

# Long-term survival and predictors of failure of opening wedge high tibial osteotomy.

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#### **Research Article**

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# Abstract Background

The primary aim was to evaluate the long-term survival of opening wedge high tibial osteotomy (HTO) for isolated osteoarthritis in the medial compartment of the knee. The secondary objective was to identify independent predictors of conversion to total knee arthroplasty (TKA).

# Methods

Two-hundred forty-seven consecutive cases of open wedge HTO performed at the study centre were retrospectively analysed. Mean age at the operation was 42,8 years (range 15-70) and most patients were male (70%). Mean follow-up was 11.6 years (6–17). Failure was defined as conversion to TKA. Kaplan–Meier and Cox regression analyses were performed.

## Results

Thirty-three of the 247 HTOs (13.4%) were converted to knee replacement, with 86.6% of the original procedures surviving at a mean 12-year follow-up. Kaplan-Meier survival estimates at 17 years for HTO were 75.5% (95% confidence interval [CI] 66.7–84.3). There was significant difference (p < 0.001) in the 17-year survival rate between obese (55.5%; 95% CI 35.3–75.6) and non-obese (79.7%; 95% CI 70.1–89.2) patients. The determinants of conversion to knee arthroplasty detected at multivariate Cox regression analysis were Body Mass Index, severity of cartilage degeneration in the medial compartment (Outerbridge grade), and age.

# Conclusions

The long-term survival of open wedge HTO for osteoarthritis in the medial compartment of the knee is satisfactory. The risk of conversion to TKA is significantly increased in obese patients. Advanced age and severity of pre-existing cartilage damage may also contribute to the risk of conversion to TKA.

## Introduction

The treatment of osteoarthritis (OA) in the medial compartment of the knee in young, active patients is challenging. High tibial valgus osteotomy (HTO) is a widely accepted procedure indicated for varus knee with symptomatic OA or overload (e.g. after medial meniscectomy) of the medial compartment [1]. Although the widespread use of total knee arthroplasty (TKA) has led to decline in HTO, this procedure has been recently shown to be cost-effective compared to knee arthroplasty in patients aged 50–60 years with medial OA of the knee [2]. Indeed, the aseptic loosening rate of knee arthroplasty is higher in younger patients due to high mechanical stress on the implant [3–5]. The basic surgical techniques of HTO

include lateral closure osteotomy and medial opening osteotomy. The latter has become the most widely used technique due to its easy control of the degree of correction and limited soft tissue dissection [6]. There has been growing interest in the literature in identifying factors influencing the outcome of trauma surgery [7] and elective orthopaedic surgery [8,9], but less data are available on determinants of long-term survivorship of opening wedge HTO in large series of patients [10–12]. The primary objective of this study was to evaluate the long-term survival of opening wedge HTO for isolated OA in the medial compartment of the knee. The secondary objective was to identify independent predictors of conversion to TKA. We hypothesized that multiple factors including age, the severity of cartilage damage in the medial compartment, and the degree of correction obtained with surgery may influence the long-term survivorship of HTO.

## **Materials And Methods**

Two-hundred ninety-six cases of opening wedge HTO were performed at the institution of three of the authors (V.I., S.N., C.Z.), a large tertiary care hospital specialized in knee surgery, between January 2005 and August 2015. Forty-five patients (49 procedures) could not be followed up. Of these, 36 patients could not be traced and nine refused to participate in the study. Hence, the study group was limited to 233 patients and 247 procedures. Inclusion criteria for the HTO were varus angle between 5 and 15 degrees, medial compartment pain, and grade II-III OA of the medial compartment as assessed by the Kellgren-Lawrence classification [13] on weight-bearing anteroposterior radiographs. Patients' preoperative and operative data were obtained from surgical records and hospital files. Patients with a body mass index (BMI) over 30 were considered obese. For preoperative planning, a full-length anteroposterior radiograph of the weight-bearing lower extremity was obtained. We used the Miniaci's method [14] to plan the correction angle. The preoperative hip-knee angle (HKA) was calculated on preoperative and postoperative radiographs. The aim of surgery was to achieve 5° tibiofemoral mechanical valgus in a one-leg standing radiograph postoperatively [15]. Telephone interviews were conducted to collect followup data from all patients or, when necessary, from their relatives. All patients gave informed consent to participate in the study. Information was obtained on any operations on their knee after the HTO procedure, their nature, and the time interval since the index procedure. The mean length of follow-up in the responders was 11.6 years (range 6 - 17). Table 1 summarizes the characteristics of patients

 Table 1. Characteristics of the patients (n = 247).

		Mean±SD or n (%)	Range		
Age at operation, years		42.8 ± 14.1	15-70		
Age at follow-up, years		54.4 ± 15.0	21-86		
Sex	Female	74 (30)			
	Male	173 (70)			
BMI, Kg/m <sup>2</sup>		26.6 ± 4.3	19-47		
Smoking	No	213 (86)			
	Yes	34 (14)			
Follow-up, yr		11.6 ± 3.5	6-17		
Preoperative radiographic HKA, degrees		173.3 ± 2.0	170-178		
SD = Standard Deviation; BMI = Body Mass Index; HKA = Hip Knee Angle					

# Surgical Technique

Diagnostic arthroscopy of the knee was routinely performed before tibial osteotomy to assess the severity of cartilage damage. Cartilage lesions were classified according to the Outerbridge classification [16]. After diagnostic arthroscopy, opening HTO was performed through a 6–8 cm skin incision, 2 cm medial to the tibial tuberosity and 2 cm below the joint line. The anterior fibers of the medial collateral ligament were detached. Guided by a Kirschner wire, a monoplanar opening wedge osteotomy was subsequently performed with an ascending bony cut starting at the medial edge of the tibia and directed toward the tibiofibular joint. The osteotomy was opened gradually using chisels and a spreader device. After reaching the expected tibial opening, the osteotomy was secured with a locking plate. The plates used in the study group included 197 VS Osteotomy Systems (Zimmer-Biomet), 46 Puddu plates (Arthrex), and 4 Tomofix plates (DePuy Synthes). An above-the-knee brace was prescribed at discharge, and full weight-bearing was allowed at four weeks postoperatively.

# Statistical analysis

The Kaplan-Meier method was used to estimate the cumulative survival at 17 years after HTO in nonobese and obese patients and the study group. Intergroup comparison was performed using a log-rank test. We performed age-adjusted univariate and multivariate Cox regression analysis to assess the effect of any explanatory variable on HTO survival. We included in the multiple regression models all the explanatory variables that showed significant association (i.e.  $p \le 0.05$ ) or a trend toward an association (i.e.  $p \le 0.10$ ) with the outcome of interest in the univariate analysis. The following confounding or explanatory variables were tested as predictors of outcome: age, sex, BMI, smoking habit, postoperative varus correction, cartilage degeneration (Outerbridge grade) of the medial compartment, type of locking plate, and use of adjunctive procedures at surgery (i.e. microfractures, platelet rich-plasma supplementation, meniscectomy). A *p* value < 0.05 was considered significant. Data were analyzed using SPSS version 26.0 software.

## Results

The surgical data of the patients are summarized in Table 2.

#### Table 2 Surgical data of patients.

	Mean (range) or n (%)			
Severity of cartilage degeneration in the medial compartment (Outerbridge grade)	0 (0)			
Ω	58 (24)			
1	43 (17)			
	47 (19)			
2	99 (40)			
3				
4				
Associated procedures	167 (68)			
None	32 (13)			
PRP supplementation	16 (6)			
Microfractures	10 (4)			
Partial meniscectomy	8 (3)			
PRP supplementation + microfractures	4 (2)			
Autologous chondrocyte implantation	4 (2)			
ACL procedures	3 (1)			
Microfractures + partial meniscectomy	2 (1)			
Partial meniscectomy + PRP supplementation	1 (0)			
Autologous chondrocyte implantation + PRP				
Postoperative radiographic HKA, degrees	183.1 (180–190)			
Surgical correction, degrees	9.8 (5-20)			
PRP = Platelet rich plasma; ACL = Anterior Cruciate Ligament; HKA = Hip Knee Angle				

Thirty-three of the 247 HTOs (13.4%) were converted to knee replacement during follow-up, with 86.6% of the original procedures surviving at an average follow-up of 11.6 years. Conversion occurred after a mean interval of 10.4 years (range 4–16) from the index procedure. Thirty-one HTO procedures were converted to TKA and 2 to unicompartmental knee arthroplasty. Kaplan-Meier survival estimates at 17 years for HTO were 75.5% (95% confidence interval [CI] 66.7–84.3) (Fig. 1). The log-rank test indicated a significant difference (p < 0.001) in the 17-year survival rate of HTO between obese (55.5%; 95% CI 35.3–75.6) and non-obese (79.7%; 95% CI 70.1–89.2) patients (Fig. 1).

When age-adjusted univariate Cox regression analysis was used to examine the determinants of the conversion of HTO to knee replacement, age (hazard ratio (HR) = 1.06; 95% CI = 1.03-1.09; P < 0.001), BMI (HR = 1.12; 95% CI = 1.05 to 1.19; p = 0.001), and the severity of cartilage degeneration (Outerbridge grade) (HR = 2.09; 95% CI = 1.28 to 3.41; p = 0.003) were directly associated with this outcome. The determinants of conversion to knee arthroplasty detected at multivariate Cox regression analysis are shown in Table 3.

Table 3

Determinants of conversion to total knee arthroplasty at the multivariate Cox regression analysis.					
	HR (95% Cl)	Chi-square difference	p		
Body Mass Index	1.08 (1.01– 1.15)	17.27	0.024		
Severity of cartilage degeneration in the medial compartment (Outerbridge grade)	1.84 (1.11- 3.06)	11.45	0.018		
Age	1.04 (1.01– 1.08)	5.39	0.028		
HR = hazard ratio; CI = confidence interval					

BMI was the most influential predictor in the model. In the Outerbridge group 4, 23/99 knees (23.2%) were converted to knee arthroplasty, with a significantly higher failure rate than in the groups with less severe cartilage involvement (i.e. Outebridge grade  $\leq$  3), where conversion occurred in 10/148 knees (6.8%) (p < 0.001). No influence of additional procedures performed at the time of surgery (microfracture, supplementation with platelet-rich plasma, or meniscectomy), type of locking plate, or postoperative angle correction on HTO survival was detected.

## Discussion

This study demonstrated that opening wedge HTO in the treatment of medial knee OA has an actual survival of 87% at a mean follow-up of about 12 years and an estimated survival of 76% at 17 years. Long-term survival rates for HTO have been highly variable in previous studies [9, 10, 12, 17–22]. Differences in the study method and surgical technique may help to explain this variability of results. Although data in the literature on the survival rate with a follow-up of more than 10 years for medial opening wedge HTO are limited [9], our results concur with studies with a shorter follow-up. Indeed, the reported survival of opening wedge HTO ranges from 72–100% at 10 years [22]. To the best of our knowledge, no previous study has reported the survival rate of opening wedge HTO in such a large cohort of patients with comparable long-term follow-up. In the current study, independent predictors for failure of HTO included older age, higher BMI, and the severity of cartilage deterioration in the medial compartment of the knee at surgery. The likelihood of conversion to knee replacement was higher in obese (i.e. BMI > 30) than in non-obese subjects. Previous studies also indicated that BMI may affect cartilage regeneration after HTO [15] and represents an independent risk factor for reduced survivorship of the

procedure [11, 12, 18, 20, 23]. In addition to the excessive and altered joint load transmission in subjects with high BMI, the effect of altered lipid metabolism and low-grade inflammation and adipokines on the joint tissues of obese patients could play a pivotal role in the progression of OA, thus leading to reduced HTO survival [24]. In our cohort of patients, the preoperative damage of articular cartilage was examined by arthroscopy at the time of osteotomy and the severity of involvement of medial compartment of the knee predicted failure of the procedure. Previous studies have indicated that the radiographic degree of OA in the medial compartment is a predictor of poor outcome [11, 12, 20, 21]. One prior study that related the severity of cartilage damage assessed arthroscopically to the long-term outcome of opening wedge HTO found that patients older than 40 years of age with advanced cartilage damage (Outerbridge 3-4) have a higher incidence of conversion to TKA [25]. In the current study, older patients were significantly more likely to require conversion to TKA than younger patients. This result is in line with most previous long-term studies that have shown a negative effect of increasing age on HTO survival [10-12, 18, 25, 26]. Articular cartilage undergoes age-related changes that increase the risk of knee OA and may limit tissue repair that occurs following HTO [27]. This study did not find significant effect of concomitant cartilage restoration techniques, including microfractures and/or platelet-rich plasma supplementation, in increasing HTO survival. Theoretically, the improved load transmission through the knee achieved by osteotomy should allow for enhanced cartilage restoration in the medial compartment of the knee. In this context, the combination of biological procedures could stimulate post-operative regeneration of articular cartilage or at least prevent the progression of medial OA. Cartilage restoration techniques and plateletrich plasma used in combination with HTO have been shown to be effective in improving function and relieving pain after surgery [28, 29]. A previous literature review [28] also found that performing concomitant microfractures can potentially delay the need for TKA after HTO in the medium term. However, the analysis was limited by the heterogeneity of techniques used for HTO and cartilage restoration, as well as inconsistency of outcome measures in previous studies. Furthermore, long-term survival has not been previously evaluated [28]. Further high-quality data are needed to determine whether cartilage restoration procedures may actually be helpful in improving the long-term HTO survival. No effect of different locking plates on HTO survival was observed in this study. There are no data in the literature on the influence of different fixation devices on the long-term outcome and survival of opening wedge HTO. However, biomechanical studies have shown that different locking plates have similar biomechanical properties and sufficient strength to ensure the healing of open wedge HTO [30, 31].

The most important strength of the present study is the survival analysis of a large cohort of patients who had undergone opening wedge HTO many years earlier. The Kaplan–Meier analysis enabled meaningful calculation of failure rates despite different follow-up times, while the Cox regression methodology allowed to evaluate the effect of several factors on failure of HTO. The present study has also several shortcomings. First, it is limited by the retrospective nature of its design. In addition, the choice of using conversion to TKA as the only indicator of failure of HTO may have underestimated the rate of poor outcomes of the procedure. In fact, some patients, especially in the older age, may refuse knee replacement despite the progression of knee OA after HTO. However, the conversion to TKA has been considered the primary endpoint in virtually all published papers reporting HTO survival.

Furthermore, knee replacement is an unambiguous event that all patients may accurately recall. Finally, it would have been useful to perform a preoperative MRI to accurately assess cartilage damage in the medial compartment of the knee before performing HTO. The cost of this examination limits its routine use, but we believe that the systematic preoperative arthroscopic examination can provide useful information to forecast the long-term outcome of HTO.

## Conclusions

The long-term survival of open wedge HTO for OA in the medial compartment of the knee is satisfactory. However, the risk of conversion to TKA is significantly increased in obese patients. Advanced age and severity of pre-existing cartilage damage may also contribute to the risk of conversion to TKA. These prognostic factors should be considered and discussed with patients when planning surgery for isolated medial compartment OA.

## Abbreviations

OA Osteoarthritis HTO High tibial valgus osteotomy TKA Total knee arthroplasty BMI Body mass index CI Confidence interval HR Hazard ratio.

## Declarations

## Ethical Approval

This is an observational study and the local Ethics Committee has confirmed that no ethical approval is required.

#### **Consent to Participate**

Informed consent was obtained from all individual participants included in the study.

#### **Consent to Publish**

Consent to publish was obtained from all participants in the study

#### Authors' Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by A.G., L.F., V.I., A.C., G.B., E.F and S.N. Data analysis was supervised by M.M. The first draft of the manuscript was written by A.G. and all authors commented on previous versions of the manuscript. The final version of the manuscript was revised by C.Z. and M.M. All authors read and approved the final manuscript.

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#### Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

#### Availability of data and materials

The authors declare that data are available upon request.

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## **Figures**



### Figure 1

Kaplan–Meier survival curve and 95 % Confidence Interval comparing non-obese (n = 207) with obese (n = 40) patients after HTO, with conversion to TKA being defined as failure.