material and methods

We used a cohort of 114 patients who had 122 lateral closing wedge HTOs, performed between 1991 and 1997 because of symptomatic medial osteoarthritis. A closing wedge technique through a transverse incision with the patient in supine position was performed in all patients. Subsequently the anterior part of the proximal tibia-fibular syndesmosis was resected. Under fluoroscopic guidance, we used a calibrated slotted wedge resection guide of Allopro (Zimmer; Winterthur, Switzerland) to remove the wedge proximal to the patellar tendon insertion. The size of the wedge was determined preoperative using the medial Hip-Knee-Ankle (HKA) angle measured from a standardized whole leg radiograph (WLR), The goal was to achieve a correction of 4 degrees in excess of neutral alignment [10]. The osteotomy was fixated with 2 step staples. All patients were mobilized on the first postoperative day, and partial weight-bearing in a standard cylinder plaster cast was allowed for 6 weeks.

Before surgery, a WLR in standing position was performed in all patients. The patient stood barefooted on the affected leg with the knee in full extension, while the contra-lateral flexed knee was supported by means of a small box. The X-ray beam was centred on the affected knee with the tube at a distance of 1.5 meters. The three-part 136/36 cm cassette with graduated grid was immediately behind the patient. The 100% anteroposterior projection was ensured during lateral fluoroscopic control by superimposing the dorsal aspect of the femoral condyles. The tube was set perpendicular to this lateral view and was moved from the proximal end to the distal end so that a WLR was obtained. We retrieved 90 preoperative WLRs; of which 5 patients with post-traumatic bone deformities, 1 patient with total hip replacement, and 1 patient with rickets were excluded for analysis. The baseline characteristics for the included 76 patients with 83 osteotomies (7 patients with staged bilateral procedures) are shown in Table 1; we found no significant differences between the study population and 31 patients with 32 osteotomies (1 patient with staged bilateral procedure) who had irretrievable WLRs.

Table 1: Baseline characteristics of the study population compared to group with irretrievable whole leg radiograph

	Study	**'Missings'**
Number of knees	83	32
Age (yrs), mean (± SD)	48.8 (±10.6)	49.6 (±10.3)
Women (%)	39	36
BMI, mean (± SD)	27.1 (± 4.3)	27.6 (± 3.1)
Ahlback medial OA (%)		
- Grade 0	5	3
- Grade 1	48	38
- Grade 2	39	53
- Grade 3	8	6

No significant differences

Failure of the osteotomy was defined as the need for conversion of HTO to a TKA. Patients' records were reviewed, and patients or relatives of the patients who had died, were interviewed via telephone to obtain the postoperative status at the time of follow-up. The average time of follow-up was 12 years (range 10-17 years). 19 osteotomies (23%) were revised to a TKA at the 10-year follow-up. The average time between the osteotomy and TKA was 6.2 (SD 2.6) years. Three patients had died from an unrelated condition 3, 8, and 10 years after the osteotomy. In none of these patients the osteotomy had been converted to a TKA.

Measurements

In 83 knees the medial HKA angle was measured, and defined as the medial angle between two lines: one line of the centre of the femur head using Mose circles to the top of the femoral notch (mechanical axis line of the femur), and a second line from the centre of the ankle to the centre of the tibial spines (mechanical axis line of the tibia) (Figure 1). The lateral distal femoral angle (LDFA) was determined to measure distal femoral bone alignment, and defined as the lateral angle formed between the mechanical axis line of the femur and the knee joint line of the femur (Figure 2) [12]. Proximal tibia varus deformity was determined by the medial proximal tibia angle (MPTA). MPTA was defined as the medial angle between the knee joint line of the tibia and the mechanical axis line of the tibia (Figure 3) [12]. The tibial bone varus angle (TBVA), which does not measure possible bone or cartilage loss of the medial tibia plateau, was used to determine constitutional tibia varus deformity. TBVA was defined as the angle between a line from the centre of the tibial spines to a point midway the proximal tibia epiphysis, and the mechanical axis line of the tibia (Figure 4) [1]. A positive values represented a varus direction of the angle described. Finally, the knee joint line convergence angle (JLCA) was assessed to determine the angle between the femoral and tibial frontal plane joint lines (Figure 5) [12]. A positive value represented a medially converged knee joint line.

Two observers (TR and IT) measured all described angles using a manual goniometer graduated in degrees, without knowledge of clinical outcome to assess interobserver reproducibility. The radiographs were re-measured by the same observers at least two weeks later, without knowledge of the results of the first readings, to assess intraobserver reproducibility. One observer (TR) was orthopaedic surgeon and experienced with reviewing WLR. The other observer (IT) was a physician attending the Orthopaedic Department. An explanation and a copy of Paley's malalignment test and Bonnin's paper were given as references to each observer [1,12].

Figure 1:
The Hip-Knee-Ankle angle (HKA) is the medial angle between a line of the center of the femur head to the top of the femoral notch, and a second line from the center of the ankle to the center of the tibial spines.

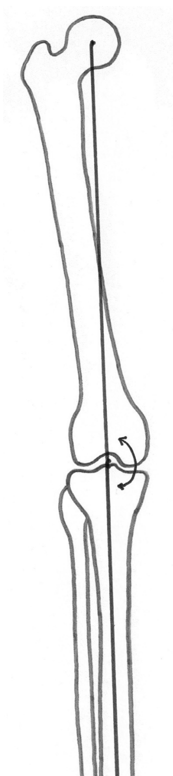


Figure 2:
Lateral distale femur angle (LDFA) is the lateral angle formed between the mechanical axis line of the femur and the knee joint line of the femur in the frontal plane.

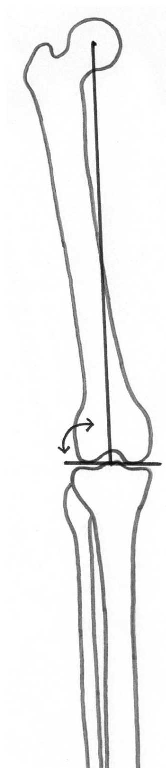


Figure 3:
Medial proximal tibia angle (MPTA) is the angle between the knee joint line of the tibia and the mechanical axis line of the tibia.

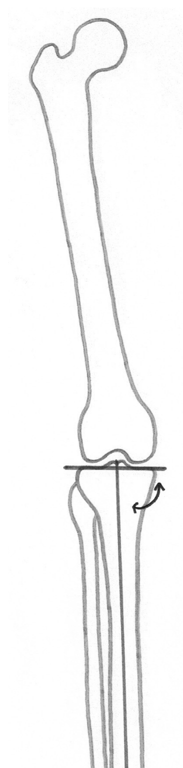


Figure 4:
Tibial bone varus angle (TBVA) is the angle between a line from the center of the tibial spines to a point midway the proximal tibia epiphysis, and the mechanical axis line of the tibia.

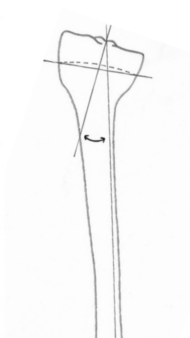
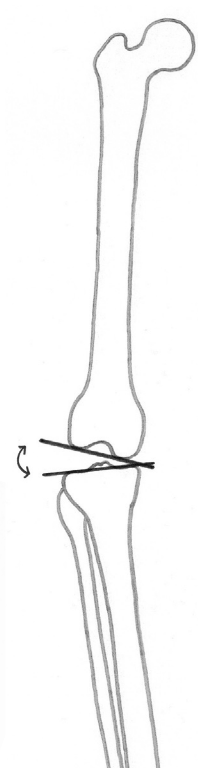


Figure 5:
The knee joint line convergence angle (JLCA) is the angle between the femoral and tibial frontal plane joint lines.



Malalignment

We considered the lower extremity varus malaligned when the HKA angle measured less than 175° [12]. When the LDFA was more than 90° the femur contributed to varus deformity, and when the MPTA angle was less than 85° the proximal tibia was a source of the varus deformity [12]. We defined constitutional tibia varus malalignment when the TBVA angle measured more than 5° [1]. JLCA was considered malaligned when the knee joint line converged more than 3°. This may be attributed to medial cartilage loss, and we also investigated the relationship (Spearman's rho correlation) between JLCA and preoperative Ahlbäck grade [12].

Statistical analysis

The SPSS statistical software version 14.0 (SPSS Inc., Chicago, Illinois) was used for statistical analysis and a p-value of 0.05 was considered to be statistically significant. The intra- and interobserver reproducibility was assessed by two-way mixed effect model, consistency definition, and expressed as intraclass correlation coefficients (ICC) that vary from zero (no agreement at all) to 1 (total agreement). We investigated the relation between conversion of HTO to TKA and preoperative malalignment; respectively varus deformity of the lower extremity (medial HKA angle < 175°), distal femur (LDFA > 90°) and proximal tibia (MPTA < 85° and TBVA > 5°), and medial convergence of the knee joint line (JLCA > 3°). We calculated odds ratios, by logistic regression analysis, to estimate the relation between failure of the osteotomy and preoperative frontal alignment factors. We performed multivariate, stepwise (backward) logistic regression and entered variables with a p-value of ≤ 0.05 into the model. The data for this investigation were collected and analyzed in compliance with the procedures and policies set forth by the Helsinki Declaration.

Results

The mean pre-HTO HKA angle of the 76 patients with 83 osteotomies was 173.1° (SD 4.1°). The mean pre-HTO distal femur alignment was in valgus with a mean of 89.1° (SD 2.4°). Pre-osteotomy proximal tibia alignment determined with the use of MPTA and TBVA measured a mean angle of 85.4° (SD 2.7°) and 6.7° (SD 4.4°), respectively. The mean pre-HTO joint line converged medially with a JLCA of 3.4° (SD 2.2°), and a positive relationship (rho = 0.3; p = 0.006) between JLCA and preoperative Ahlbäck grade of OA was found. The intra and interobserver agreements were excellent for HKA (ICC's of 0.94; 0.95), and good for MPTA (ICC's of 0.84; 0.88) and LDFA (ICC's of 0.79; 0.75). JLCA assessment showed reasonable intra and interobserver agreement (ICC's of 0.69; 0.70). However, determination of TBVA had poor intra and interobserver agreement (ICC's of 0.52; 0.48). The probability of survival for HTO was 77% (SD 4%) at 10-years follow-up. Using the logistic regression model, HKA angle < 175° and JLCA > 3° were identified as preoperative risk factors for conversion to arthroplasty (p = 0.03 and p = 0.006). There was a 4 times (95% CI; 1.2 –

13.3) higher chance of conversion to arthroplasty for patients with preoperative HKA < 175°, and a 6 times (95% CI; 1.7 – 24.3) higher risk for knee replacement in patients with a preoperative JLCA > 3°. Preoperative frontal plane varus deformity of distal femur (LDFA > 90°), or the proximal tibia (MPTA < 85° and TBVA > 5°) showed no significant relationship with HTO failure after 10 years (Table 2).

Table 2. Predictors of HTO conversion to arthroplasty at 10-years follow-up

	OR	**P-value**
HKA < 175°	4.0 (1.2 – 13.3)	0.025
LDFA > 90°	1.6 (0.5 – 5.1)	NS
MPTA < 85°	1.1 (0.4 – 3.0)	NS
TBVA > 5°	0.99 (0.3 – 3.0)	NS
JLCA > 3°	6.4 (1.7-24.3)	0.006

HKA = medial hip-knee-ankle angle
LDFA = lateral distal femoral angle
MPTA = medial proximal tibia angle
TBVA = tibial bone varus angle
JLCA = joint line convergency angle

Discussion

Careful operative technique, adequate correction, but most of all proper patient selection seem to predict long-term outcomes of HTO. Anatomical conditions that determine knee deformity in the frontal plane have been described to influence the success of valgus correction osteotomy [1,5,15]. We used a historic cohort of patients who had undergone lateral closing wedge osteotomy for symptomatic medial osteoarthritis, to determine the role of preoperative axial parameters of varus alignment in the failure of HTO. Although the indication and technique were standardized in our clinic the present study was not prospective. Indicated for operation were only patients with knee motion more than 90 degrees and with less of 15 degrees of flexion contraction, without collateral laxity greater than the expected from the diminished joint space on physical examination, and with a medial HKA angle no less than 165°. Our analysis was limited that no knee scores or radiographs were used to measure knee function or varus deformity at the time of follow-up. The outcomes were merely based on failure of the surgical procedure. However, we considered TKA to be a clear end-point for HTO failure because avoiding knee replacement is one of the main reasons to perform HTO. Another limitation of this study was that we were able to retrieve 74% of all radiographs at 10 years follow-up. Nonetheless, we noted no significant baseline differences for the group of patients who had irretrievable images compared to the study group (Table 1). In a population with symptomatic knee osteoarthritis, knee function impairment may lead to large changes in projected angles when simultaneous flexion and rotation occur [3]. We used standing WLR with lateral fluoroscopy to ensure 100% anteroposterior projection. Earlier we reported high intra- and interobserver agreement of the measurement of the HKA angle with the use of this radiological technique [2]. This study demonstrated also good agreement for the measurement of MPTA (0.84; 0.88) and LDFA (0.79; 0.75), and reasonable agreement for JLCA (0.69; 0.70).

The influence of lower extremity varus deformity on outcome after HTO remains under debate. A preoperative tibiofemoral angle > 9° has been described as a predictor of HTO failure and patient dissatisfaction after HTO [5]. Another recent analysis, however, found no influence of the preoperative angle [4]. In both studies, the determination of the cut-off angles was not well specified. We defined the lower extremity varus malaligned when the medial HKA angle measured less than 175° [12], and found a significant relation between HKA angle < 175° and conversion to TKA after 10 years. Varus alignment correlates significantly with knee adduction moment [9], and Prodromos et al. reported that patients with low preoperative knee adductor moments had substantially better clinical results after HTO than patients with high knee adduction moments [13]. Another explanation might be that the HKA angle correlates well with the grade of medial compartment osteoarthritis [2]. Advanced stages of osteoarthritis have been reported to increase the revision rate of osteotomy [11]. In our clinic we did not use preoperative stress views, but patients with collateral laxity greater than the expected from the diminished joint space on physical examination, were not eligible for osteotomy. That probably explains the significant ($p = 0.006$) correlation we observed between JLCA converging medially and preoperative Ahlbäck grade of OA. Therefore, the size of the medial converged JLCA measured on a standing WLR, most likely represents the amount of medial joint space narrowing due to loss of medial cartilage. Spahn et al. demonstrated that a medial joint space width less than 5 mm and tibial exophytes, or severe chondral damage of the medial tibia plateau predict a poor result after HTO [14]. This study also showed that JLCA > 3° was a strong predictor of HTO failure. In a retrospective analysis of 29 patients (37 osteotomies) who underwent HTO because of medial osteoarthritis, preoperative varus inclination of the distal femur was significantly associated with poor results after a mean follow-up of 7.4 years. The authors argued that assessing the preoperative slope of the distal femur was important because it may predict recurrence of varus deformity [15]. Recurrent varus has been reported to increase the risk of HTO revision by re-osteotomy or arthroplasty [11]. Our series of 83 osteotomies was limited that no varus deformity was measured at the time of follow-up. The mean preoperative LDFA, however, was in mild valgus (89.1º) which suggests that excessive tilt of the joint surface after tibial osteotomy is not likely to be expected. This may explain that we did not identify preoperative distal femur varus inclination as a risk

factor for HTO conversion to TKA after 10 years.
Tibia deformation is mainly due to both constitutional deformation and degenerative changes, and some have suggested that favourable candidates for HTO include patients who have proximal bowing of the tibia [1,8]. In a series of 217 patients who underwent lateral closing wedge HTO because of symptomatic medial osteoarthritis, clinical results seemed to be better with increased bowing at 6 years follow-up [1]. Constitutional bowing is hard to distinguish from degenerative bone deformity with standard measurement techniques that assess the tibial plateaus. TBVA measurement with the use of the proximal growth cartilage scar has been proposed to determine constitutional deformity of the proximal tibia [1]. This may be helpful because possible bone loss of the medial tibia plateau will not be measured. However, when assessing TBVA on WLR, we found poor intraobserver reproducibility ($r = 0.52$) and unacceptable low agreement between the 2 observers ($r = 0.48$), mainly due to uncertain identification of the old epiphyseal growth plate. Jenny et al. also reported low interobserver agreement ($r = 0.41$) for defining the morphology of the proximal tibia with the use of this method [6]. TBVA assessment, therefore, seems not a reliable method, and MPTA measurement may be more suitable to recognize constitutional tibia bone deformity in patients with low grade OA. In this study the majority of patients (92%) had medial compartment OA less than Grade 3 using the Ahlbäck scoring system of knee osteoarthritis, which radiological indicates no bone loss of the proximal tibia. We considered MPTA < 85° constitutional bowing of proximal tibia [12], but found no significant relationship with HTO failure after 10 years.
In summary we found that lower extremity varus deformity and medial convergence of the knee joint line predict failure of closing wedge HTO after a 10-year follow-up. In contrast, we found no evidence that varus bowing of the proximal tibia or distal femur influences long-term survival of HTO.

Acknowledgments
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Conflict of interest
The authors declare that they have no conflict of interest.

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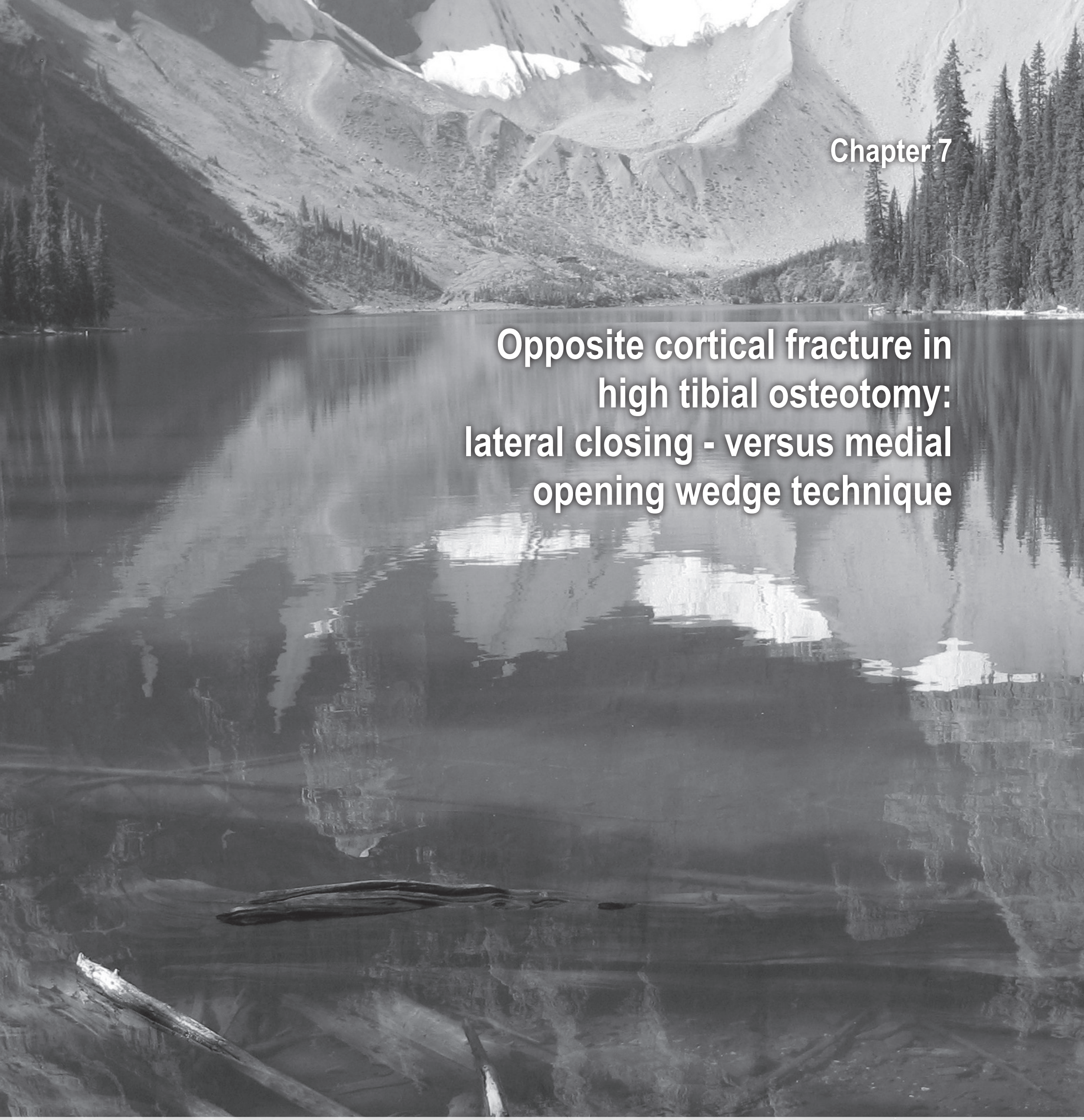

Chapter 7

Opposite cortical fracture in high tibial osteotomy: lateral closing - versus medial opening wedge technique

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Abstract

Background and purpose

High tibial valgus osteotomy (HTO) aims to correct the mechanical axis, most often, in medial compartmental osteoarthritis of the knee. Loss of operative correction may threaten the long-term outcome. In both a lateral closing wedge and a medial opening wedge procedure the opposite cortex of the tibia is usually not osteotomized leaving 1 cm bone intact as fulcrum. However, a fracture of this cortex may lead to loss of correction; this was analysed in the present study.

Patients and methods

We used a prospective cohort of 92 consecutive patients previously reported by Brouwer et al. (2006). The goal in that randomized controlled trial was to achieve a correction of 4 degrees in excess of physiological valgus. The present study evaluated in retrospect the 1-year radiographical effect of opposite cortical fracture. Opposite cortex fracture was identified on the posteroanterior radiographs in supine position on the first day after surgery.

Results

44 patients with a closing wedge HTO (staples and cast fixation) and 43 patients with an opening wedge HTO (non-angle stable plate fixation) were used for analysis. 36 patients (0.8) in the closing wedge group, and 15 patients (0.4) in the opening wedge group had an opposite cortical fracture; ($p < 0.0001$). At 1-year the closing wedge group with opposite cortex fracture had a valgus position with a mean HKA angle of 3.2 (SD 3.5) degrees of valgus. However, the opening wedge group with opposite cortex disruption achieved varus malalignment with a mean HKA angle of 0.9 (SD 6.6) degrees of varus.

Interpretation

Opposite cortex fracture is more common for the lateral closing wedge technique. However, medial cortex disruption has no major consequences, and generally does not lead to malalignment. Lateral cortex fracture in the medial opening wedge technique, with the use of a non angle-stable plate, leads more often to varus malalignment.

Introduction

High tibial valgus osteotomy (HTO) is a generally accepted treatment of medial unicompartmental osteoarthritis of the knee with varus alignment, especially in younger active patients (Virolainen et al. 2004). A successful outcome of the osteotomy relies on proper patient selection, and achievement and maintenance of adequate operative correction (Hernigou et al. 1987, Berman et al. 1991, Spahn et al. 2006). The two most commonly used surgical techniques are the closing wedge HTO with fibular osteotomy and, more recently popularised, the opening wedge HTO with plate fixation. Avoidance of opposite cortex fracture in HTO can be difficult, and is generally limited by the angular size of the wedge. A fractured medial cortex in a lateral closing wedge osteotomy may lead to progressive movement of the distal tibia into a varus position (Kessler et al. 2002). Instability at the opening wedge osteotomy site due to disruption of the lateral cortical hinge potentially results in displacement of the osteotomy, and may contribute this way to recurrent varus deformity (Miller et al. 2005).

Opposite cortical fracture in HTO is an adverse event, for which one can not randomize the patient. The highest practicable level of evidence to evaluate the consequences of intra-operative opposite cortex fracture in HTO, will be a retrospective analysis of a well-designed randomized controlled trial. Therefore, we used a cohort of 92 patients who were included in a prospective level I study on two different techniques of HTO, described extensively by Brouwer et al. (2006). The objective of the present analysis was to determine the effects of opposite cortical fracture on whole leg alignment; both for closing and opening wedge osteotomy.

Patients and methods

The patients included in this study were part of a randomized, controlled and consecutive trial published by Brouwer et al. (2006); comparing a lateral closing wedge and a medial opening wedge osteotomy in 92 patients. The goal in that trial was to achieve a correction of 4 degrees in excess of physiological valgus. For the closing wedge group a slotted wedge resection guide of Allopro (Zimmer; Winterthur, Switzerland) was used under fluoroscopic guidance. The anterior part of the proximal fibular head was resected and the osteotomy was fixated with 2 staples. After surgery a standard cylinder plaster cast was applied for 6 weeks. The opening wedge HTO was created with the Puddu HTO instrumentation (Arthrex; Naples, Florida, USA), and performed under fluoroscopic guidance to control the correction during the surgical procedure; the osteotomy was fixated with the non-angle stable Puddu plate. If the wedge was more than 7.5 mm, the open wedge was filled with bone from the ipsilateral iliac crest. All patients were mobilized on the first postoperative day, and partial weight-bearing was allowed for 6 weeks. This analysis focuses on the radiographical effect of opposite cortical fracture on the whole leg alignment in both techniques at the 1-year follow-up. Standardised radiography was performed preoperatively, and on the first day and 12 months after surgery.

1 patient was lost to follow-up (closing wedge), and in 3 patients (closing wedge; 2 and opening wedge; 1) we were not able to retrieve the radiographs made 1 day after surgery to determine opposite cortical fracture. In another patient (opening wedge) the 1-year postoperative whole leg radiograph had not been made, because of emergency treatment of an unrelated condition. Thus, the study population consisted of 87 of the original 92 patients (Table 1).

Table 1: Baseline characteristics of the total study population and separately for the two intervention groups.

	Total (n = 87)	Closing wedge HTO (n = 44)	Opening wedge HTO (n = 43)
Sex, male : female	55 : 32	25 : 19	30 : 13
Age, [years], mean (SD)	50 (8.6)	50 (8.1)	50 (9.1)
HKA angle [a] [°], mean (SD)	5.9 (3.0)	6.6 (3.1) [b]	5.3 (2.8) [b]
Ahlbäck grade			
medial compartment			
0	2	1	1
1	74	39	35
2	11	4	7
lateral compartment			
0	80	39	41
1	7	5	2

[a] positive angle represents varus alignment, negative angle represents valgus alignment
[b] $p = 0.05$ for the difference between the two intervention groups

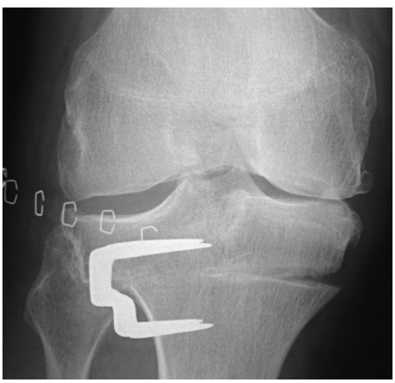
Measurements

The grade of radiographical osteoarthritis was scored according to Ahlbäck (1968) and measured on standard short posteroanterior radiographs in standing position. The mechanical axis (Hip-Knee-Ankle angle; HKA angle) was measured on a whole leg radiograph in standing position before surgery and 1 year after surgery (Brouwer et al. 2003). Opposite cortical fracture of the osteotomy site was scored from the posteroanterior radiographs in supine position on the first day after surgery by one assessor (TMR), blinded for the 1-year postoperative radiographical outcome (Figure 1). When cortical disruption was noted in the lateral closing wedge group, we also looked for a gap. A gap was defined as a more than 2 mm width between the disrupted opposite cortex fragments occurred (Figure 2).

Figure 1: Opposite cortical fracture on the first day after surgery (radiograph in supine position)

Closing-wedge HTO | Opening-wedge HTO

Figure 2: Opposite medial cortical fracture with a gap in closing-wedge HTO on the first day after surgery (radiograph in supine position)



Statistical analysis

Distribution analysis of the HKA was tested by the Shapiro-Wilk test. The data of the HKA were not normally distributed, therefore Mann-Whitney-Wilcoxon U-test was used to analyse between-group differences. The χ^2 (chi-squared) test was used to compare the percentage of opposite cortical fractures between the groups. We used the SPSS program statistical software version 10.1 (SPSS Inc., Chicago, Illinois) and a p-value of 0.05 was considered to be statistically significant.

Results

44 patients had a closing wedge HTO and 43 patients had an opening wedge HTO. 36 patients (0.8) in the closing wedge group, and 15 patients (0.4) in the opening wedge group were identified with an opposite cortical fracture; this difference between the two osteotomy techniques was highly significant ($p < 0.0001$). The relative risk of an opposite cortical fracture in closing wedge - compared to opening wedge HTO was 8 (95% CI 3-23).

Closing wedge HTO

The mean preoperative HKA angle for the closing wedge group was 6.7 (SD 2.9) degrees of varus in the group with a cortex fracture and 6.0 (SD 4.1) degrees of varus in the patients without opposite cortical disruption. At the 1-year follow-up the mean postoperative HKA angle was 3.2 (SD 3.5) degrees of valgus in the closing wedge group with cortex fracture and 2.5 (SD 3.7) degrees of valgus without cortex fracture; these differences were not statistically significant (Table 2). Of the 36 patients with a medial cortex fracture, 18 showed no gap. In 18 patients we observed a gap of more than 2 mm between the opposite cortex fragments. When a gap was seen on the first day postoperative radiograph the mean 1-year postoperative HKA angle was more in valgus compared to the group with opposite cortex fracture without a gap ($p = 0.05$) (Table 3); respectively 4.3 (SD 3.4) and 2.1 (SD 3.4) degrees of valgus. In the group with a gap 7 patients had a valgus of more than 4 degrees compared to 6 patients without a gap; this difference was not significant. No significant deviation form the planned 4 degrees in excess of physiological valgus was seen in any of the subgroups at 1-year follow-up.

Opening wedge HTO

The opening wedge group with (4.9 degrees; SD 3.2) and without (5.5 degrees; SD 2.5) opposite cortical fracture showed no significant difference in the mean preoperative HKA angle of varus. The 1-year postoperative mean HKA angle was 0.9 (SD 6.7) degrees of varus in the group with cortex fracture, and 2.3 (SD 4.0) degrees of valgus in the group without cortex disruption (Table 2). This difference in postoperative alignment between the two groups almost reached statistical significance ($p = 0.057$) 1 year after surgery. The group of patients with opposite cortical fracture achieved less accurate correction with deviation from the planned 4 degrees in excess of physiological valgus at 1-year follow-up ($p = 0.04$). The group without cortex fracture did not deviate significantly from the planned correction 1 year after surgery.

Table 2: Whole leg alignment (Hip-Knee-Ankle angle) for closing and opening wedge high tibial osteotomy groups with or without opposite cortical fracture.

	Closing wedge HTO (n = 44) Mean (SD)		Opening wedge HTO (n = 43) Mean (SD)	
Opposite cortex fracture	Yes (n = 36)	No (n = 8)	Yes (n = 15)	No (n = 28)
HKA angle [a], degrees				
- preoperative	6.7 (2.9)	6.0 (4.1)	4.9 (3.2)	5.5 (2.5)
- postoperative	-3.2 (3.5)	-2.5 (3.7)	0.9 (6.7) [b]	-2.3 (4.0) [b]

[a] positive angle represents varus alignment, negative angle represents valgus alignment
[b] p = 0.057 for postoperative HKA angle difference with and without cortex disruption, opening wedge group

Table 3: Whole leg alignment (Hip-Knee-Ankle angle) for closing wedge osteotomy stratified for medial cortex fracture pattern.

	Opposite cortex fracture (n = 36) [a]		
	no gap (n = 18)	gap (n = 18)	
HKA angle [b], degrees			
- preoperative	6.1 (2.9)	7.2 (2.9)	p = 0.25
- postoperative	-2.1 (3.4)	-4.3 (3.4)	p = 0.05

[a] mean (SD)
[b] positive angle represents varus alignment, negative angle represents valgus alignment

Discussion

Opposite cortical fracture in closing - and opening wedge HTO seems an operative complication not entirely preventable when correcting a large varus deformity. Pape et al. (2004) reported that the capacity for plastic deformation of the medial cortex of the proximal tibia might have been exceeded in closing osteotomies with a larger wedge size (> 8 degrees), leading to a non-displaced fracture during the operation. Böhler et al. (1999) argued that valgus correction of the tibia plateau by removal of a wedge as much as 10 degrees is possible without fracturing the medial cortex. However, another cadaver study by Kessler et al. (2002) permitted far less maximal angular correction (7 degrees for both the closing and opening wedge technique) that can be applied to human tibias without fracturing the cortex at the apex of the wedge. This was underscored by Spahn et al. (2003) who reported in a series of 55 patients treated with opening wedge HTO using the Puddu spacer plate (mean wedge correction angle of 9.7 degrees; SD 1.9), 8 lateral cortical fractures. In our patients the primary outcome was to achieve a correction of 4 degrees in excess of physiological valgus at one-year follow-up, leading to a mean correction angle of 11 (SD 3.1) degrees in the closing wedge and 9 (SD 2.8) degrees in the opening wedge group. The magnitude of the wedge sizes may be the reason for a high rate of unintentional opposite cortical fracture seen in both the closing – (four fifths) and opening wedge technique (one third). Also, with the closing wedge technique it can be difficult to remove the wedge completely, especially at its apex at the medial side. Consequently, closing the wedge may cause fracturing at the medial osteotomy site. This probably explains the significant higher rate of opposite cortex fracture compared to the opening wedge technique.

Study limitations

The study patients were part of a randomized, controlled and consecutive trial on two osteotomy techniques (Brouwer et al. 2006). Few clinical studies have reported on the effect of opposite cortical fracture in HTO that may lead to loss of correction. We realize that subgroup analysis in such a trial has its statistical limitations. However, it is impossible to randomize for adverse events such as opposite cortex fracture in HTO. With this analysis we focused on the 1-year radiological effect of intra-operative opposite cortex disruption in both techniques. A limitation might be that we did not make a whole leg radiograph the first day postoperatively because the patient could not stand on his operated leg; therefore we can not discriminate between insufficient correction or loss of correction during the one year follow-up.

Closing wedge HTO

It has been advised to maintain the medial cortex of the proximal tibia in lateral closing wedge HTO to provide sufficient stability and avoid a decreasing cortical contact area of tibial segments (Miniaci et al. 1989, Coventry et al. 1993). Progressive movement into a varus position may otherwise occur (Myrnerts 1980, Insall et al. 1984). However, our data do not support this statement. The aimed correction was achieved even more often in the closing wedge group with medial cortex fracture and a gap of the medial cortex fragments (Table 3). With the closing wedge technique, posteromedial bony remnants may act like a more lateral hinge when closing the wedge, and probably cause fracture and gaping at the medial osteotomy site with pronounced valgisation. Pape et al. (2004) detected no loss of valgus correction on full weight-bearing standing radiographs in patients with a fractured medial cortex of the proximal tibia after a closing wedge procedure either; they used an L-shaped rigid plate, which is supposed to offer high primary stability. Radiostereometric findings indicate a less stable situation for closing wedge osteotomy when bone staples with a plaster cast are used (Magyar et al. 1999). Harrison and Waddell (2005), however, noted no change in femoral-tibial alignment with the use of staples and a long-leg cast.

Opening wedge HTO

Unharmed opposite lateral cortex largely dictates the stability after opening wedge HTO regardless of implant design (Stoffel et al. 2004). Agneskircher et al. (2006) also stated that in composite tibias, independent of the implant, axial loading is well tolerated with an intact lateral cortical bridge. Our results seem to justify these findings in a clinical setting. With the use of the non-angle stable Puddu plate, 1-year postoperative the mean HKA angle was 2.3 degrees of valgus in the opening wedge group without cortex fracture (Table 2). In our study however, 15 of 43 patients fractured the opposite tibia cortex, and achieved less accurate correction with a mean HKA angle of 0.9 degrees of varus at 1 year follow-up. Hernigou et al. (1987) reported lateral cortex fracture as a complication of medial opening wedge HTO, resulting in displacement of the osteotomy and recurrent varus malalignment before osteotomy union in 12% of all their patients. In our series 4 patients with lateral cortex disruption were re-operated within 1 year; 2 patients because of non-union and 2 patients required re-valgisation osteotomy due to the recurrent varus deformity (Brouwer et al. 2006). Disruption of the lateral cortex causes increased micromotion at the osteotomy site, and this instability likely contributes to the high incidence of delayed union and non-union after medial HTO (Miller et al. 2005). The Puddu plate proved unable to oppose the instability, which was also reported by others (Spahn et al. 2003). Mechanical studies have shown that when the lateral cortex is injured, angle-stable implants provide superior primary stability compared to the Puddu plate (Stoffel et al. 2004, Agneskircher et al. 2006). The angle stable design protects the lateral cortex and prevents lateral displacement. Furthermore, the use of a spacer with an angle-stable plate seems to increase primary stiffness even more (Spahn et al. 2006). When unintentional opposite cortical fracture occurs, we suggest the use of an angle-stable implant, which has the best biomechanical properties in internal fixation after medial opening wedge HTO.

Conclusion

We conclude that fracturing of the opposite cortex in HTO is much more common in the lateral closing than in the medial opening wedge technique. Nevertheless medial cortex fracture in closing wedge osteotomy with the use of staples and plaster has no major consequences, and can be managed successfully in the vast majority of patients. It does not generally lead to recurrence of varus malalignment 1 year after surgery. However, lateral cortex fracture in the medial opening wedge technique is an unstable situation. The use of a non-angular stable Puddu plate seems to provide insufficient primary stability, and leads more often to varus malalignment.

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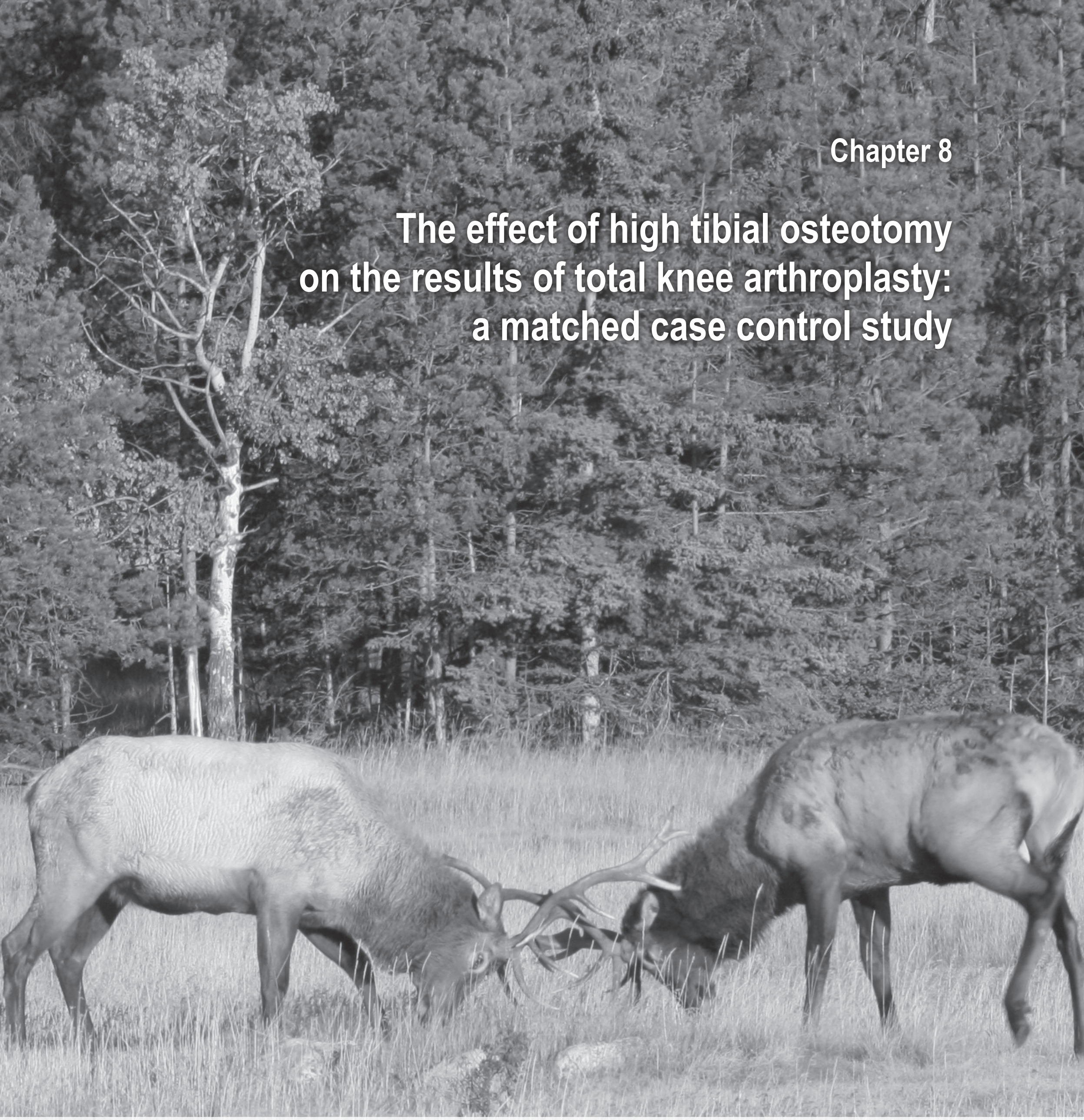
Chapter 8

The effect of high tibial osteotomy on the results of total knee arthroplasty: a matched case control study



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Abstract

Background: We performed a matched case control study to assess the effect of prior high tibia valgus producing osteotomy on results and complications of total knee arthroplasty (TKA).

Methods: From 1996 until 2003 356 patients underwent all cemented primary total knee replacement in our institution. Twelve patients with a history of 14 HTO were identified and matched to a control group of 12 patients with 14 primary TKA without previous HTO. The match was made for gender, age, date of surgery, body mass index, aetiology and type of prosthesis. Clinical and radiographic outcome were evaluated after a median duration of follow-up of 3.7 years (minimum, 2.3 years). The SPSS program was used for statistical analyses.

Results: The index group had more perioperative blood loss and exposure difficulties with one tibial tuberosity osteotomy and three patients with lateral retinacular releases. No such procedures were needed in the control group. Mid-term HSS, KSS and WOMAC scores were less favourable for the index group, but these differences were not significant. The tibial slope of patients with prior HTO was significantly decreased after this procedure. The tibial posterior inclination angle was corrected during knee replacement but posterior inclination was significantly less compared to the control group. No deep infection or knee component loosening were seen in the group with prior HTO.

Conclusion: We conclude that TKA after HTO seems to be technically more demanding than a primary knee arthroplasty, but clinical outcome was almost identical to a matched group that had no HTO previously.

Background

Medial unicompartmental osteoarthritis of the knee is a common clinical problem. In the active patient with a life expectancy of 20 years or more a high tibia valgus osteotomy (HTO) is a generally accepted treatment that can result in excellent pain relief and function improvement. However results seem to deteriorate in time and an overall failure rate of 24% at 10 years has been reported [1]. Most likely due to the natural course of unicompartmental osteoarthritis progression of symptoms occurs and this group of patients may require knee replacement.

Difficult exposure of the tibia due to soft tissue scaring, patellar mechanism eversion difficulties, reduction of the amount of tibia bone stock, tibia plateau tilting, retained osteosynthesis and subacute infection are technical points to be dealt with when performing a total knee arthroplasty (TKA) after proximal tibia osteotomy [2]. Another important factor influencing the outcome of TKA after HTO is patient selection [3]. Patient cohort disparity may therefore be one of the causes that some report substandard total knee arthroplasty outcome after a high tibial osteotomy [4,5,6] while others see no clinical or radiographic difference for TKA with or without an osteotomy [7,8].

Randomized controlled trials (RCTs) are considered the ideal and highest level of evidenced based medicine [9]. However, an RCT may not be an appropriate standard of evidence for evaluating most surgical treatments. Very few operations can be randomized for ethical, scientific, or practical reasons. Numerous "good" surgical practices have evolved into "standard of care" without being randomized against placebo or ineffective treatment options [10]. An RCT on the effect of previous HTO on TKA outcome would hardly be ethical. The young, active patient with symptomatic medial compartmental osteoarthritis would be denied of standard operative care by not performing tibial osteotomy as a placebo-control arm. Thus the highest practicable level of evidence will be a representative observational study [10].

We conducted a case control study to assess the influence of high tibia valgus osteotomy on results and complications of total knee replacement. In the aim to prevent cohort disparity we matched for diagnosis, time of follow-up, body weight and significant risk factors for failure of TKA [11] to select an ideal comparison group.

Methods

Between January 1996 and June 2003, a series of 356 all cemented primary total knee arthroplasties (TKA) was performed in the author's institution. Sixteen patients with a history of 18 proximal tibial osteotomies prior to total knee replacement were identified. Two patients had died and two patients were lost tot follow up.

The index group was compromised of 14 knees in 10 women and 2 men who underwent total knee replacement 4.8 (range 1.3 – 8.9) years after HTO. A lateral closing wedge technique through a transverse incision with the patient in supine position was performed in all patients. The osteotomy was fixated with two step staples. After surgery a standard cylinder plaster cast was applied for 6 weeks. All patients were mobilised on the first postoperative day, and partial weight-bearing with the use of two crutches was allowed for 6 weeks. After bony healing the staples were removed in all knees except one; in 9 knees before, in 3 during, and in one knee after joint replacement. Symptomatic medial compartment osteoarthritis was diagnosed in all cases. The median age at the time of total knee surgery was 60 (range 51 – 75) years and the median body mass index (BMI) of this group was 31.3 (range 26.2 – 41.5) kg/m^2. Nine patients had surgery prior to tibial osteotomy, including four who had meniscectomy, one who had arthroscopy with debridement, one who had a cartilage transplantation, one who had a failed valgus closing wedge tibia osteotomy performed in another institution, and two who had surgery because of a fracture around the knee.

This group was matched with a control group of 14 primary total knees in 12 patients

selected from the same cohort of patients with total knee replacement. The match was made for gender, age, date of surgery, BMI, aetiology and type of prosthesis (Table 1). Ten patients in the control group underwent prior surgery before knee replacement. Six patients had a meniscectomy, two had surgery because of a fracture around the knee, one had a diagnostic arthroscopy to evaluate posterior cruciate ligament insufficiency and one had a peroneal nerve release. The indication for TKA was symptomatic osteoarthritis in all patients.
Two types of cruciate retaining all cemented total knee prosthesis (Kinemax, Howmedica International Inc, Co.Clare, Ireland and Genesis II, Smith & Nephew, Memphis, U.S.A.) were used in both groups. One patient in the index group needed a posteriorly stabilized knee prosthesis and was matched to a patient in the control group with the same type of prosthesis.

Patients in both groups underwent clinical and radiographic evaluation at a minimum follow up of two years. Pre- and postoperative data of knee range of motion were available for all patients. Knee pain was measured by a visual analogue scale (VAS (0 – 10)) [12]. Knee function was evaluated by the Hospital for Special Surgery Score (HSS), the Knee Society Score (KSS) and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) [13,14,15].
Pre- and postoperative radiography of the knee included an anteroposterior radiograph in standing position to measure the femorotibial angle (FTA) [16]. A true lateral radiograph of the knee in at least 30 degrees of flexion was used to determine the length of the patella tendon according to Insall-Salvati (IS ratio) [17]. The posterior inclination angle of the tibia plateau (PI) was measured on a lateral radiograph according to Moore-Harvey [18]. The Kellgren-Lawrence and Ahlbäck scores were used to determine the level of osteoarthritis [19,20]. Fixation of the knee components was evaluated using the Knee Society Roentgenographic Evaluation System [21].

The SPSS program was used for the statistical analyses. A p-value of 0.05 was considered statistically significant. The sample size was calculated based on an expected inferior clinical result for the index group. An inferior result was defined as 15 points difference in HSS score. To detect such a difference with one-sided testing (α = 0.05 and power of 80%) we needed to include 12 patients in each group. The data for this investigation were collected and analyzed in compliance with the procedures and policies set forth by the Helsinki Declaration, and all patients gave their informed consent.

Results

No significant differences were noted between the two groups with respect for gender, age, time of follow-up, American Society of Anaesthesiologists (ASA) risk score [22] and type of knee prosthesis ratio (Table 1).) Both groups showed overweighted patients with a higher median BMI for the index group; this was, however, not significantly different from the control group.

Table 1: Demographic data for 14 knees with a closing wedge high tibia osteotomy prior to TKA (index group) and 14 knees with a primary TKA (control group)

Demographic	**Index**	**Control**
Gender, female : male	10 : 2	10 : 2
Age, median years	60 (51 – 75)	61 (51 – 75)
Follow-up, median years	3.7 (2.3 – 8.8)	4.0 (2.3 – 8.3)
BMI, median kg/m2	31.1 (26.2 – 41.5)	28.6 (24.5 – 37.3)
ASA,		
1	1	2
2	10	10
3	3	2
OA, Kellgren-Lawrence score		
Grade 2	1	1
Grade 3	12	9
Grade 4	1	4
OA, Ahlbäck score		
Grade 1	4	4
Grade 2	6	8
Grade 3	3	1
Grade 4	1	1
Prosthesis, Kinemax : Genesis	11 : 2	10 : 3

The different levels of osteoarthritis before knee replacement were equally distributed in both groups using the Kellgren-Lawrence and Ahlbäck grading systems (Table 1).
All total knees in both groups were approached by the standard medial parapatellar incision.

The median operative time in the index group was not significantly different from the control group (p = 0.173) with 120 (range 95 – 165) minutes compared to 115 (range 90 - 135) minutes; respectively. The patient group with a previous osteotomy suffered from more perioperative blood loss with a median of 450 (range 100 - 915) ml compared to a median blood loss of 225 (range 100 - 600) ml in the control group; this difference was not significant (p = 0.071). The index group required one tibial tuberosity osteotomy and three lateral retinaculum releases. The control group needed no tuberosity osteotomy or lateral releases. There was a trend (p = 0.092) towards the use of a thicker polyethylene tibial component composite in the index group, with a mean thickness of 10 (range 8 - 18) mm compared with a median of 8 (range 8 – 12) mm in the control group.

Postoperative complications

No infections were seen in both groups postoperatively. Two patients, one in each group, were mobilized under anaesthesia because of limited range of motion.

Clinical and radiological outcome

The range of motion postoperative showed no significant difference between both groups (Table 2).

Table 2. Range of motion in both groups before and after TKA

		Index *	Control *	Significance
Flexion	Pre TKA	100 ° (60 – 150)	120 ° (90 – 130)	NS
	Post TKA	110 ° (95 – 130)	120 ° (80 – 130)	NS
Extension	Pre TKA	0 ° (- 15 – 0)	0 ° (- 40 – 0)	NS
	Post TKA	0 ° (-10 – 5)	0 ° (- 20 – 10)	NS

* The values are given as the median (range)
- Negative value indicates extension deficit

The postoperative knee flexion in the index and control group had a median of 110 ° (range 95 – 130 °) and 120 ° (range 80 – 130 °), respectively. The postoperative median VAS score was 4.5 (range 0 - 9) in the index group and 3.7 (range 0 - 9) in the control group; this difference was not significant. The functional outcome analysed by the HSS, KSS and WOMAC scores is presented in Table 3. Although all scores were worse for the index group no significant differences were noted.

Table 3. Functional outcome in both groups after TKA

		Index *	Control *	Significance
Score	[0 – 100]			
HSS		78.5 (48 – 91)	82 (57 – 95)	NS
KSS	Knee	79 (45 – 105)	90 (45 – 110)	NS
	Function	70 (10 – 90)	80 (20 – 100)	NS
WOMAC	Pain	57.5 (30 – 100)	80 (20 – 100)	NS
	Stiffnes	43.8 (12.5 – 100)	62.5 (12.5 – 100)	NS
	Function	56.6 (17 – 100)	66.1 (14 – 100)	NS

* The values are given as the median (range)

The radiographic results for both groups are given in Table 4 and 5. The index group had a significant (p < 0.0001) increase of the median FTA from - 3 º (range -9 – 0 º) before HTO to 3 º (range -2 – 9 º) before TKA. The PI (p = 0.04) and the IS ratio (p = 0.03) were both significantly decreased after HTO from 6 º (range -2 to 14 º) to 3 º (range -13 to 16 º) and from 1.06 (range 0.74 – 1.29) to 0.95 (range 0.58 – 1.20), respectively.
Subsequently there were significant differences between the index and control groups according to the preoperative PI (3 º (range -13 to 16 º) versus 6.5 º (range 4 to 16 º)) and preoperative IS ratio (0.95 (range 0.58 – 1.20) versus 1.07 (range 0.76 – 1.29)).
Postoperative, the two groups showed no significant differences for anteroposterior alignment, femoral component placement and patellar height.

Table 4. Radiological outcome in both groups before TKA

	Index *			Index *	Control *	
	pre HTO	pre TKA	P	pre TKA	pre TKA	P
FTA[a]	- 3.0 º (- 9 ; 0)	3.0 º (-2 ; 9)	< 0.0001	3.0 º (-2 ; 9)	2.0 º (-3 ; 11)	NS
PI [b]	6.0 º (- 2 ; 14)	3.0 º (-13 ; 16)	0.04	3.0 º (-13 ; 16)	6.5 º (4 ; 16)	0.04
IS [c]	1.06 (0.74 ; 1.29)	0.95 (0.58 ; 1.20)	0.002	0.95 (0.58 ; 1.20)	1.07 (0.76 ; 1.29)	0.05

* The values are given as the mean (range)
- Negative value indicates varus alignment
[a] Femorotibial angle
[b] Posterior inclination tibia plateau
[c] Patella height: Insall-Salvati ratio

Table 5. Radiological outcome in both groups after TKA

		Index *	Control *	Significance
Alignment [a]		5.0 º (- 4 – 14)	6.0 º (- 4 – 9)	NS
Femoral component [b]		2.0 º (- 3 – 8)	2.0 º (- 5 – 8)	NS
Tibial component [c]		7.0 º (0 – 12)	12.0 º (2 – 20)	p = 0.026
Insall – Salvati ratio		1.25 (0.90 – 1.79)	1.10 (0.90 – 1.46)	NS
Loosening [d]	Femoral (mm)	N =1 (3)	N = 2 (2 + 3)	NS
	Tibial (mm)	0	N = 1 (9)	NS
	Patella (mm)	0	0	NS

* The values are given as the median (range)
- Negative value indicates varus alignment
[a] Femorotibial angle (FTA)
[b] Flexion angle femoral component
[c] Posterior inclination tibial component
[d] Loosening according to the Knee Society Roentgenographic Evaluation System

The tibial component was placed with significantly (p = 0.025) less posterior slope in the index group, respectively 7 º (range 0 to 12 º) and 12 º (range 2 to 20 º) in the control group. Both groups had an increase of patella height postoperatively, which was only significant for the study group (p = 0.002).
The Knee Society Roentgenographic Evaluation System revealed one patient with a numeric score of 3 for the femoral component in the index group. No radiological tibial or patellar loosening was seen in the index group. The control group had two patients with radiological femoral component loosening with a score of 2 and 3, respectively. Scores of four or less are probably not significant [21].
One patient in the control group showed a numeric score of 9 for the tibial component with malposition. This knee was successfully revised 26 months after total knee replacement. No patellar loosening was seen in the control group.

Discussion and conclusion

Proximal tibial osteotomy is a well-accepted treatment of medial unicompartmental osteoarthritis of the knee with varus malalignment in young and active patients [1]. In general, however, progression of disease will occur and ultimately many patients require

TKA. In the present study osteotomy delayed total knee replacement with a median of 4.8 years. This amount of time bought before performing arthroplasty compares well with other studies [23,24].

Conflicting results of TKA after HTO have been reported. Some studies identify no clinical or radiographic difference in outcome for TKA with or without a previous osteotomy [7,8] while others see substandard TKA outcome after HTO [5,6]. Technical difficulties such as soft tissue scarring, patella infera, limb malalignment, reduced bone stock of the proximal tibia, tibial plateau tilting and retained osteosynthesis material have been recognized to contribute to suboptimal components positioning and soft-tissue balancing [2,3]. Risk of selection bias in non-randomised studies may be another cause of differences in outcome [25]. Patients who had a previous osteotomy are a highly selected population with presumably an unfavourable demographic status [3]. We attempted to minimise selection bias by controlling for known prognostic factors. That is why we conducted a case control study matched for diagnosis, time of follow-up, BMI, gender, age and type of prosthesis. We realise, however, that the present study cannot address the problem of unknown or immeasurable prognostic factors.

In our matched case control study we found less favourable results for a total knee replacement after previous osteotomy compared to a primary knee arthroplasty. Knee replacement after closing wedge tibial osteotomy showed a trend towards prolonged median operative time and a greater amount of blood loss. Hardware removal during knee implant surgery only occurred in three knees, and surgical records showed no difficulties in taking out the step staples. A more plausible reason may have been the significant decline in patellar height (mean IS ratio = 0.93). Patellar tendon shortening, and a decreased distance from the tubercle to the joint after closing wedge osteotomy proximal to the tuberosity, make patellar eversion more difficult [23]. In our series we had to perform three lateral retinacular releases and one tuberosity osteotomy to facilitate eversion of the patella and the patellar ligament. Soft tissue balancing in the valgus knee after closing wedge osteotomy could have been another reason. The trend to use a thicker insert in the study group suggests significantly more lateral dissection.

Our index group developed no flexion contracture post closing wedge osteotomy and the knee range of motion after knee replacement did not differ between the two groups. The alignment considering the femorotibial angle was corrected close to the optimal 6 degrees of valgus in both groups. No significant differences were noted. The femoral component was placed in mild flexion but did not differ between the two groups. The tibial posterior inclination however was significantly decreased after osteotomy (Table 4). We managed to restore the posterior slope during knee replacement but posterior inclination was still significantly less compared to the control group (Table 5). Loss of tibial slope has been

described after closing wedge osteotomy and is associated with patella infera. Also a relative elevation of the posterior cruciate ligament can occur leading to PCL insufficiency [26]. In our series we just needed one posterior stabilized knee arthroplasty due to PCL insufficiency. We were able to correct patella infera, and the patellar height after TKA in the index group did not differ significant from the control group. Especially after excluding one patient in the index group with bilateral patella alta after re-insertion of traumatic bilateral patella tendon rupture the patellar ratio (median IS ratio = 1.19) equalled that of the control group (median IS ratio = 1.10).
Literature suggests that after primary knee joint replacement substantial improvements in the scores for physical health, such as those for pain and physical functioning seem to take place within the first 3 to 6 months after surgery. Studies with longer-term follow-up describe long-lasting improvement [27]. Deehan et al. also found an enduring improvement in KSS at 3 and 12 months after revision surgery, which was comparable with the improvement in KSS for primary TKA. Successive surgical revision, however, had a negative influence on reported functional outcome [28]. In our series, after a median follow-up of 3.7 years, HSS, KSS and WOMAC scores showed inferior results for the patients who underwent TKA after tibial osteotomy; possibly due to the low numbers of patients these differences in function scores did not reach significance.

The last decade medial opening wedge HTO with special implants for internal fixation has gained popularity in the treatment of varus gonartrosis. Opening wedge osteotomy is advocated to be technically easier and a fibular osteotomy is not required. To our knowledge no results have yet been published on the effect on subsequent TKA. However, since larger implants are necessary in open wedge osteotomy, implant removal should not be combined with total knee arthroplasty. A recent RCT showed significantly more patellar descent and tibial slope increase after opening wedge HTO compared to the closing wedge technique [29]. This might cause exposure and patellar eversion problems during knee replacement. The advantage of opening wedge osteotomy is preservation of bone stock with tensioning of the medial collateral ligament. This may result in a more conservative amount of bone removed during knee joint replacement. Consequently, joint line elevation by the use of a thicker than desired tibial component in balancing the ligaments, is less likely. Furthermore, unlike closing wedge osteotomy, the relative position of the medullary canal is not altered. This may facilitate tibial component placement by intramedullary guidance. Future studies, however, have to confirm whether these aspects of the opening wedge osteotomy technique influence conversion to a TKA.

Correction osteotomy in relatively young patients with osteoarthritis of the medial compartment has good results and delays knee replacement [30]. Arthroplasty in the young patient can have adverse effects. In an update study of data from the Swedish Knee Arthroplasty Register younger age was associated with an increased risk of prosthetic revision [31]. An analysis of the Mayo Clinic total joint register confirms the significance of age in knee replacement. Ten-year knee prosthetic survivorship for patient who were 55 years or younger was 83% compared with 94% for those older than 70 years ($p < 0.0001$) [11]. It has been described that the survivorship for knee arthroplasties without prior surgery is significantly greater than for knees with prior operative treatment [11]. In our series, however, we did not encounter any TKA revisions because of loosening or infection in the group of patients receiving TKA after prior HTO during the course of our evaluation.

Ethical considerations, but also the absence of equipoise in performing randomisation due to the fact that outcomes of operations are related to their mechanisms of action as well as to patient's cooperation with treatment plans, rules out an RCT to assess the effects on TKA outcome after previous osteotomy [10]. A cohort study using comparison groups matched for patient-selection factors that affect survivorship of TKA will be the best available level of evidence. Our matched control study tends to show that total knee replacement after proximal tibial osteotomy is a therapeutic option technically more demanding than a primary knee arthroplasty. Medium-term results are less favourable for the osteotomized patient although not significantly worse. We are in need of more well-designed observational studies in order to conduct a meta-analysis to develop grades of recommendation in performing TKA after HTO.

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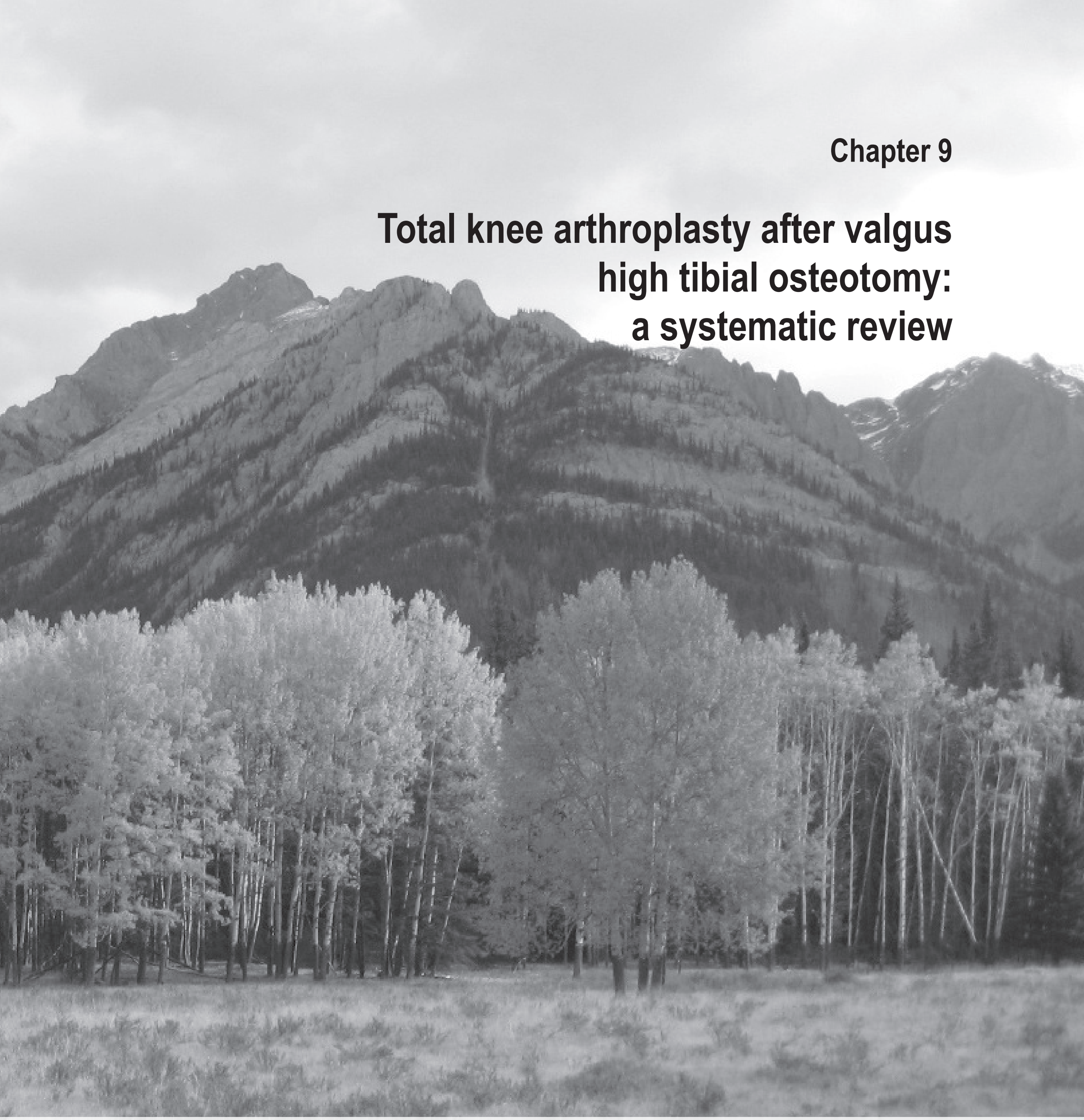

Chapter 9

Total knee arthroplasty after valgus high tibial osteotomy: a systematic review

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Abstract

Background: Previous osteotomy may compromise subsequent knee replacement, but no guidelines considering knee arthroplasty after prior osteotomy have been developed. We describe a systematic review of non-randomized studies to analyze the effect of high tibial osteotomy on total knee arthroplasty.

Methods: A computerized search for relevant studies published up to September 2007 was performed in Medline and Embase using a search strategy that is highly sensitive to find nonrandomized studies. Included were observational studies in which patients had total knee arthroplasty performed after prior high tibial osteotomy. Studies that fulfilled these criteria, were assessed for methodologic quality by two independent reviewers using the critical appraisal of observational studies developed by Deeks and the MINORS instrument. The study characteristics and data on the intervention, follow-up, and outcome measures, were extracted using a pre-tested standardized form. Primary outcomes were: knee range of motion, knee clinical score, and revision surgery. The grade of evidence was determined using the guidelines of the GRADE working group.

Results: Of the 458 articles identified using our search strategy, 17 met the inclusion criteria. Fifteen studies were cohort study with a concurrent control group, one was a historical cohort study and one a case-control study. Nine studies scored 50% or more on both methodological quality assessments. Pooling of the results was not possible due to the heterogeneity of the studies, and our analysis could not raise the overall low quality of evidence. No significant differences between primary total knee arthroplasty and total knee arthroplasty after osteotomy were found for knee range of motion in four out of six studies, knee clinical scores in eight out of nine studies, and revision surgery in eight out of eight studies after a median follow-up of 5 years.

Conclusions: Our analysis suggests that osteotomy does not compromise subsequent knee replacement. However, the low quality of evidence precludes solid clinical conclusions.

Background

High tibial osteotomy (HTO) is an accepted surgical treatment of medial unicompartmental osteoarthritis (OA) of the knee with varus mal-alignment in young patients. However, there is no sound evidence that an osteotomy is more effective than alternative non-operative therapies, such as valgus bracing or laterally wedged insoles [1]. Furthermore, results seem to deteriorate with time and this group of patients may require total knee replacement [2]. Success of primary total knee arthroplasty (TKA) with knee osteoarthritis is well established, and about 85% of patients are satisfied with the surgical outcome [3]. When considering osteotomy in the early treatment of medial compartment knee OA, subsequent TKA should not be compromised, and results should not deteriorate more rapidly than after primary TKA alone [4]. In the past, there have been reports of technical difficulties after failed HTO that influenced outcomes of knee replacement; however these studies were criticized due to patient selection bias [5,6].

The aim of this study was to collect the best available scientific evidence from clinical studies examining TKA after HTO compared with primary TKA, and determine whether an osteotomy influences clinical outcome after TKA. Although randomized controlled trials (RCT) are considered the ideal and highest level of evidence in making decisions about the care of individual patients, numerous "good" surgical practices have evolved into "standard of care" without being randomized against placebo or ineffective treatment options [7]. This probably explains why no RCT has been published on the effect of TKA with previous HTO or not, and that high-quality observational studies constitute the best available evidence [8]. We conducted a systematic review of non-randomized studies to analyze the effect of HTO on subsequent TKA, which may help facilitate the decision-making on performing osteotomy in the younger individual.

Methods

Identification of studies

A search of all relevant studies published in Medline and Embase up to September 2007 was performed to identify those investigating TKA after earlier HTO. The search strategy combined all phases of the optimal non-randomized studies strategy and used fixed method B, based on the study of Furlan et al. [9]. Key words used were: arthroplasty, replacement, knee, and osteotomy, and cohort studies (or controlled study, or follow-up studies, or prospective studies, or risk factors, or cohort.mp, or compared.mp, or groups.mp or multivariate.mp). Finally, all the references in the identified studies were checked to detect any additional published data.

Two reviewers (TR, MR) assessed the studies and whether they met the following inclusion criteria:

- patients in the study had TKA performed after prior HTO;
- the study had an observational design between 4 and 7 using the taxonomy of study designs described by Deeks et al. (controlled before-and-after, concurrent cohort, historical cohort, or case-control studies) [10];
- the article was written in English, German, or Dutch;
- full text was available for the article;

Disagreements on inclusion were resolved by discussion, and the final decision of a third reviewer (JV) was not necessary.

Methodologic quality

Two reviewers (TR, MR) assessed the methodologic quality independently from each other. In order to avoid conflict of interest two other reviewers (RB, DM) re-assessed one study that was (co)-authored by TR and MR [11]. The critical appraisal of observational studies tool

(Deeks) [10] and the methodological index for non-randomized studies (MINORS) form [12] were used. Disagreements were resolved in a consensus meeting. The maximum quality score was 12 for both forms. The measure of agreement between the two reviewers (TR, MR) is presented as kappa. The methodologic quality was used as an additional criterion for inclusion, and studies had to be of high quality to be selected for final review. High quality was based on a summary quality score, and defined as presenting an adequate concurrent cohort study that fulfilled 50% or more of the validity criteria on both quality instruments [13].

Data extraction

Two reviewers (TR, MR) independently extracted the study characteristics and data on the intervention (operation time, lateral ligamental release, tuberosity osteotomy, tibial component insert), clinical outcome measures (postoperative knee range of motion (ROM) and clinical knee scores), and revision surgery (aseptic loosening, patellar loosening, deep infection, miscellaneous), using a pre-tested standardized form. Agreement on data extraction was reached by consensus.

Evidence synthesis

The grade of evidence was determined following the guidelines of the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) working group [14]. GRADE acknowledges the primacy of RCT, but in addition recognizes circumstances in which high-quality observational studies generate high-quality evidence of treatment effects [15]. Grades of evidence are divided into the following categories: high, moderate, low, and very low; randomized trials are considered of high, observational studies of low, and any other evidence of very low quality. The similarity of estimates of effect across studies (consistency), and the extent to which people, interventions, and outcome measures are similar to those of interest (directness) may lower or raise the grade of evidence. We judged that quality of life of patients receiving knee arthroplasty will mostly be affected by knee function, pain, and adverse events such as aseptic loosening or infection, and considered postoperative ROM, postoperative knee scores and revision surgery as critical outcome measurements. The lowest quality of evidence for any of the outcomes was used for rating overall quality of evidence, as suggested by the GRADE working group. The data for this review were collected and analyzed in compliance with the procedures and policies set forth by the Helsinki Declaration.

Table 1: Identified observational studies reviewed for design and quality

		Design		Quality assessment	
	study	**Year**	**Deeks classification**	**Deeks tool**	**Minors list**
1	van Raaij [11]	2007	concurrent cohort (5)	9	8
2	Haslam [4]	2007	concurrent cohort (5)	8	7
3	Huang [16]	2002	concurrent cohort (5)	7	7
4	Karabatsos [17]	2002	concurrent cohort (5)	7	7
5	Meding [18]	2000	concurrent cohort (5)	8	7
6	Haddad [19]	2000	concurrent cohort (5)	8	7
7	Nizard [20]	1998	concurrent cohort (5)	8	7
8	Amendola [21]	1998	concurrent cohort (5)	6	6
9	Mont [22]	1994	concurrent cohort (5)	7	8
10	Parvizi [5]	2003	concurrent cohort (5)	5	9
11	Walther [23]	2000	concurrent cohort (5)	4	4
12	Toksvig-Larsen [24]	1998	concurrent cohort (5)	6	4
13	Bergenudd [25]	1997	concurrent cohort (5)	6	5
14	Gill [26]	1995	concurrent cohort (5)	5	4
15	Jackson [27]	1994	case-control (7)	3	2
16	Windsor [6]	1988	historical cohort (6)	3	4
17	Katz [28]	1987	concurrent cohort (5)	5	6

Those articles were selected with high quality on both instruments (≥ 50% or ≥ 6 points)

Table 2. Baseline characteristics of the 9 reviewed manuscripts

author, year		eligible knees, N	knees lost to follow-up, N	included patients, N	TKA, N	women, %	OA, %	time bought by HTO†, years	age at TKA†, years	follow-up†, years	patients with missing data, N
Van Raaij, 2007 [11]	HTO	18	4	12	14	83	100	4.8	60	3.7	0
	control	342	-	12	14	83	100	NA	61	4.0	0
Haslam, 2007 [4]	HTO	78	27	40	51	48	100	4.8	65	12.6	0
	control	-	-	44	51	48	100	NA	65	12.6	0
Huang, 2002 [16]	HTO	-	-	15	17	87	100	8	61	5	0
	control	-	-	14	17	86	100	NA	62	5	0
Karabatsos, 2002 [17]	HTO	-	-	20	22	50	95	8.4	59	5.2	3
	control	-	-	20	21	50	95	NA	60	4.7	3
Meding, 2000 [18] a	HTO	39	-	39	39	31	97	8.7	67	7.5	0
	control	39	-	39	39	31	97	NA	67	6.8	0
Haddad, 2000 [19]	HTO	50	0	42	50	62	100	7.3	65	6.2	2
	control	-	-	42	50	57	100	NA	66	-	1
Nizard, 1998 [20]	HTO	63	6	55	63	85	100	9.7	72	4.5	5
	control	537	-	-	63	78	100	NA	71	4.0	-
Amendola, 1998 [21]	HTO	42	-	39	42	36	100	5.4	64	3.1	-
	control	168	-	39	41	49	100	NA	65	3.1	-
Mont, 1994 [22]	HTO	80	7	73	73	49	89	5	62	6.1	0
	control I b	974	-	73	73	49	89	NA	64	6.0	0
	control II c	974	-	73	73	49	88	NA	64	6.2	0

NA = not applicable
- = not mentioned in manuscript
† = the values are given as the average
a = patient group received bilateral TKA after unilateral HTO and served as own control
b = matched for pre-TKA deformity (within 5°)
c = matched for pre-HTO deformity (only varus knees)

Table 3. Intraoperative results for TKA with – compared to without prior HTO for the 9 reviewed manuscripts

author, year		TKA, N	operation time, minutes	lateral ligamental release	tibial tuberosity osteotomy	tibial component insert
van Raaij, 2007 [11]	HTO	14	120	3	1	10 mm
	control	14	115	0	0	8 mm
Haslam, 2007 [4]	HTO	51	-	-	-	-
	control	51	-	-	-	-
Huang, 2002 [16]	HTO	17	168 a	5	-	-
	control	17	142 a	0	-	-
Karabatsos, 2002 [17]	HTO	22	170 b	7 c	-	-
	control	21	118 b	2 c	-	-
Meding, 2000 [18]	HTO	39	-	4	-	-
	control	39	-	1	-	-
Haddad, 2000 [19]	HTO	50	23 min longer d	22	-	difference; NS
	control	50	-	-	-	
Nizard, 1998 [20]	HTO	63	-	15 e	7 f	-
	control	63	-	1 e	1 f	-
Amendola, 1998 [21]	HTO	42	-	6	-	-
	control	41	-	2	-	-
Mont, 1994 [22]	HTO	73	-	-	-	-
	control	73	-	-	-	-

- = not mentioned in manuscript

[a] $p = 0.002$, [b] $p < 0.0001$, [c] $p = 0.0089$, [d] $p < 0.02$, [e] $p = 0.0001$, [f] $p = 0.03$

NS = no significant difference after TKA with - compared to without prior HTO

Table 4. Postoperative outcome measures after TKA with - compared to without prior HTO for the 9 reviewed manuscripts. Follow-up time on a median of 5 years.

author, year		patients, N	knee range of motion,°	HSS	KSS knee	KSS function	WOMAC	Baltimore knee score; excellent/good, %
van Raaij, 2007 [11]	HTO	12	110	79	79	70	NS	-
	control	12	120	82	90	80		-
Haslam, 2007 [4]	HTO	40	91[a]	79	-	-	-	-
	control	44	106[a]	80	-	-	-	-
Huang, 2002 [16]	HTO	15	-	-	83	75	-	-
	control	14	-	-	85	72	-	-
Karabatsos, 2002 [17]	HTO	17	-	-	-	-	NS	-
	control	17	-	-	-	-		-
Meding, 2000 [18]	HTO	39	113	-	89	81	-	-
	control	39	118	-	90	84	-	-
Haddad, 2000 [19]	HTO	40	93	87	91	70	-	-
	control	41	103	89	89	66	-	-
Nizard, 1998 [20]	HTO	50	101	79	74[b]	67	-	-
	control	-	105	83	81[b]	64	-	-
Amendola, 1998 [21]	HTO	39	101[c]	86	-	-	-	-
	control	39	115[c]	89	-	-	-	-
Mont, 1994 [22]	HTO	73	-	-	-	-	-	47[d],[e]
	control I	73	-	-	-	-	-	64[d]
	control II	73	-	-	-	-	-	68[e]

HSS = Hospital for Special Surgery score (maximum 100 points)
KSS = Knee Society clinical rating system score (maximum 100 points)
WOMAC = Western Ontario and McMaster University Osteoarthritis Index
- = not mentioned in manuscript
NS = no significant difference after TKA with - compared to without prior HTO
[a] $p = 0.006$, [b] $p = 0.0001$, [c] $p < 0.005$, [d] $p < 0.01$, [e] $p < 0.001$

Table 5. Revision surgery after TKA with - compared to without prior HTO for the 9 reviewed manuscripts. Follow-up time on a median of 5 years.

author, year		TKA, N	aseptic loosening, N	patellar loosening, N	deep infection, N	other, N
van Raaij, 2007 [11]	HTO	14	0	0	0	2
	control	14	0	0	1	2
Haslam, 2007 [4]	HTO	51	4	1	0	0
	control	51	2	0	0	1
Huang, 2002 [16]	HTO	17	0	0	0	6
	control	17	0	2	0	4
Karabatsos, 2002 [17]	HTO	22	0	0	0	0
	control	21	0	0	0	1
Meding, 2000 [18]	HTO	39	1	3	0	2
	control	39	0	1	0	2
Haddad, 2000 [19]	HTO	50	1	-	1	11
	control	50	1	-	2	8
Nizard, 1998 [20]	HTO	63	0	1	0	13
	control	63	0	0	0	10
Amendola, 1998 [21]	HTO	42	0	1	0	3
	control	41	1	0	0	0
Mont, 1994 [22]	HTO	73	-	-	-	-
	control	73	-	-	-	-

- = not mentioned in manuscript

Table 6. Quality assessment of the grade of evidence of the observational studies comparing TKA with – and without prior HTO

	Quality assessment				No of knees		Summary of findings Effects		
No of studies	Design	Quality	Consistency	Directness	HTO	no HTO		Quality	Importance
Range of motion (6)									
	observational	no serious limitations	no important inconsistency	direct	251	251	4/6 studies no difference	low	critical
Knee clinical scores (9)									
	observational	no serious limitations	no important inconsistency	direct				low	critical
HSS (5/9)					212	212	5/5 studies no difference		
KSS (5/9)					175	176	4/5 study no difference		
other (3/9)					106	105	2/3 studies no difference		
Revision surgery because of (a)septic loosening (8)									
	observational	no serious limitations	no important inconsistency	direct	298	296	8/8 studies no difference	low	critical

Results

Included studies

Of the 458 articles identified using our search strategy, 17 met the inclusion criteria (Table 1). After the methodological quality assessment nine studies scored 50% or more on both quality scores and were included in this review: van Raaij [11]; Haslam [4]; Huang [16]; Karabatsos [17]; Meding [18]; Haddad [19]; Nizard [20]; Amendola [21] and Mont [22]. The mean score was 7.6 (range, 6 - 9) for the Deeks tool and corresponded with a 63% score. For the MINORS form the mean score was 7.1 (range, 6 - 8) and corresponded with a 59% score. The measure of agreement (kappa) between the two reviewers (TR, MR) was 0.86 for the Deeks tool quality score, and 0.95 for the MINORS form quality score. Disagreement occurred mainly because of reading errors and differences in interpretation of the comparability of group criteria.

For the nine studies included, all studies had a follow-up matched (for at least three characteristics) pair comparison design. An overview of the characteristics is presented in Table 2. There were a total of 371 TKAs with previous HTO compared to 369 primary TKAs. A lateral closing wedge technique was used in four studies, one study presented results after valgus dome osteotomy, and four studies described combined or unknown osteotomy techniques. Osteotomy delayed TKA with a median of 7 (5 – 10) years. In one study patients served as their own controls when receiving bilateral knee replacement after unilateral HTO. One study presented two comparison groups; one was matched by pre-TKA deformity and the other by pre-HTO deformity. All populations, but one (59 years), had a mean age beyond 60 years at TKA surgery. Four studies contained more women than men; between 89 and 100% of patients were diagnosed with knee osteoarthritis. All studies reported on primary knee prosthesis designs, and the use of revision tibial components was not mentioned. Seven studies presented all cemented TKAs in almost all cases (94 – 100%). Only one study described a singular prosthesis design. Patella replacement was mentioned in four studies; in two studies all patients received patellar resurfacing, in one study about half of the patients, and in one study approximately 10% of the patients. The average follow-up after TKA was at least three years in all studies; with a median follow-up of 5 (3 – 13) years.

Study results

Intra-operative results are shown in Table 3. Four studies reported on operation time which in three studies was significantly prolonged (median of 26 minutes) for patients receiving TKA after prior osteotomy (index group) compared with primary TKA (control group). In seven studies more lateral ligamental releases (median of 6) were necessary in the index group in comparison to the control group. Significant differences were found in two studies. Two studies found that more tibial tuberosity osteotomies were performed in the index group, and one of the studies noted a significant difference. No significant differences were reported in the distribution for thickness of the tibial inserts in two studies. The postoperative ROM (Table 4) was mentioned in six studies, and these studies detected less knee motion for the index group with a median of 10° (4° – 14°) in comparison to the control group. Two studies noted significant differences. All studies presented a knee score (Table 4) which contained pain and function evaluation; Hospital for Special Surgery score (HSS) in five studies, Knee Society clinical rating system score (KSS) in five studies, Western Ontario and McMaster University Osteoarthritis Index (WOMAC) in two studies, and the Baltimore knee score in one study. HSS and WOMAC scores were less favorable for the index group. All these differences, however, were not significant. Although the KSS knee score of the index group was lower in four out of five studies, only one study reported a KSS knee score significantly lower than the control group. The KSS function score of the index group was higher in three out of five studies, but no significant differences were found. One study used the Baltimore Knee score and detected a result in the index group significantly inferior to the control group. All studies but one reported on revision surgery after TKA (Table 5). In eight studies no significant differences between both groups were described for aseptic loosening, deep infection or other additional interventions. Seven studies reported on patellar loosening and found no significant differences between the index and control groups. One study commented on staged patellar re-surfacing for persistent patellofemoral symptoms, and described no differences between both groups.

Grade of evidence

No important inconsistencies among the nine studies were found in the direction of effect and the size of differences in effect; prolonged operation time, extra operative procedures, less postoperative knee ROM, and no increase of revision surgery was noticed for patients receiving TKA after prior HTO in the studies reflecting on the aforementioned outcomes. All studies described patients in their 6^{th} or 7^{th} decade of life receiving TKA because of symptomatic knee osteoarthritis. Knee replacement, regardless of prosthesis type, has more or less the same relative effects across most patients, therefore we judged the evidence obtained as direct [29]. Table 6 shows the overall quality assessment of the grade of evidence of the nine high-quality observational studies comparing TKA with - to TKA without prior HTO. We found no strong association among the studies and the overall quality of evidence, therefore, remained low.

Discussion

Patients who require TKA for a failed HTO comprises a significant portion of those patients undergoing TKA [22]. Previous surgery may influence subsequent knee replacement, but so far, no guidelines considering TKA after prior osteotomy have been developed, and no grading of existing evidence has been determined. To our knowledge the present study is the first systematic review of existing literature on this topic. We used a limited search strategy in finding relevant non-randomized studies. Earlier Furlan et al. showed that the sensitivity of limited search strategies for a fixed set of controlled vocabulary and text words was between 95 and 100% [9]. We assessed the quality of the retrieved studies with established forms, and we found good interobserver agreement for both the Deeks tool and MINORS form (kappa 0.86 and 0.95; respectively).

Well-designed observational studies may provide high quality of evidence in circumstances described by the GRADE working group. The present study, however, could not raise the current low quality level of evidence. All studies presented relative small sample sizes, and pooling of the data would have provided a more precise association with the clinical outcomes. The heterogeneity of the studies, mainly due to differences in gender, osteotomy techniques, and time of follow-up, made quantitative pooling of the data impossible and a systematic review represented the best available method to synthesize the current literature [30]. This obviously limits the validity of the conclusions that can be extracted form this analysis.

Surgical methods have been recognized to be important factors in the longevity of knee implants [31]. Subperiosteal exposure of the proximal tibia and eversion of the patellar mechanism are more difficult in the post-osteotomy knee due to soft tissue scaring. Ligamentous imbalance may also compromise the implant procedure. Seven studies reported that more lateral ligamental releases were necessary for the post-osteotomy patients, and two studies found that more tibial tuberosity osteotomies were performed. These additional procedures may contribute to a significantly prolonged operation time for patients receiving TKA after prior osteotomy in three out of four studies. Many surgeons feel that intra-operative factors such as duration of the procedure may lead to inferior outcome after knee replacement. Earlier a logistic regression analysis showed that superficial infection was highly correlated with deep wound infection, which is a big threat to a successful outcome following knee joint replacement. Longer operating time, however, was no predictor of wound infection in 1181 patients undergoing TKA surgery [32]. Exposure difficulties and alterations in knee anatomy may compromise precision and accuracy of the surgical technique [31]. Especially tibial component fixation may be an issue after osteotomy due to the loss of metaphyseal bone stock. A revision tibial component with a canal filling stem will increase the mechanical stability of tibial fixation [33]. On the other hand, a stemmed implant may prevent accurate placement of the tibial tray due to the asymmetric positioning of the medullary canal after HTO. Previous osteotomy may also influence patellar tracking leading to subluxation or rotatory instability. Malalignment and instability are major causes of early failure, and most revisions are performed within 5 years of primary arthroplasty [34]. After a median follow-up of 5 years we found no significant differences in TKA failure for the patients receiving TKA after previous osteotomy compared to primary TKA in all eight studies reporting on revision surgery. All studies presented in our review reported on primary knee prostheses, and did not describe the use of revision components. Earlier, a matched radiosteriometric study also showed no difference in failure rate after 10 years for primary knee components in patients with or without prior HTO [24]. Substantial improvements in the scores for physical health, such as those for pain and physical functioning seem to take place within the first 3 to 6 months after primary knee joint replacement, and studies with longer-term follow-up describe a lasting effect [35]. All six studies that discussed knee motion reported less range of motion with a median of 10° for patients receiving TKA after osteotomy compared to primary TKA patients. Two studies even noted significant inferior results. However, a multivariate analysis suggested that when determining the success of knee arthroplasty surgery ROM is far less important than overall function [36]. At mid-term follow-up this review could not detect any significant differences between both groups for overall function evaluated by standard knee clinical scores in eight out of nine studies.

Surgical treatment options for younger patients with unicompartmental OA of the knee remain controversial. Arthroplasty may have adverse effects. In an update study of data from the Swedish Knee Arthroplasty Register younger age was associated with an increased risk of prosthetic revision [37]. The cumulative revision rate for unicompartmental arthroplasty (UKA) was even higher than for TKA, and after removal of UKA loss of bone stock required significantly more osseous reconstructions in total knee revision compared with TKA after HTO [26,37]. One of the main reasons to perform HTO is delaying arthroplasty. The present review shows that the use of HTO postpones primary TKA for a median of 7 years in this subgroup of patients. This may be particular beneficial for patients with early onset knee OA, whose primary TKA might wear out before they die if they did not have the HTO.

Conclusions

In summary our analysis represents the best available evidence on TKA after prior osteotomy, which seems to suggest that osteotomy does not compromise subsequent TKA. However, the overall low quality of evidence could not be raised by this review. Therefore, knee arthroplasty register data or multi-center high-quality observational studies are needed to produce larger numbers and potentially generate higher quality of evidence to reach more solid conclusions.

Competing interests

The authors declare that they have no competing interests.

Authors' contribution

TR designed the study, acquired the data and drafted the manuscript. MR contributed substantially to the acquisition of data, carried out the statistical analysis and has been involved in interpretation of the data. AF and JV participated in the study design, and have been involved in critically revising the manuscript for important intellectual content. All authors read and approved of the final manuscript.

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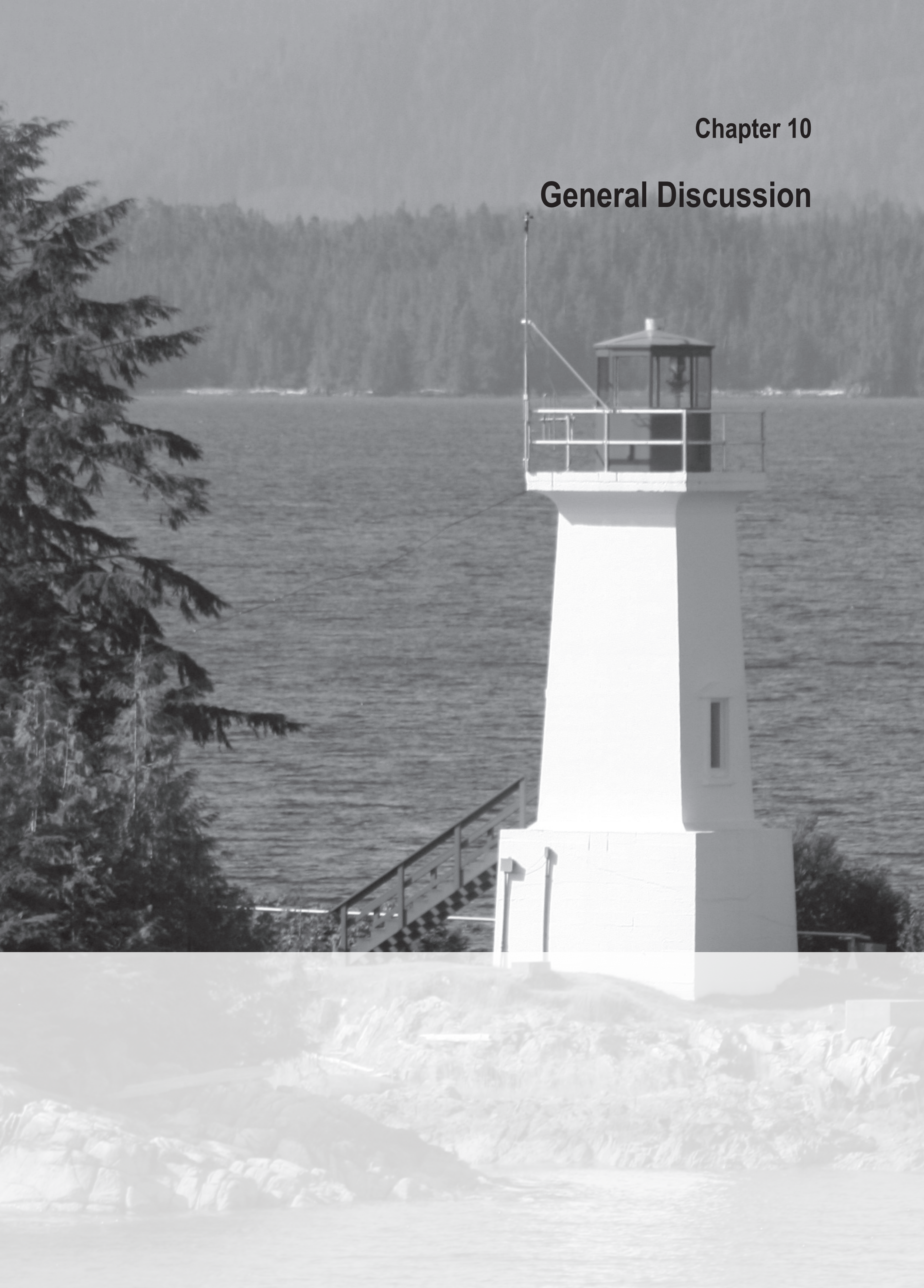
Chapter 10

General Discussion



Introduction

Osteoarthritis (OA) has a major impact on functioning and independence and ranks among the top ten causes of disability worldwide [1,2]. Knee OA is the most common joint disorder, and symptomatic disease occurs in 6% of adults 30 years of age or older. [3] The lifetime risk of developing symptomatic knee OA has even been estimated to be around 45%. [4] OA of the knee is defined as a multifactorial disease that is a result of both biologic and mechanical events. [5] Many patients, however, present with unicompartmental knee OA, which is generally caused by a mechanical problem with secondary inflammatory changes. [6,7] This explains why anti-inflammatory or structure-modifying OA drugs have not been able to halt or change the natural course of this disease; probably because the underlying mechanical problem is not addressed. Alterations in the mechanical stresses on knee joint tissues, on the other hand, have not only been shown to improve symptoms but also to reduce risk of development of radiographic knee OA. [8] Most non-operative devices and surgical methods currently used in early stages of the disease, share the goal of altering joint biomechanics. This thesis addresses some aspects of the mechanical treatment of unicompartmental knee OA, and focuses on the medial compartment of the knee because it is almost 10 times more frequently involved than the lateral compartment. [9]

Alignment in symptomatic varus osteoarthritis of the knee

Knee alignment is a determinant of load distribution, and the importance was underscored by Sharma et al. who found malalignment associated with OA progression. [10] Adequate measurement of knee alignment, therefore, is important, and a full-limb radiograph is considered the gold standard to assess knee alignment. However, in clinical practice, due to expenses and cumbersome procedures, knee alignment is often measured on a regular knee radiograph. This method allows defining the anatomic axis in the knee, and correlation between mechanical and anatomical axis angles has been reported. [11] Strangely enough different methods of assessing the anatomic axis are still used in literature. Despite the fact that the femoral anatomic-axis intersects the knee joint line medial to the knee joint center [12], the knee joint center is frequently presented as a landmark to assess anatomic alignment. [13] We found that this method underestimates varus malalignment. [14] This may explain that some found an association between knee alignment and medial OA progression [15], while others did not. [16] Anatomic knee axis determined by the angle between the mid-diaphyseal lines of the femur and tibia may be more accurate to assess knee alignment because of its strong correlation with the Hip-Knee-Ankle (HKA) angle. [14] However, we observed poor interobserver agreement when a regular knee radiograph was used. Future research may focus on the optimal size of the knee radiograph because avoiding full-limb radiographs will not only diminish radiation exposure, but will also cut costs which make large epidemiology studies on knee OA and alignment more feasible. Epidemiology studies are needed to understand and clarify the role of knee alignment in the etiology of medial knee OA. In everyday practice, however, the HKA angle remains standard of care to determine knee alignment, and serves as a guide for conservative management and surgical planning in the individual patient with symptomatic medial OA.

Non-operative treatment of symptomatic varus osteoarthritis of the knee

In the non-invasive treatment of medial knee OA, valgus bracing has been shown to have an effect on knee pain and function. There is also some evidence that foot orthoses have additional beneficial effects in the treatment of symptomatic knee OA. [17] In our comparative trial the laterally wedged insole improved pain 10% from baseline, which was the same effect we noted for valgus bracing after 6 months follow-up. According to the OMERACT-OARSI set of responder criteria for clinical trials in OA [18], about one sixth of our patients benefited from either the insole or brace intervention. [19] Few good clinical studies with appropriate terms of follow-up have been published on orthoses or bracing in the treatment of medial compartment knee OA. A recent crossover RCT found laterally wedged shoe insoles not efficacious in patients with medial knee OA treated for 6 weeks. The vast majority of participants (93%) had symptomatic medial tibiofemoral OA Kellgren-Lawrence (K-L) ≥ grade 3. [20] Ogata et al. suggested earlier that laterally wedged insoles are more effective in early medial compartment knee OA. [21] Based on explorative subgroup analysis we found that almost half of our patients with medial OA K-L < grade 2 responded to the laterally wedged insole after 6 months. [19] This subset of patients may be ideal for future research on the effectiveness of wedged insoles.

Valgus knee bracing and laterally wedged insoles probably work by unloading the diseased medial compartment. Significant correction of varus malalignment has been described for both modalities in small groups of patients with the use of less than optimal radiographs. [22,23] Based on the results of this thesis we found no evidence that a 10 millimeter laterally wedged leather inlay or an unloader valgus brace significantly alter varus malalignment in the frontal plane of the knee. Other adaptive mechanisms that reduce the load on the medial knee compartment, may account for the positive effect of non-invasive treatment. It has been noted that walking in stiff shoes significantly increases knee stresses compared to walking barefoot. [24] A shoe inlay may potentially reduce stiffness by acting as a shock-absorber. Different types of insoles should be studied to determine the optimal material and wedge size so that appropriate recommendations regarding footwear can be made. Bracing has been suggested to improve joint-position sense and reduce muscle contractions, which may normalize walking. [25,26] Studies on the gait of small amount of patients have indeed shown that knee bracing as well as insoles can reduce the estimated medial compartment load by decreasing the adduction moment about the knee significantly. [27] Peak adductor moment is a strong predictor of radiographic progression in patients with medial compartment OA.

[28] Further research into the effect of both non-invasive therapies should focus on gait analysis in combination with long-term clinical outcome scores.

Operative treatment of symptomatic varus osteoarthritis of the knee

In the surgical treatment of medial knee OA, valgus producing high tibial osteotomy (HTO) is well accepted, especially in active patients. The updated Cochrane review (13 studies with 693 patients) presented in this thesis, provided no evidence that HTO is more effective than non-operative treatment. [29] None of the included studies compared osteotomy with non-operative treatment, most likely because patients who undergo surgery are highly selected. The most important indication for osteotomy is symptomatic medial knee OA unresponsive to extensive non-operative treatment. This makes a RCT on the effect of osteotomy compared to non-operative treatment inappropriate. Osteotomy has evolved into "standard of care" without being randomized against placebo or other treatment options. This is common for many surgical procedures. [30] Although HTO is well established not all patients benefit from this type of surgery. Our findings suggest that women less likely gain from corrective osteotomy. [31] In this thesis we also analysed the influence of different sources of knee deformity on HTO. It has been suggested that patients with congenital bowing of the proximal tibia benefit more from a valgus correction osteotomy. [32] We found no evidence that varus bowing of the proximal tibia influences long-term survival of HTO. [33] Instead, varus deformity of the lower extremity and medial convergence of the knee joint line were identified as preoperative risk factors for HTO failure. Both factors have a positive correlation with advanced stages of OA [33,34], which is known to increase the revision rate of osteotomy. [35,36] Based on this thesis, ideal candidates for corrective osteotomy are males with low-grade medial compartmental OA. Future osteotomy research should focus on women with advanced OA of the medial knee compartment. This group may provide the equipoise needed to compare osteotomy with non-operative treatment as well as surgical treatment alternatives. [37,38,39]

Besides patient selection, proper surgical techniques are very important in the success of the HTO procedure. [40,41,42] The results of our latest Cochrane review do not justify a conclusion about effectiveness of specific surgical techniques. The purpose of tibial osteotomy, regardless of the technique used, is to unload the arthritic compartment by an osseous angular deviation in the frontal plane. [43] The two most common surgical techniques include 1) closing wedge HTO with fibular osteotomy and, more recently popularised, 2) opening wedge HTO with plate fixation. In both techniques the goal is to achieve and maintain adequate correction, which can be adversely affected by intra-operative fracturing of the opposite tibia cortex. In this thesis we describe that opposite cortex fracture is more common for the lateral closing wedge technique. In general this does not lead to malalignment. Opposite cortex fracture in the medial opening wedge technique (with the use of a non-locking plate) commonly leads to loss of correction and varus malalignment. [44] Patients with mild valgus alignment after HTO have a better outcome [42], and a retrospective analysis recommended an overcorrection between 3 - 7 degrees of valgus. [45] Longer-term evaluation of our RCT on closing wedge versus opening wedge HTO may provide a definitive answer to the optimal size of correction.

Interestingly, a cadaver study showed that the extremity alignment necessary to unload the medial side is approximately 25 degrees of valgus. [46] This amount of correction is unacceptable in a clinical setting, and may explain why HTO cannot halt the progression of medial knee OA. [47] In this thesis we describe that 25% of patients undergoing HTO are revised to a TKA after 10-years follow-up. [31] In our institution that accounted for 3% of patients receiving a cemented primary TKA. This small subgroup of patients formed the base of a matched case control study. In our mind, it is essential that patients undergoing HTO be informed of the likely consequences of the surgery. We found that clinical outcome of TKA after HTO was almost identical to a matched group that had no prior HTO. [48] Others found less favourable outcomes [49], and to synthesize the results we conducted a systematic review. Of the 458 articles identified, 17 met the inclusion criteria, and only 9 studies (335 patients) scored 50% or more on the methodological quality assessment. Our review suggested that osteotomy does not seem to compromise subsequent TKA. [50] Knee arthroplasty registry data or multi-center observational studies, however, are needed to generate higher quality of evidence to reach more solid conclusions.

Strength and Limitations

Although pain with knee OA is considered chronic, fluctuations in knee pain are frequent. Studying treatment modalities can be challenging because of methodological and logistic difficulties. [3] Our insole versus brace trial was limited in that the assessor was also the caregiver. Methodological strength would have been gained by blinding the assessor for follow-up measurements by using an independent assessor. The follow-up period was 6 months, which is relatively short for a chronic disease like knee OA. Moreover, our power permitted us to detect a 15% difference in pain reduction from baseline between both groups. In hindsight, this may have been quite optimistic. We only observed small effects for both the insole and brace groups, which prevented us from drawing strong conclusions. The results of the explorative subgroup analysis may be flawed by statistical and methodological limitations.

In particular circumstances subgroup analyses can provide the highest practicable level of evidence (for example it is impossible to randomize for adverse events). In this thesis we tested two osteotomy techniques [51] to study the effect of opposite cortex fracture in HTO. To the best of our knowledge, this is the only prospective clinical study to address this problem in both a closing and opening wedge HTO. Although prospective randomized trials are

considered the highest level of evidence, it is not always feasible to conduct a RCT due to the lack of equipoise. No randomized trials have been published on TKA after prior HTO. We designed a matched case control study to assess the effect of prior osteotomy on results and complications of total knee replacement. The study however lacked power with small numbers, and the majority of outcome measures did not reach significance despite strong trends. In an attempt to increase power we reviewed the existing literature with a limited search strategy highly sensitive in finding relevant nonrandomized studies. A meta-analysis was not possible due to the heterogeneity of the studies, and conclusions on the outcome of TKA after prior HTO remained weak.
HTO failure was assessed in historic cohorts. We realise that retrospective studies are limited and cannot address the problems of all known and unknown prognostic factors that may explain osteotomy failure. Knee replacement was considered a failure, because arthroplasty is a clear and objective end-point. Other end-points that may be more valuable and informative include grade of correction achieved, postoperative alignment, OA progression, and clinical knee scores.

Comment

There is evidence that varus deformity increases the risk of medial OA progression and development. [10,16] Correction of malalignment may improve symptoms and preserve cartilage. [52] Based on this thesis, we found no evidence that non-operative treatment (laterally wedged insole or valgus unloader brace) alters the alignment in the frontal plane. Valgus producing osteotomy, on the other hand, does correct varus malalignment, and may halt disease progression especially in males with mild varus deformity. The preferred osteotomy technique and optimal amount of correction, however, remain unclear, and may be influenced by age, gender, BMI, OA grade, or accompanying knee pathology (e.g. ligamentous instability). Although varus malalignment in the frontal plane is an indicator of medial compartment load it only provides a static impression of stresses on the knee surface. Gait analyses show the whole dynamics of knee loading, and especially the peak adduction moment is a strong predictor of OA progression. [28] This may provide a better tool to evaluate different therapeutic options for the individual patient.

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Chapter 11

Summary

Chapter 1: Knee osteoarthritis (OA) is the most common joint disorder, and in the Netherlands approximately 17% of the population aged 45 years and over suffer from knee OA. Patients with OA of the medial compartment often have a varus malalignment; the mechanical axis and load bearing passes through the medial compartment. Malalignment may have an impact on the development and progression of knee OA.

Chapter 2: Although therapeutic procedures such as knee osteotomy and knee replacement depend on proper knee alignment assessment, determination of knee alignment remains under debate. We evaluated if femorotibial (FT) measurement on short knee films may be used in clinical settings. The angle formed between the mid-diaphyseal line of the femur and the tibia (FTa), and the angle between the line from the midpoint of the femoral diaphysis through the knee joint center and the mid-diaphyseal line of the tibia (FTb) were assessed to determine anatomic knee alignment on a conventional knee image. Then, the accuracy of alignment was compared to the gold standard Hip-Knee-Ankle (HKA) angle on a whole leg radiograph (WLR). Measurements of the radiographs in 68 participants (ISRCTN92527149) with symptomatic medial compartmental knee OA, showed that conventional knee image cannot substitute WLR in the radiographic assessment of knee alignment due to either poor correlation (= 0.34) or interobserver agreement (ICC = 0.37). As a consequence possible misinterpretation of alignment in the individual patient may occur.

Chapter 3: Knee braces as well as foot orthoses may have beneficial effects in the treatment of knee osteoarthritis. A prospective randomized controlled clinical trial was conducted at a university medical center to compare both interventions head-tot-head. In 91 patients with symptomatic medial compartmental knee osteoarthritis, a 10-millimeter laterally wedged insole (index group, n = 45) was compared to a valgus brace (control group, n = 46). At 6 months of follow-up no significant differences in pain and functional outcomes were detected between both groups. Both interventions had no effect on knee varus malalignment. Patients in the insole group complied significantly ($P = 0.015$) better to their intervention. According to the OMERACT-OARSI criteria, about one sixth of our patients responded to the allocated intervention. Subgroup analysis showed a better effect for the insole in patients with mild medial OA. Our results suggest that a laterally wedged insole may be an alternative to valgus bracing in the non-invasive treatment of medial knee OA. Insoles are safe, easier to apply and generate fewer costs than knee bracing, which represents a huge potential in the treatment of symptomatic medial knee OA.

Chapter 4: The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE (Current contents, Health STAR) were searched up until May 2007 in this update review to identify all clinical trials concerning an osteotomy for knee OA. Thirteen studies involving over 693 people were included; 11 studies were included in the original review, and two studies and one longer follow-up study were included in this update. All studies concerned a high tibial osteotomy (HTO) for medial compartment OA of the knee.

Six studies, in which two studies were included in this update, compared two techniques of HTO. One study compared HTO alone versus HTO with additional treatment. Four studies compared within the same type of HTO, different peri-operative conditions (two studies) or two different types of post-operative treatment (two studies). Two studies, including the longer follow up, compared HTO with unicompartmental joint replacement. No study compared an osteotomy with conservative treatment. Based on 13 studies, we conclude that there is 'silver' level evidence (www.cochranemsk.org) that valgus HTO improves knee function and reduces pain. There is no evidence whether an osteotomy is more effective than conservative treatment and the results so far do not justify a conclusion about effectiveness of specific surgical techniques.

Chapter 5: Controversies about factors affecting survival of HTO still exist. We retrospectively analyzed a cohort of 104 consecutive patients, mean age 49 years, who had closing wedge HTO performed between 1991 and 1996. The probability of survival for HTO was 75% (SD 4%) at 10 years with knee replacement as the end point. Ideal candidates for corrective osteotomy are males with symptomatic medial compartmental osteoarthritis Ahlbäck grade 1, who 10 years after surgery have an almost 10 times lower probability of failure of HTO than women with more degenerative changes.

Chapter 6: Anatomical conditions that determine knee deformity in the frontal plane have been described to influence the success of valgus correction osteotomy. Preoperative frontal plane varus deformity of the lower extremity, proximal tibia and distal femur, and medial convergence of the knee joint line, were assessed on a WLR in 76 patients, who had closing wedge HTO performed between 1991 and 1997, because of symptomatic medial OA. Only varus deformity of the lower extremity (< 175°), and medial convergence of the knee joint line (> 3°) were identified as preoperative risk factors for conversion to arthroplasty ($p = 0.03$ and $p = 0.006$). Our findings suggest that constitutional varus deformities of the proximal tibia and distal femur do not influence long-term survival of HTO. In contrast, lower limb varus deformity and medial joint line convergence predict failure of closing wedge HTO after 10 years.

Chapter 7: In both a lateral closing wedge and a medial opening wedge procedure a fracture of the opposite cortex of the tibia may lead to loss of correction, and may threaten long-term osteotomy outcome. 44 patients with a closing wedge HTO (staples and cast fixation) and 43 patients with an opening wedge HTO (non-angular stable plate fixation), who were enrolled in a RCT to achieve a correction of 4 degrees in excess of physiological valgus, were used for analysis. 36 patients (0.8) in the closing wedge group, and 15 patients (0.4) in the opening wedge group had an opposite cortical fracture; ($p < 0.0001$). At 1-year the closing wedge group with opposite cortex fracture had a valgus position with a mean HKA angle of 3.2 (SD 3.5) degrees of valgus. However, the opening wedge group with opposite cortex disruption achieved varus malalignment with a mean HKA angle of 0.9 (SD 6.6) degrees of varus. Although opposite cortex fracture is more common for the lateral closing wedge technique, medial cortex disruption has no major consequences, and generally does not lead to malalignment. Lateral cortex fracture in the medial opening wedge technique with the use of a non angular-stable plate, however, leads more often to varus malalignment.

Chapter 8: When considering osteotomy in the early treatment of symptomatic medial compartmental OA, subsequent total knee arthroplasty (TKA) should not be compromised. We performed a matched case control study to assess the effect of prior HTO on results and complications of TKA. From 1996 until 2003 356 patients underwent all cemented primary TKA in our institution. Twelve patients with a history of 14 HTO were identified and matched to a control group of 12 patients with 14 primary TKA without previous HTO. The index group had more perioperative blood loss and exposure difficulties with one tibial tuberosity osteotomy and three patients with lateral retinacular releases. No such procedures were needed in the control group. Mid-term knee clinical scores were less favorable for the index group, but these differences were not significant. The tibial slope of patients with prior HTO was significantly decreased after this procedure ($p = 0.04$). The tibial posterior inclination angle was corrected during knee replacement but posterior inclination was significantly less compared to the control group ($p = 0.025$). No deep infection or knee component loosening were seen in the group with prior HTO. We conclude that TKA after HTO seems to be technically more demanding than a primary knee arthroplasty, but clinical outcome was almost identical to a matched group that had no HTO previously.

Chapter 9: Conflicting results of TKA after osteotomy, however, have been reported. We performed a search for relevant studies published up to September 2007 in MEDLINE and EMBASE to synthesize these results. The overall grade of evidence was determined using the guidelines of the GRADE working group. Of the 458 articles identified, 17 met the inclusion criteria and were assessed for methodologic quality. Nine observational studies were of high quality. Pooling of the results was not possible due to the heterogeneity of the studies. The operative time for patients with previous osteotomy was significantly prolonged in three out of four studies. No significant differences between primary TKA and TKA after osteotomy were found for knee range of motion in four out of six studies, knee clinical scores in eight out of nine studies, and revision surgery in eight out of eight studies. This review found that the best available evidence on TKA after prior HTO was of low quality. Based on this evidence, previous osteotomy does not appear to hamper total knee arthroplasty after a median follow-up of 5 years.

Chapter 10 summarizes the main findings, and includes the strengths and limitations of the studies presented. Furthermore, the results are interpreted and the implications on patient care and future research are discussed.

Chapter 12

Samenvatting

Hoofdstuk 1: Gonartrose is de meest voorkomende aandoening van de gewrichten. In Nederland heeft ongeveer 17% van de bevolking van 45 jaar en ouder last van slijtage van het kniegewricht. Patiënten met slijtage van het mediale knie compartiment hebben vaak een varus been. De mechanische beenas en de belasting van de knie verlopen dan door het aangedane mediale compartiment. Afwijkingen van de normale as zijn wellicht van invloed op de ontwikkeling en toename van gonartrose.

Hoofdstuk 2: De behandeling van gonartrose is vooral gebaseerd op een verandering van de belasting van de knie. Een nauwkeurige bepaling van de standsafwijking van de knie is dus van belang. Met standaard voorachterwaartse knie opnames werd bekeken of de femorotibiale (FT) hoek meting gebruikt kan worden om de juiste afwijking van de stand van de knie te bepalen. De hoek tussen de mid-diafysair lijnen van het femur en de tibia (FTa) en de hoek tussen een lijn van het midden van de diaphysis naar het centrum van de knie en de mid-diafysair lijn van de tibia werden bepaald op een standaard knie röntgenopname in voorachterwaartse richting. De nauwkeurigheid van deze metingen werd vergeleken met de gouden standaard „Hip-Knee-Ankle“ (HKA) hoek op een lange been opname. De metingen in 68 patiënten met symptomatische artrose van het mediale compartiment van de knie, laten zien dat een standaard knie opname de lange been opname niet kan vervangen bij het nauwkeurig bepalen van de stand van de knie vanwege enerzijds een slecht correlatie (= 0.34) en anderzijds een slechte overeenkomst tussen de waarnemers (ICC = 0.37). Dit kan leiden tot een verkeerde interpretatie van de stands afwijking van de knie in de individuele patiënt.

Hoofdstuk 3: Er bestaan aanwijzingen dat patiënten met symptomatische mediale gonartrose baat hebben bij een knie brace of voet orthose. Een knie brace wordt echter vaak niet goed verdragen. Wij onderzochten met een prospectieve gerandomiseerde studie of patiënten beter af zijn met een steunzool met een laterale wig verhoging. Eénennegentig patiënten met symptomatische mediale gonartrose werden geïncludeerd; 45 patiënten werden behandeld met een steunzool met een 10 millimeter laterale wig verhoging en vergeleken met een controle groep van 46 patiënten behandeld met een valgiserende knie brace. Na 6 maanden werden er geen significante verschillen gevonden in pijn- of klinische knie scores. Volgens de OMERACT-OARSI criteria reageerde een zesde van patiënten in de steunzool en brace groepen op hun behandeling. De varus afwijking van de knie werd door geen van beide behandelingen gecorrigeerd. Patiënten in de steunzool groep droegen hun interventie significant ($p = 0.015$) langer dan de brace groep. Een subgroep analyse liet zien dat de steunzool het beste werkte in patiënten met milde mediale gonatrose. Deze studie liet zien dat een steunzool met laterale wig verhoging even goed werkt als een valgiserende brace. Steunzolen zijn veilig, makkelijk aan te meten en goedkoper dan knie braces. Dit maakt de steunzool met laterale wig verhoging tot een mogelijk alternatief in de conservatieve behandeling van symptomatische mediale gonartrose.

Hoofdstuk 4: De valgiserende tibiakoposteotomie (VTO) speelt een belangrijke rol in de chirurgische behandeling van mediale gonartrose. Een systematische literatuur studie werd verricht voor de Cochrane Library naar de resultaten van een osteotomie. Alle gerandomiseerde en klinisch gecontroleerde prospectieve studies op het gebied van een correctie osteotomie wegens unicompartimentele gonartrose werden in MEDLINE en EMBASE (tot mei 2007) opgezocht. Dertien studies met 693 patiënten werden geïncludeerd: 11 studies werden geïnclueerd en geanalyseerd in een eerder verschenen overzicht artikel, en 2 studies en 1 vervolgstudie werden in dit artikel geïncludeerd. In alle studies werd een VTO voor de behandeling van mediale gonartrose geanalyseerd. Zes studies, waarvan 2 in dit hoofdstuk, vergeleken 2 verschillende operatietechnieken. Eén studie vergeleek VTO met VTO en een aanvullende behandeling. Vier studies met 1 osteotomietechniek vergeleken verschillende omstandigheden rond de operatie (2 studies) en 2 verschillende behandelingen na de operatie (2 studies). Twee studies, waarvan 1 studie met een langere follow-up tijd, vergeleken VTO met een unicompartimentele knie prothese. Geen van de geïncludeerde studies vergeleek VTO met een conservatieve behandeling. De resultaten van de 13 geanalyseerde studies suggereren dat een correctie osteotomie voor verbetering van de knie functie en pijnverlichting zorgt. Er is echter geen bewijs dat een osteotomie effectiever is dan conservatieve behandeling van gonartrose en het blijft onduidelijk welke osteotomie techniek het beste gebruikt kan worden.

Hoofdstuk 5: Er bestaat nog steeds onduidelijkheid welke preoperatieve factoren het succes van een VTO bepalen. Een groep van 104 opeenvolgende patiënten (gemiddelde leeftijd 49 jaar), behandeld met een gesloten VTO tussen 1991 en 1996, werd daartoe retrospectief geanalyseerd. Na 10 jaar was 75% (SD 4.2%) van de VTO's niet omgezet naar een totale knie prothese (TKP). Vrouwen en een artrose graad van 2 of meer volgens de Ahlbäck classificatie, werden geïdentificeerd als preoperatieve risicofactoren die revisie van VTO naar TKP voorspellen. Deze studie laat zien dat mannen met symptomatische mediale gonartrose en Ahlbäck graad 1 ideale kandidaten zijn voor een corrigerende osteotomie. Zij hebben 10 jaar na de ingreep, bijna 10 keer minder kans op VTO falen dan vrouwen met een verder gevorderd stadium van artrose.

Hoofdstuk 6: Met name tibia vara wordt genoemd als een mogelijke voorspeller van het succes van VTO op de lange termijn. Zesenzeventig patiënten, behandeld met een gesloten VTO tussen januari 1991 en december 1997 wegens symptomatische mediale gonartrose, werden retrospectief geanalyseerd. Naast tibia vara werden preoperatieve varus afwijkingen van het gehele been en het distale femur, en de richting van de knie gewrichtsspleet in het frontale vlak op een standaard lange been opname bepaald. Varus van het gehele been (< 175°), en het convergeren van de knie gewrichtsspleet naar mediaal (> 3°) werden geïdentificeerd als preoperatieve risicofactoren die revisie van VTO naar knie prothese op de lange termijn voorspellen ($p = 0.03$ and $p = 0.006$). Deze studie laat echter geen invloed van tibia vara op het resultaat van een gesloten VTO na 10 jaar zien.

Hoofdstuk 7: Verlies van correctie leidt tot een slechter resultaat van een VTO, en kan direct na de operatie optreden door een doorbraak van de overliggende cortex van de osteotomie. Vierenveertig patiënten met een gesloten VTO (krammen en gips) en 43 patiënten met een open VTO (1e generatie Puddu plaat) werden gebruikt om het effect van een overliggende cortex doorbraak te analyseren. Alle patiënten maakten eerder deel uit van een prospectief, gerandomiseerd onderzoek waarbij het doel was om een overcorrectie van 4 graden valgus te bewerkstelligen. Zesendertig patiënten (0.8) in de gesloten VTO groep en 15 (0.4) in de open VTO groep hadden een overliggende cortex doorbraak ($p < 0.0001$). Na 1 jaar was de HKA hoek in de gesloten HTO groep met cortex doorbraak 3.2 graden (SD 3.5) in valgus. De open VTO groep met cortex doorbraak bereikte echter een varus stand met een HKA hoek van 0.9 graden (SD 6.6) na 1 jaar. Hoewel een overliggende cortex doorbraak significant meer voorkomt bij de gesloten osteotomie techniek leidt dit meestal niet tot correctieverlies. Een cortex doorbraak bij de open techniek, waarbij geen hoekstabiele plaat wordt gebruikt, leidt vaker tot een varus standsafwijking.

Hoofdstuk 8: Een VTO is een goede behandeling van symptomatische mediale gonartrose, maar moet een mogelijke knie prothese in de toekomst niet in de weg staan. Wij onderzochten het effect van een voorafgaande VTO op de resultaten en de complicaties van een TKP door middel van een matched case-control studie. Tussen 1996 en 2003 werd bij 356 patiënten een gecementeerde totale knie prothese geplaatst. Twaalf patiënten met 14 VTO's in de voorgeschiedenis (index groep) werden geïdentificeerd en gematched met een controle groep van 12 patiënten met 14 primaire TKP's zonder VTO in de voorgeschiedenis. Er werd meer perioperatief bloedverlies in de index groep gezien. De knie benadering was met 1 tuberositas osteotomie en 3 laterale retinaculum klievingen lastiger voor de index groep. In de controle groep werd bij geen van de patiënten dergelijke procedures uitgevoerd. De klinische knie scores waren minder gunstig voor de index groep vergeleken met de controle groep. Significante verschillen konden echter niet worden aangetoond. De hellingshoek van het tibiale plateau was significant afgenomen bij patiënten die in het verleden een HTO hadden ondergaan. De tibiale posterieure inclinatie werd peroperatief hersteld maar bleef significant achter bij de controle groep. Diepe wondinfecties of prothese loslating werden niet gezien in de index groep. Wij concluderen dat een kniegewricht vervangende operatie na een VTO technisch lastiger is maar dat de klinische resultaten van een TKP na VTO bijna gelijk zijn aan een matched controle groep welke geen HTO in de voorgeschiedenis had.

Hoofdstuk 9: In de literatuur worden tegenstrijdige resultaten van een TKP na een eerdere VTO beschreven. In MEDLINE en EMBASE (tot september 2007) werd gezocht naar relevante studies om het effect van een osteotomie op een knie prothese en het niveau van het bewijs in de literatuur te bepalen. De richtlijnen van de GRADE werkgroep werden gehanteerd om het niveau te bepalen. 17 van de 458 gevonden studies voldeden aan de inclusie criteria en de kwaliteit van hun methodologie werd onderzocht. 9 studies waren van een hoge kwaliteit en werden nader geanalyseerd. De resultaten konden niet worden samengevoegd omdat de studies te heterogeen waren. In 3 van de 4 studies was de operatietijd significant langer bij patiënten met een TKP na VTO. Echter er konden geen significante verschillen worden aangetoond tussen de TKP groepen met en zonder osteotomie in het verleden, voor kniefunctie in 4 van de 6 studies, klinische scores in 8 van de 9 studies en revisie chirurgie in 8 van de 8 studies. Wij vonden het bewijs in de literatuur van lage kwaliteit. Gebaseerd op dit bewijs concluderen wij, dat na een mediane follow-up van 5 jaar, een VTO het resultaat van een TKP niet in de weg staat.

Hoofdstuk 10 is een samenvatting van de belangrijkste bevindingen in dit proefschrift en bespreekt de sterke en zwakke punten van de studies. Daarnaast worden de resultaten met betrekking tot patiëntenzorg en toekomstig onderzoek besproken.

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Mr. L. van Raaij (LLM), paranimf

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Mr. R. Sanders (BA), paranimf

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Curriculum vitae

Tom van Raaij was born on Saint Jacob´s day 1971 in Delft, the Netherlands. In 1989 he graduated from the Eemland College (VWO) in Amersfoort, and went on to study Medicine at Leiden University Medical School. After a research fellowship at Yale University, New Haven, USA, he received his University Medical Degree "Arts-examen" in 1997. Until 1999 he worked as a resident at the General Surgery Department of the Westeinde Hospital (Medical Center Haaglanden) in The Hague. A short stay in the UK as a Senior House Officer in Accident and Emergency Medicine at the Royal Liverpool University Hospital made him decide to pursue a career in Orthopaedic Surgery. One year after his residency at the Department of Orthopaedic Surgery of the Erasmus Medical Center Rotterdam (former Dijkzigt Hospital), headed by professor J.A.N. Verhaar, he started his 2-year training program in General Surgery at the Deventer Hospital in Deventer (Head: dr. M. Eeftinck Schattenkerk) in 2001. From 2003 until 2007 he continued his Orthopaedic training: 3 years at the Erasmus Medical Center Rotterdam (Head: prof.dr. J.A.N. Verhaar) and 1 year at the St Elisabeth Hospital in Tilburg (Head: dr. J. de Waal Malefijt). In 2007 he worked as an Orthopaedic surgeon (chef de clinique) at the Franciscus Hospital in Roosendaal, before starting his fellowship in Orthopaedic Trauma at the Foothills Medical Centre, University of Calgary, Canada (Head: professor R.B. Buckley, MD, FRCS (C)) in 2008 and 2009. Since 2009 he works as an Orthopaedic surgeon at the Martini Hospital in Groningen together with dr. C.L.E. Gerritsma-Bleeker, dr. J.J.A.M. van Raaij, drs. M.S. Sietsma, dr. R.W. Brouwer and drs. B.L.E.F. ten Have. The author is married to Astrid Hartwijk, with whom he shares a magnificent little dude: Faas Ole Willem.

PhD Portfolio Summary

Summary of PhD training and teaching activities

Name PhD student: Tom M. van Raaij Erasmus MC Department: Orthopaedics Research School:	PhD period: 2004 – 2009 Promotor(s): prof.dr. J.A.N. Verhaar Supervisor:

1. PhD training	**Year**	**Workload (Hours/ECTS)**
General academic skills		
- Biomedical English Writing and Communication	2008	12 ECTS
- Research Integrity		
Research skills		
- Statistics: Principles and practice of clinical research course, 5-6 November 2008, Toronto, Canada	2008	1 ECTS
- Methodology	2004-2008	12 ECTS
In-depth courses (e.g. Research school, Medical Training)		
- Resident of Orthopaedic surgery, Erasmus University Medical Center Rotterdam, the Netherlands	2004-2006	90 ECTS
- Clinical researcher, Department of Orthopaedics, Erasmus University Medical Center, Rotterdam, the Netherlands.	2007	30 ECTS

Presentations Raaij T van, Takacs I, Reijman M, Verhaar J. Varus inclination of the proximal tibia or the distal femur does not influence high tibial osteotomy outcome. Fall meeting NOV, Utrecht, October 10th 2008.	2008	1 ECTS
Raaij T van, Brouwer R, Reijman M, Bierma-Zeinstra S, Verhaar J. Conventional knee radiography hampers valid alignment measurement in the individual patient with osteoarthritis of the knee. Nordic Orthopaedic Federation (NOF), Amsterdam, the Netherlands, June 12th 2008.	2008	1 ECTS
Raaij T van, Brouwer R, Reijman M, Bierma-Zeinstra S, Verhaar J. The effect of bracing and lateral-wedged insoles on knee alignment in patients with varus gonarthrosis. Annual meeting Dutch Orthopaedic Association (NOV), Maastricht, the Netherlands, January 11th 2008.	2008	1 ECTS
Raaij T van, Reijman M, Brouwer R, Jakma T, Verhaar J. Pre-operatieve risicofactoren die de overleving van een gesloten wig tibiakoposteomie bepalen. Fall meeting NOV, Veldhoven, 2007.	2007	2 ECTS
Raaij T van, Vlieger R de, Reijman M, Verhaar J, Brouwer R. The effect of cortex disruption in closing – and opening wedge high tibial osteotomy. Annual meeting NOV, Rotterdam, the Netherlands, February 1st 2007.	2007	2 ECTS
Raaij TM van, Bakker W, Reijman M, Verhaar JAN. Het effect van een hoge tibia osteotomie op het resultaat van een totale knie prothese. Een matched case-control studie. Fall meeting NOV, Veldhoven	2006	2 ECTS

International conferences Kadaver cursus: shoulder, knee arthroscopy and osteotomy, Arthex, 11 – 16 October 2004, Naples, Florida, USA	2004	1 ECTS
Innovations in minimally invasive knee joint surgery, Smith and Nephew, 16 – 18 February 2006, Munster, Germany	2006	1 ECTS
Seminars and workshops		
- Basiscursus Osteotomie (rond de knie), St Maartens-kliniek, October 24th 2003, Nijmegen, the Netherlands	2003	0,5 ECTS
- Advanced Course Osteotomies of the lower leg, St Maartenskliniek, 6 –7 October 2006, Nijmegen, the Netherlands	2006	1 ECTS
- Teaching Workshop in Medical Education, April 2008, Calgary, Canada.	2008	1 ECTS
Didactic skills		
- Teaching co-assistenten/medical students patient assessment skills and basic orthopaedics knowledge	2004-2007	4 ECTS
Other -		

2. Teaching activities	**Year**	**Workload (Hours/ECTS)**
Lecturing		
- Congres MUSC (musculoskeletal science center) Rotterdam, the Netherlands, April 20th 2004; oral presentation: „Resultaten van conservatieve therapie van unicompartimentele gonarthrosis door middel van een knie brace (RCT)"	2004	0.25 ECTS
- Rogo Cluster dag, September 9th 2005, Den Haag, the Netherlands; oral presentation: "Knikkende knieen: antecurverende tibiakoposteotomie"	2005	2 ECTS

- Orthopedie wetenschapsdag, November 15th 2006, Rotterdam, the Netherlands; oral presentation: „Arthrose en bot: is zagen een goede optie?” - Treatment of knee osteoarthritis, an educational lecture for HAIO’s at the Huisartsen instituut, Erasmus MC; July 2006, Rotterdam, the Netherlands	2006 2006	0.25 ECTS 0.5 ECTS
Supervising practicals and excursions - teaching co-assistenten basic skills of physical knee examination	 2004-2006	 3 ECTS
Supervising Master’s theses - W. Bakker: TKA after osteotomy: a matched case control study - R. de Vlieger: Effect of opposite cortical disruption in high tibial osteotomy - C. Demmendal: Dexa-scan analyses in patients with symptomatic medial knee osteoarthritis treated with a valgus brace or a laterally wedged insole	 2004 2006 2006	 3 ECTS 3 ECTS 3 ECTS
Other - Supervision of elective research project by I. Takacs: Varus inclination of the proximal tibia does not influence high tibial osteotomy outcome	 2007	 3 ECTS

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