Joint line obliquity after high tibial osteotomy:

assessment and clinical implications

Tianshun Xie

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Joint line obliquity after high tibial osteotomy: assessment and clinical implications

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by

Tianshun Xie

born on 8 August 1990

Supervisor
Dr. I. van den Akker-Scheek

Co-supervisors
Dr. H.C. van der Veen
Dr. R.W. Brouwer

Assessment Committee
Prof. S.M.A. Bierma-Zeinstra
Prof. J.N. Doornberg
Prof. F.P.J.G. Lafeber

Paranymphs
Hui Dong
Ting Jiang

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Chapter 1

General introduction

In 2020, osteoarthritis affected 595 million people worldwide, constituting 7.6% of the global population [1]. The pathological changes in osteoarthritis comprise a destructive process that disrupts the homeostasis of both articular cartilage and subchondral bone, potentially leading to the narrowing of the joint space [2]. Characterized by pain, stiffness, and restricted joint motion, osteoarthritis significantly diminishes patients' quality of life [3]. A substantial amount of these people suffering from osteoarthritis are diagnosed with knee osteoarthritis. In 2019, the worldwide prevalence of knee osteoarthritis was recorded at 364.6 million cases. Older age (>65 years old) and obesity (Body mass index >32.5 kg/m2) have been identified as noteworthy risk factors associated with accelerated knee osteoarthritis [4, 5]. Regarding age, by the year 2050, the population aged over 65 is projected to surpass the population aged between 15 and 24 [2]. The global prevalence of obesity has witnessed a substantial increase, rising from 4.6% in 1980 to 14% in 2019 [6]. Projections suggest that by 2030, the global prevalence of obesity could reach 50% [7]. As the population ages and obesity prevalence continues to rise, the prevalence of knee osteoarthritis is expected to increase, exacerbating the existing situation [8, 9].The prevalence of knee osteoarthritis has a profound socioeconomic impact on societies and healthcare systems globally [10]. Therefore, effective management and treatment are necessary for addressing knee osteoarthritis.

Non-surgical treatment of knee osteoarthritis

The conventional first-line approach for addressing symptomatic knee osteoarthritis involves non-surgical conservative treatments, offering advantages in terms of cost-effectiveness and minimized risks as opposed to surgical treatment [3]. The OsteoArthritis Research Society International (OARSI) provides practical recommendations for guiding the non-surgical management of knee osteoarthritis, drawing from expert opinion and high-quality evidence [11]. In accordance with the OARSI guideline [11], it is suggested that key non-surgical interventions for knee osteoarthritis should comprise arthritis education and structured land-based exercise programs. Furthermore, the OARSI guideline underscores the importance of weight loss in managing knee osteoarthritis, emphasizing that obesity poses a risk factor for the progression of this condition, and a strong recommendation of topical non-steroidal anti-inflammatory drugs (NSAIDs) [12]. These conservative treatments prevent and postpone the necessity of surgical intervention for symptomatic knee osteoarthritis [12].

Surgical management of knee osteoarthritis

When non-surgical treatments do not sufficiently relieve pain and enhance function as knee osteoarthritis progresses, surgical interventions are considered. Total knee arthroplasty (TKA) is a surgical procedure to replace a damaged knee joint with an artificial prosthesis, often used for treating severe knee osteoarthritis [13]. Although TKA is considered one of the most successful surgical interventions, providing prompt relief from pain and enhancing functionality, the durability of a knee artificial prosthesis is finite, and signs of wear and tear may gradually emerge over time [14]. A study involving 48000 primary TKAs showed a 20% failure rate at 15 years follow-up [15]. Consequently, a revision prosthesis is required when the primary TKA fails, introducing heightened surgical complexity and increased risks into the revision procedure [16].

In cases of uni-compartmental knee osteoarthritis accompanied by malalignment, addressing malalignment takes precedence, necessitating additional surgical treatment options. In a systematic review conducted by Stoddart et al. [17], involving 3786 patients, it was found that isolated medial knee osteoarthritis accounted for 27% of knee osteoarthritis cases. Moreover, the hip-knee-ankle angle, denoting lower limb alignment, is measured between the mechanical axes of the femur and tibia in an anteroposterior long-leg standing radiograph, typically ranging from 1° to 1.5° in varus in healthy individuals [18, 19]. In a study performed in Rotterdam, the Netherlands, involving 2664 knees, Brouwer et al. [20] concluded that an increasing lower limb malignment is associated with both the progression and development of knee osteoarthritis. Also, other authors concluded that varus malalignment of the lower limb is an independent risk factor for the progression of medial knee osteoarthritis [21]. For these patients with medial knee osteoarthritis and varus malalignment, a valgus-producing high tibial osteotomy (HTO) is typically performed [22]. The HTO involves a controlled wedge-shaped osteotomy in the proximal tibia based on preoperative planning, and repositioning of the cut tibial segment to achieve the desired realignment [22]. HTO shifts the mechanical axis laterally, reducing medial compartment load, alleviating symptoms, and enhancing quality of life [23, 24]. Consequently, HTO is increasingly valuable in deferring the requirement for a TKA, preserving the patient's natural knee joint, and mitigating the necessity for possible future revision TKA [24].

Outcomes of high tibial osteotomy

When performing an HTO, two different techniques are commonly used: lateral closing-wedge and medial opening-wedge HTOs [25]. Both the lateral closing-wedge and medial opening-wedge HTOs demonstrate favourable clinical results. As per Ollivier et al.'s systematic review encompassing 7087 lateral closing-wedge or medial opening-wedge

HTOs [22], TKA can be postponed for over 15 years in 44% to 93% of patients, with more than 77% expressing satisfaction during a mean follow-up period exceeding 10 years. In the systematic review by Ekhtiari et al. [26], involving 1189 patients undergoing HTO, 87% returned to sports with 79% surpassing preoperative levels, 85% returned to work with 66% exceeding preoperative levels, and 90% resumed sports or work within the first postoperative year. Cheng et al.'s systematic review of 2840 knees demonstrated significant improvements in patient-reported outcomes after lateral closing-wedge or medial opening-wedge HTOs, including Hospital for Special Surgery Knee Score, Lysholm score, and Visual Analog Scale pain score [25].

Although the lateral closing-wedge HTO and medial opening-wedge HTO are both the prevailing choices in clinical practice [25], the two techniques yield varying outcomes. Lee et al. [27] found that medial opening-wedge HTO increased the leg length by on average 6.96 mm, whereas lateral closing-wedge HTO decreased it by 1.95 mm on average. A discrepancy in leg length can impact lower limb alignment, joint function and stability, and gait pattern [27]. Sun et al. [28] indicated that lateral closing-wedge HTO was associated with a higher incidence of opposite cortical fractures. Furthermore, opting for a lateral closing-wedge HTO may be preferable when a significant correction is needed, compared to medial opening-wedge HTO [27].

History of high tibial osteotomy

The idea of using osteotomy for deformity correction dates as far back as the sixteenth century [29]. The application of HTO starts in the mid-20th century. In 1961, Jackson and Waugh et al. [30] reported 11 cases of osteotomies at the proximal tibia for the treatment of symptomatic knee osteoarthritis with valgus or varus malalignment. In 1973, Coventry et al. [31] published their experience with lateral closing-wedge HTO involving 226 patients, further bolstering the technique's popularity. In 1979, Fujisawa et al. [32] conducted a study that explored the optimal weight-bearing point for achieving the desired correction in HTO, based on arthroscopic findings, leading to the establishment of the 'Fujisawa point' positioned 30% to 40% laterally from the midpoint of the tibial plateau. In 1987, the effectiveness of medial opening-wedge HTO was established as Hernigou et al. presented long-term results from a study involving 93 patients [33].

Planning of high tibial osteotomy

Effective preoperative planning is crucial for the success of HTO [34]. In valgus-producing HTO for treating medial knee osteoarthritis, a targeted alignment post-correction is typically set at 4-degree valgus (a range of 2-6 degrees valgus) [35, 36]. To attain the desired alignment following HTO, a correction point is needed to be established at the knee joint during preoperative planning, typically observed in anteroposterior long-standing radiographs. To date, consensus on the optimal correction point remains elusive. While the Fujisawa point is commonly used (typically choosing 62-62.5% of the tibial plateau from the medial edge) [37], also the lateral tibial spine as the optimal point (approximately 58.3%) is now considered [38]. Using the Fujisawa point and the lateral tibial spine as optimal point have shown similar outcomes, with the latter aiding in joint geometry preservation and exhibiting a lower risk of patellofemoral cartilage deterioration [39].

How to measure knee joint line obliquity

Although a valgus-producing HTO is a powerful technique for addressing medial knee osteoarthritis, it concurrently results in an increased knee joint line obliquity (KJLO) in the frontal plane [40], especially in cases requiring significant correction [41]. This issue has garnered clinical attention in recent years, prompting both biomechanical and clinical investigations in this area. Nevertheless, previous studies lack consensus in defining KJLO [40], employing varying criteria, including the use of distinct knee joint lines and reference lines to establish an angle for assessing KJLO. The knee joint line is determined by the tangential lines of the proximal tibia, distal femur, or the middle knee joint space [42]. The KJLO is assessed by the angle formed between the knee joint line and a reference line, which can be based on the ground floor, the tibial mechanical axis, or lower limb weight-bearing line [43-45] (**Figure 1**).

Consequences of increased knee joint line obliquity after high tibial osteotomy

A previous finite element analysis study indicated that an increase in KJLO after HTO can lead to a notable rise in shear stress directed towards the lateral knee compartment [41]. This increase in obliquity has been shown to substantially alter the distribution of contact stress within the knee joint, as indicated by a prior cadaver study [48], with higher pressure observed at the medial tibial intercondylar eminence and the lateral meniscus.

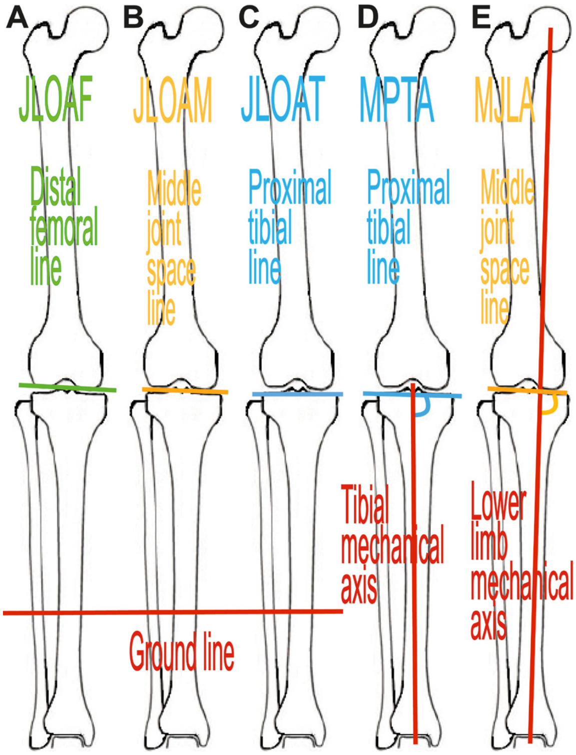

Figure 1. Measurement methods for knee joint line obliquity [46]
A. Joint line orientation angle by femoral condyles (JLOAF), the angle between distal tangential line of femoral condyles (green) and ground line (red) [45]. **B.** Joint line orientation angle by middle knee joint space (JLOAM), the angle between line at middle knee joint space (yellow) and ground line (red) [44]. **C.** Joint line orientation angle by tibial plateau (JLOAT), the angle between proximal tangential line of tibial plateau (blue) and ground line (red) [47]. **D.** Medial proximal tibial angle (MPTA), the angle between proximal tangential line of tibial plateau (blue) and tibial mechanical axis (red) [43]. **E.** Mikulicz joint line angle (MJLA), the angle between line at middle knee joint space (yellow) and lower limb mechanical axis (red) [43].

Considerate debate continues regarding whether these biomechanical changes have clinical implications. Previous studies have yielded varying results concerning the impact of KJLO on patient-reported outcomes and the survival rate of HTO [47, 49-51]. One potential explanation for the differences in results is the diverse methods employed for assessing KJLO, leading to variability in the association between KJLO and clinical consequences. Moreover, previous studies have often lacked rigorous control over confounding variables when comparing increased KJLO and acceptable KJLO groups following HTO [40]. Furthermore, the available evidence on the relationship between increased KJLO and HTO survivorship is constrained by the limited number of patients included (less than 120 cases) in the previous studies and the regression model is not used for analysis [49, 52].

Total knee arthroplasty after high tibial osteotomy

HTO typically demonstrates a commendable long-term survival rate, ranging between 44% and 93% over a span of 15 years follow-up [22]; however, its efficacy may diminish over time [53]. HTO is considered to buy time before a TKA is necessary. In cases where HTO is no longer effective, a TKA often serves as an alternative solution. Nonetheless, the question of whether a prior HTO can impact the outcomes of a subsequent TKA remains a topic of debate [54-57]. An investigation comparing TKA with prior HTO and primary TKA without prior HTO in terms of patient-reported outcomes and radiological parameters is therefore necessary.

Thesis objectives

This thesis aims to address the implications of knee joint line obliquity issues in patients who undergoing high tibial osteotomy with medial knee osteoarthritis and varus malalignment. The central focus is to understand the influence of an increased knee joint line obliquity on clinical outcomes of these patients. The objectives include:

To investigate the methodology for measuring knee joint line obliquity, including a description of current techniques used and to recommend the preferred knee joint line obliquity measurement method in high tibial osteotomy.
To explore the influence of increased knee joint line obliquity on patient-reported outcomes, radiological results, and the survivorship of lateral closing-wedge high tibial osteotomy.
To assess the disparities between total knee arthroplasty following high tibial osteotomy and primary total knee arthroplasty without prior high tibial osteotomy, with a focus on contrasting patient-reported outcomes and radiological parameters.

By accomplishing these goals, this thesis contributes to a better understanding of the clinical challenges associated with increased knee joint line obliquity after high tibial osteotomy and total knee arthroplasty performed in patients who have previously undergone high tibial osteotomy.

Thesis outline

Part I - How to measure knee joint line obliquity
Chapter 2 is a scoping review that provides a concise overview of contemporary measurement methods for knee joint line obliquity and the radiographic techniques

employed to evaluate knee joint line obliquity in knees with valgus-producing high tibial osteotomy. The debate regarding the most suitable method for measuring knee joint line obliquity remains ongoing.

Chapter 3 constitutes a cross-sectional study focuses on identifying the preferred measurement method for knee joint line obliquity. This chapter directly addresses the contentious issues introduced in Chapter 2 and presents a recommended approach for measuring knee joint line obliquity.

Part II - Consequences of increased knee joint line obliquity after high tibial osteotomy

Chapter 4 is a systematic review that delves into the clinical and radiological outcomes associated with knee joint line obliquity following a lateral closing-wedge high tibial osteotomy. Controversy surrounds the potential influence of increased knee joint line obliquity on subsequent outcomes after high tibial osteotomy, making this a central focus of the chapter.

Chapter 5 is a cohort study that investigates the influence of increased knee joint line obliquity on clinical and radiological outcomes following a lateral closing-wedge high tibial osteotomy. The study design employs a one-on-one matching method to effectively manage potential confounding variables in outcome comparisons. This chapter builds upon and addresses the contentious issues introduced in Chapter 4.

Chapter 6 is a cohort study that explores the influence of increased knee joint line obliquity and other perioperative factors on the survival of lateral closing-wedge high tibial osteotomy. This study draws upon a substantial patient dataset comprising 463 knees for its analysis.

Part III - Total knee arthroplasty after high tibial osteotomy

Chapter 7 is a cohort study that examines the scenario in which a high tibial osteotomy is not effective anymore. This study conducts a comprehensive comparison of clinical outcomes and radiological parameters between hight tibial osteotomy that undergo conversion to total knee arthroplasty and primary total knee arthroplasty without prior high tibial osteotomy. This study design incorporates a one-on-one matching method to ensure the robustness of the analysis by mitigating bias arising from imbalanced between-group variables.

The thesis ends with **Chapter 8,** that offers a comprehensive discussion of the studies encompassed within the thesis, outlines the limitations of this thesis, and gives prospective directions for future research.

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Part I

How to measure knee joint line obliquity

Chapter 2

Assessing joint line obliquity in valgus-producing high tibial osteotomy: a scoping review of the literature

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Tianshun Xie
Reinoud W. Brouwer
Inge van den Akker-Scheek
Hugo C. van der Veen

This Chapter has been submitted

Abstract

Purpose

To summarize currently used knee joint line obliquity (KJLO) measurement methods, including their measurement reliability, and the radiographic techniques used in valgus-producing high tibial osteotomy.

Methods

The databases PubMed, Embase, and Web of Science were searched from inception up to February 2023, with an updated search in May 2023, to identify articles that measured KJLO on radiographs in valgus-producing high tibial osteotomy.

Results

Thirty clinical articles were included. There were five different KJLO measurement methods reported, including joint line orientation angle by femoral condyles (JLOAF), joint line orientation angle by middle knee joint space (JLOAM), joint line orientation angle by tibial plateau (JLOAT), Mikulicz joint line angle (MJLA), and medial proximal tibial angle (MPTA), of which the JLOAT was the most commonly used. KJLO was measured on anteroposterior full-length standing radiographs with either single-leg or double-leg patient stance position, with no standardized bipedal distance on double-leg stance radiographs. Moderate-to-excellent measurement reliability was reported for intraobserver and interobserver MPTA, and good-to-excellent for intraobserver JLOAT and JLOAM and for interobserver JLOAT, JLOAM, and MJLA.

Conclusion

There is no consensus on how to measure KJLO or on which radiographic technique should be used. When measuring joint line orientation angles on anteroposterior full-length double-leg stance radiographs, controlling the bipedal distance with feet together is suggested when possible. Future research is needed to determine the measurement differences between the five KJLO measurement methods and to identify the preferred, ideal one.

Introduction

Valgus-producing high tibial osteotomy is a powerful surgical procedure performed for medial knee osteoarthritis in patients with varus malalignment, aiming to realign the lower limb weight-bearing line from the affected medial knee compartment to the relatively healthy lateral side, slow down knee osteoarthritis progression, and postpone knee arthroplasty [1, 2]. However, this surgical process could introduce an increased knee joint line obliquity (KJLO) in the frontal plane [3-5].

Excessive KJLO can lead to a notable rise in shear stress and a redistribution of contact stress within the knee joint [6-8]. However, controversial evidence exists regarding the relationship between postoperative KJLO and patient-reported outcomes, status of medial knee cartilage, and the long-term surgical survivorship subsequent to valgus-producing high tibial osteotomy [9]. The variance in KJLO measurement methods and radiographic techniques used may contribute to this controversy, so evaluation of KJLO and hence decision-making remain difficult in patients with suspected excessive KJLO. The purpose of this scoping review was to summarize currently used KJLO measurement methods, including their measurement reliability when possible, and the radiographic techniques used in valgus-producing high tibial osteotomy.

Methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline for scoping reviews [10].

Search strategy

A literature search was conducted on 18 February 2023 in three online electronic databases: PubMed, Web of Science, and Embase, with an updated search on 1 May 2023. Articles were retrieved from the date of online database inception up to the search date. The search strategies of the three databases, which were optimized by a librarian, are shown in **Table 1**.

Table 1. Search Strategy

Online Database	Search String
PubMed	("Osteoarthritis, Knee" [Mesh] OR "Knee" [Mesh] OR "Knee Joint" [Mesh] OR knee* [tiab]) AND ("Osteotomy" [Mesh] OR osteotom* [tiab]) AND (joint line obliquit* [tiab] OR joint line orientat* [tiab] OR jlo [tiab])
Web of Science	TS= "knee*" AND TS= "osteotom*" AND TS= ("joint line obliquit*" OR "joint line orientat*" OR "jlo")
Embase	("knee osteoarthritis"/exp OR "knee"/exp OR knee*:ab,ti,kw) AND ("osteotomy"/exp OR osteotom*:ab,ti,kw) AND ("joint line obliquit*":ab,ti,kw OR "joint line orientat*":ab,ti,kw OR jlo:ab,ti,kw)

Article selection and data extraction

Articles meeting the following criteria were included: KJLO was measured in patients planned for valgus-producing high tibial osteotomy, and the KJLO measurement method was clearly described. Articles on nonpatient research such as cadaveric studies and finite element analysis studies were excluded. No language restriction was used in the article selection.

Article selection and data extraction process: (1) duplicate articles were manually excluded from the search outcome; (2) title, abstract, and full text were independently assessed by two reviewers (TX and HV) by checking the predefined criteria; (3) relevant references of the included articles were manually searched for additional articles; (4) information on publication year, study location, separate patient groups, osteotomy techniques, stance position in filming, KJLO measurement method used and its measurement reliability when possible, and preoperative KJLO mean values were extracted from each included article (TX); (5) two reviewers (TX and HV) achieved consensus on included articles and extracted information in discussion meetings, and a third reviewer (IvdAS) was consulted if there was disagreement between the two reviewers.

Grading measurement reliability

The measurement reliability of radiological parameters is usually evaluated by the intraclass correlation coefficient (ICC) between two measurements of the same observer (intraobserver reliability) and between the measurements of two observers (interobserver reliability). ICC values < 0.5, 0.5-0.75, 0.75-0.9, and >0.9 represent the grades of poor, moderate, good, and excellent measurement reliability, respectively [11].

Results

The search strategy identified 188 articles, containing 105 duplicates. Of the remaining 83 articles, 55 were excluded based on the predefined inclusion and exclusion criteria. The updated searching and screening resulted in 2 additional articles. In the end, 30 clinical articles were included. A flowchart of the article selection process is presented in **Figure 1**. The extracted information from the included articles is summarized in **Table 2** and below.

Eighteen clinical studies (18/30, 60.0%) used the double-leg stance position at filming [4, 5, 12-27], three with bipedal distance: Sohn et al. [20] and Victor et al. [22] controlled bipedal distance with both feet together, Bartholomeeusen et al. [12] defined hip joint adduction until the touching of medial sides of the upper legs, knees, and ankles. Four clinical studies used single-leg stance position at filming (4/30, 13.3%) [3, 28-30]. The remaining eight clinical studies did not mention any stance position details (8/30, 26.7%) [31-38].

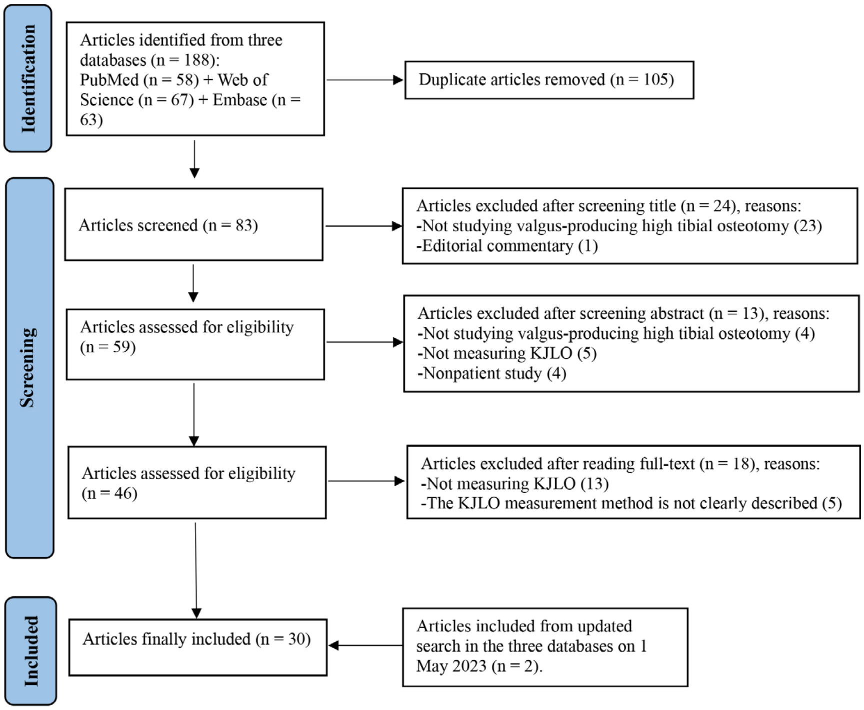

Figure 1. Literature Selection Process by PRISMA flowchart

KJLO radiographic techniques

All studies used an anteroposterior full-length standing radiograph for KJLO measurement. Variation was seen in the standing position for single-leg stance or double-leg stance at filming and in bipedal distance on double-leg stance radiographs.

KJLO measurement methods

Five different KJLO measurement methods were reported, including joint line orientation angle by tibial plateau (JLOAT), joint line orientation angle by middle knee joint space (JLOAM), joint line orientation angle by femoral condyles (JLOAF), Mikulicz joint line angle (MJLA), and medial proximal tibial angle (MPTA). For clarification purposes, the five KJLO measurement methods are illustrated in **Figure 2.** Twenty-one clinical studies used JLOAT to measure KJLO (21/30, 70.0%) [4, 12, 13, 17-27, 29, 30, 32, 34-36, 38], three used JLOAM (3/30, 10.0%) [14, 33, 37], three used JLOAF (3/30, 10.0%) [3, 15, 28], and one used MPTA (1/30, 3.3%) [31]. Two clinical studies performed two KJLO measurement methods to assess KJLO (2/30, 6.7%), one using JLOAT and MPTA [16], and the other using MJLA and MPTA [5].

Table 2. Summary of Included Articles

Authors (year, location)	Osteotomy techniques (separate patient groups)	KJLO measurement methods	Radiographic techniques	KJLO mean values, Preoperative *(postoperative)*	KJLO mean values, Preoperative *(postoperative)*	
					Intraobserver ICC	Interobserver ICC
Babis et al. (2008, USA) [4]	LCW HTO	JLOAT	Double-leg stance	-0.5° *(NM)*	-0.5° *(NM)*	-0.5° *(NM)*
Victor et al. (2014, Belgium) [22]	HTO	JLOAT	Double-leg stance with feet together	NM *(NM)*	NM *(NM)*	NM *(NM)*
Lee KM et al. (2015, Korea) [33]	MOW HTO	JLOAM	NM	0.3° *(4.4°)*	0.3° *(4.4°)*	0.3° *(4.4°)*
Oh et al. (2016, Korea) [17]	MOW HTO	JLOAT	Double-leg stance with patella distance equal to shoulder width	-0.7° *(1.3°)*	-0.7° *(1.3°)*	-0.7° *(1.3°)*
Kim CW et al. (2017, Korea) [14]	MOW HTO	JLOAM	Double-leg stance	-0.4° *(3.2°)*	-0.4° *(3.2°)*	-0.4° *(3.2°)*
Akamatsu et al. (2018, Japan) [28]	MOW HTO (postoperative MPTA>95°/≤95°)	JLOAF	Single-leg stance	0.7°/ -0.1° *(5.7°/3.2°)*	0.7°/ -0.1° *(5.7°/3.2°)*	0.7°/ -0.1° *(5.7°/3.2°)*
Goshima et al. (2019, Japan) [13]	MOW HTO	JLOAT	Double-leg stance with patella distance equal to shoulder width	-2.3° *(1.4°)*	-2.3° *(1.4°)*	-2.3° *(1.4°)*
Park JY et al. (2019, Korea) [37]	MOW HTO	JLOAM	NM	-0.8° *(2.9°)*	-0.8° *(2.9°)*	-0.8° *(2.9°)*
Bartholomeeusen et al. (2020, Belgium) [12]	MOW HTO	JLOAT	Double-leg stance with medial sides touching upper legs, knees, and ankles	1.81° *(3.46°)*	1.81° *(3.46°)*	1.81° *(3.46°)*
Goto et al. (2020, Japan) [31]	LCW HTO	MPTA	NM	NM *(96.6°)*	NM *(96.6°)*	NM *(96.6°)*
Kim JE et al. (2020, Korea) [32]	MOW HTO	JLOAT	NM	0.79° *(2.72°)*	0.79° *(2.72°)*	0.79° *(2.72°)*
Kubota et al. (2020, Japan) [29]	MOW HTO	JLOAT	Single-leg stance	1.1° *(2.6°)*	1.1° *(2.6°)*	1.1° *(2.6°)*

Table 2. Continued.

Authors (year, location)	Osteotomy techniques (separate patient groups)	KJLO measurement methods	Radiographic techniques	KJLO mean values, Preoperative *(postoperative)*	KJLO mean values, Preoperative *(postoperative)*	
					Intraobserver ICC	Interobserver ICC
Park JG et al. (2020, Korea) [36]	MOW HTO	JLOAT	NM	0.5° *(3.6°)*	0.5° *(3.6°)*	0.5° *(3.6°)*
Song et al. (2020, Korea) [38]	MOW HTO	JLOAT	NM	NM *(NM)*	NM *(NM)*	NM *(NM)*
Kim GW et al. (2021, Korea) [15]	MOW HTO	JLOAF	Double-leg stance	NM (5.5°/0.9°)	NM (5.5°/0.9°)	NM (5.5°/0.9°)
Lee SJ et al. (2021, Korea) [34]	MOW HTO	JLOAT	NM	2.1° *(3.3°)*	2.1° *(3.3°)*	2.1° *(3.3°)*
Miyazaki et al. (2021, Japan) [35]	MOW HTO	JLOAT	NM	-1.0° *(2.4°)*	-1.0° *(2.4°)*	-1.0° *(2.4°)*
Park JG et al. (2021, Korea) [19]	MOW HTO (preoperative MPTA ≥85°/<85°)	JLOAT	Double-leg stance	2.2°/ -0.4° *(5.3°/3.5°)*	2.2°/ -0.4° *(5.3°/3.5°)*	2.2°/ -0.4° *(5.3°/3.5°)*
Park JG et al. (2021, Korea) [18]	MOW HTO	JLOAT	Double-leg stance	0.7° *(4.5°)*	0.7° *(4.5°)*	0.7° *(4.5°)*
Akamatsu et al. (2022, Japan) [3]	MOW HTO	JLOAF	Single-leg stance	1.4° *(6.3°)*	1.4° *(6.3°)*	1.4° *(6.3°)*
Hiramatsu et al. (2022,Japan) [23]	MOW HTO	JLOAT	Double-leg stance with knees at shoulder width	-0.66° *(3.0°)*	-0.66° *(3.0°)*	-0.66° *(3.0°)*
Kubota et al. (2022, Japan) [30]	MOW HTO (rod/ MPTA)	JLOAT	Single-leg stance	1.3°/ -0.7° *(3.4°/1.4°)*	1.3°/ -0.7° *(3.4°/1.4°)*	1.3°/ -0.7° *(3.4°/1.4°)*
Kawashima et al. (2022, Japan) [24]	MOW HTO	JLOAT	Double-leg stance	-0.5° *(2.8°)*	-0.5° *(2.8°)*	-0.5° *(2.8°)*
Kim JS et al. (2022, Korea) [16]	MOW HTO (postoperative MPTA 85°~90°/ 90°~93°/ 93°~95°/95°~102°)	JLOAT	Double-leg stance	-1.02°/ -1.01°/ -0.66°/ 0.06° *(-0.10°/0.26°/1.57°/5.14°)*	-1.02°/ -1.01°/ -0.66°/ 0.06° *(-0.10°/0.26°/1.57°/5.14°)*	-1.02°/ -1.01°/ -0.66°/ 0.06° *(-0.10°/0.26°/1.57°/5.14°)*
		MPTA		83.81°/ 84.75°/ 84.46°/ 84.63° *(89.12°/92.06°/93.52°/96.04°)*	83.81°/ 84.75°/ 84.46°/ 84.63° *(89.12°/92.06°/93.52°/96.04°)*	83.81°/ 84.75°/ 84.46°/ 84.63° *(89.12°/92.06°/93.52°/96.04°)*

Table 2. Continued.

Authors (year, location)	Osteotomy techniques (separate patient groups)	KJLO measurement methods	Radiographic techniques	KJLO mean values, Preoperative *(postoperative)*	KJLO mean values, Preoperative *(postoperative)*	
					Intraobserver ICC	Interobserver ICC
Park SB et al. (2022, Korea) [25]	MOW HTO (unilateral/ primarily bilateral/ secondarily bilateral treated limbs)	JLOAT	Double-leg stance	1.2°/1.7°/1.1° *(3.1°/3.3°/2.7°)*	1.2°/1.7°/1.1° *(3.1°/3.3°/2.7°)*	1.2°/1.7°/1.1° *(3.1°/3.3°/2.7°)*
Rosso et al. (2022, Italy) [5]	MOW HTO	MJLA MPTA	Double-leg stance	88.3° *(90.6°)* 85.1° *(91.5°)*	88.3° *(90.6°)* 85.1° *(91.5°)*	88.3° *(90.6°)* 85.1° *(91.5°)*
Sohn et al. (2022, Korea) [20]	MOW HTO (postoperative MPTA ≥95°/<95°)	JLOAT	Double-leg stance with feet together	3.5°/0.7° *(6.0°/3.7°)*	3.5°/0.7° *(6.0°/3.7°)*	3.5°/0.7° *(6.0°/3.7°)*
Tseng et al. (2022, Taiwan) [21]	MOW HTO	JLOAT	Double-leg stance	-0.7° (*NM*)	-0.7° (*NM*)	-0.7° (*NM*)
Abs et al. (2023, France) [27]	MOW HTO	JLOAT	Double-leg stance	3.0° *(5.6°)*	3.0° *(5.6°)*	3.0° *(5.6°)*
Jeong et al. (2023, Korea) [26]	MOW HTO	JLOAT	Double-leg stance	NM (*NM*)	NM (*NM*)	NM (*NM*)

[a] *Knee joint line obliquity (KJLO); Medial opening wedge high tibial osteotomy (MOW HTO); Lateral closing wedge high tibial osteotomy (LCW HTO); Medial proximal tibial angle (MPTA); Mikulicz joint line angle (MJLA); Not mentioned (NM).*

[b] *Intraclass correlation coefficient (ICC) is graded following Koo et al.'s guideline [11].*

[c] *All studies use anteroposterior full length standing radiographs.*

[d] *For joint line orientation angle by femoral condyles (JLOAF), joint line orientation angle by middle knee joint space (JLOAM) and joint line orientation angle by tibial plateau (JLOAT), a positive value (+) indicates a medial opening angle, a negative value (-) indicates a lateral opening angle.*

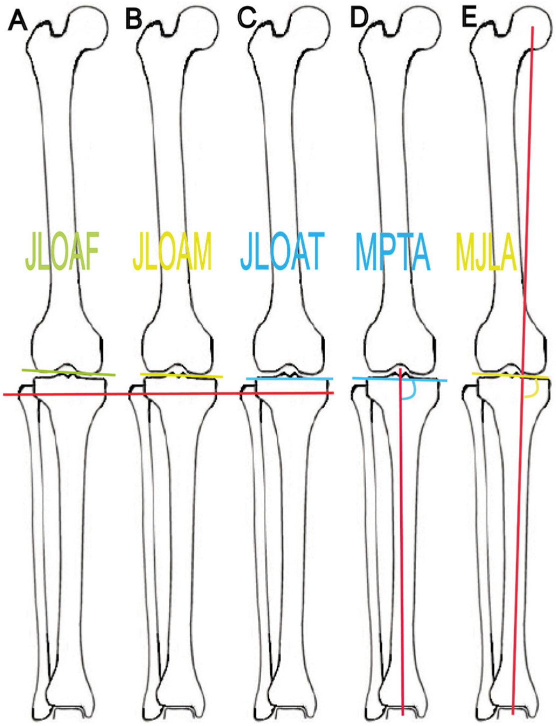

Figure 2. Illustration of KJLO Measurement Methods
A. Joint line orientation angle by femoral condyles (JLOAF) is formed by the knee joint orientation line measured by the tangential line of the femoral condyles (green) and the ground line (red) [28].
B. Joint line orientation angle by middle knee joint space (JLOAM) is formed by the knee joint orientation line measured by the line connecting the midpoints of medial and lateral knee joint space (yellow) and the ground line (red) [33].
C. Joint line orientation angle by tibial plateau (JLOAT) is formed by the knee joint orientation line measured by the tangential line of the tibial plateau (blue) and the ground line (red) [22].
D. Medial proximal tibial angle (MPTA) is the medial angle between the tangential line of the tibial plateau (blue) and the tibial mechanical axis (red) [16].
E. Mikulicz joint line angle (MJLA) is the medial angle between the middle knee joint space line (yellow) and the lower limb weight-bearing line (red) [5]. The weight-bearing line connects the femoral head centre and ankle joint centre. [52].

KJLO measurement reliability

Twenty-two clinical studies reported ICC outcomes of the KJLO measurement method used [5, 13, 14, 16-21, 24-27, 29, 30, 32-38]. Moderate-to-excellent measurement reliability was found for intraobserver and interobserver MPTA, and good-to-excellent for intraobserver JLOAT and JLOAM and for inter-observer JLOAT, JLOAM, and MJLA. There is a lack of reporting on intraobserver measurement reliability in measuring MJLA. No intraobserver or interobserver measurement reliability was reported in measuring JLOAF.

Discussion

The most important finding of this review is that the literature shows large variability in KJLO measurement methods and radiographic techniques used, which implies there is no consensus on which measurement method or radiographic technique should be used to assess KJLO.

Although JLOAT is the most commonly used KJLO measurement method, it is reported to be influenced by single-leg and double-leg stance positions as well as by bipedal distance in the double-leg stance position. According to Paley et al. [39], for healthy individuals, JLOAT measures 0° at the single-leg stance position and at the double-leg stance position with feet together. It reaches 3° lateral opening at the double-leg stance position with a bipedal distance equal to pelvis width [39]. Lee et al. [40] found that a 10-cm bipedal distance increase could introduce a 3.7° JLOAT mean measurement change on anteroposterior full-length double-leg stance radiographs. Rosso et al. [5] indicated that JLOAT was an unreliable KJLO measurement method, as measurement could be affected by the leg position relative to the ground. Since the three joint line orientation angles (JLOAT, JLOAM, JLOAF) are all formed by the ground line, it is reasonable to speculate that bipedal distance may also influence measurements of JLOAM and JLOAF. Hence to use joint line orientation angles for measuring KJLO on double-leg stance radiographs, a key procedure is to control and standardize the bipedal distance. The present review recommends using the at-attention stance position with feet together when physiologically possible. In this way, the measurements of joint line orientation angles on double-leg stance radiographs could be compared to their measurements on single-leg stance radiographs.

Whether single-leg and double-leg stance positions and bipedal distance in the double-leg stance position influence MJLA measurement remains unclear. Although studies have reported that the MPTA measurement was not affected by stance position, whether this measurement is influenced by bipedal distance on double-leg stance radiographs has not been identified. Bardot et al. [41] and Yazdanpanah et al. [42] found no statistically significant differences in MPTA measurements between single-leg and double-leg stance positions on anteroposterior full-length standing radiographs ($p > 0.05$). This finding could be explained by MPTA being measured based on the anatomical geometry of the tibial bone, thus the measurement is independent of the patient's stance position at filming. Unlike the measurements of joint line orientation angles, the measurements of MJLA and MPTA do not take the ground line into account. A reasonable hypothesis is that bipedal distance does not influence measurements of MJLA and MPTA. Future research is needed to verify this hypothesis.

There is no consensus on the preferred, ideal radiographic technique to be used for measuring KJLO in anteroposterior full-length single-leg stance or double-leg stance radiographs. In the included studies of this review, double-leg stance radiographs are used more frequently than single-leg stance radiographs, though each has its respective advantages and deficiencies. Na et al. [43] and Hiranaka et al. [44] reported that single-leg stance radiographs may be a superior radiographic technique for assessing dynamic lower limb alignment, as they are better at illustrating the loaded knee condition during gait by only providing weight-bearing on the affected knee joint. Conversely, Specogna et al. [45] found that single-leg stance radiographs did not provide more representative measurements describing the condition of knee joint under dynamic load, and recommended using double-leg stance radiographs in surgical assessment for medial knee osteoarthritis. Double-leg stance radiographs provide a comparison of radiographic features between the affected knee and its contralateral side, and patients with severe pain and/or instability of the affected knee joint may be unable to take a single-leg stance radiograph.

As the included studies lack ICC outcome reporting on intraobserver and interobserver for the JLOAF and intraobserver for the MJLA, it is not yet possible to identify a superior method from the five KJLO measurement methods based on their measurement reliability.

Factors affecting knee joint space width may influence measurement of JLOAM and MJLA. According to the definitions, JLOAM and MJLA are formed by the knee joint orientation line that measures the middle knee joint space, so confounding factors affecting knee joint space width may need to be taken into consideration in measuring them, such as meniscus and cartilage thickness, knee osteoarthritis severity grade, lateral knee laxity, and medial knee tightness [46-48]. Research is needed to find out how these confounding factors influence KJLO measurements.

In the included clinical studies, the heterogeneity of the radiographic techniques used makes it difficult to give a comprehensive comparison of the preoperative KJLO mean values between the five KJLO measurement methods. As mentioned, single-leg stance position and double-leg stance position, including bipedal distance, could influence measurements of JLOAT, JLOAM, and JLOAF. In addition, some included studies only provide the preoperative KJLO mean values from each separate patient group without presenting the overall preoperative KJLO mean values: this also encumbers determining the measurement differences between the five KJLO measurement methods in this review.

To evaluate KJLO, the preferred, ideal measurement method is suggested not to be influenced by the single-leg or double-leg stance positions or by bipedal distance in the double-leg stance position on anteroposterior full-length standing radiographs. In that way, KJLO measurements can be compared between different patients using various radiographic techniques. Reproducibility of this preferred, ideal measurement method is likewise recommended, as it has good intraobserver and interobserver measurement reliability and is not influenced by confounding factors such as knee osteoarthritis severity and knee joint laxity grades.

Obtaining a 100% anteroposterior projection full-length standing radiograph is crucial towards ensuring KJLO measurement accuracy in the frontal plane. To achieve this, it is recommended to use the position of a fully extended knee and the patella facing forward during the filming process [39, 49, 50]. Besides standardizing the filming position, a lateral fluoroscopic control targeting the posterior femoral condyles helps guarantee a 100% anteroposterior full-length standing radiograph [51].

Based on the findings of this scoping review, more research is needed to determine the preferred, ideal KJLO measurement method that can be used regardless of the anteroposterior full-length standing radiographic technique used. A well-designed study that investigates preoperative KJLO measurement differences between the five KJLO measurement methods by the same radiographic technique would be required.

Conclusion

There is no consensus on how to measure KJLO or on which radiographic technique should be used. When measuring joint line orientation angles on anteroposterior full-length double-leg stance radiographs, controlling the bipedal distance with feet together is suggested. Future research is needed to determine the measurement differences between the five KJLO measurement methods and to identify the preferred, ideal one.

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Chapter 3

Assessment of joint line obliquity and its related frontal deformity using long-standing radiographs

Tianshun Xie
Hugo C. van der Veen
Inge van den Akker-Scheek
Reinoud W. Brouwer

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Abstract

Purpose

To investigate how radiographic techniques and osteoarthritis grade influence measurements of knee joint line obliquity (KJLO) and KJLO-related frontal deformity, and to propose preferable KJLO measurement methods.

Methods

Forty patients with symptomatic medial knee osteoarthritis indicated for high tibial osteotomy were assessed. Measurements were compared between single-leg and double-leg standing radiographs for KJLO measurement methods including joint line orientation angle by femoral condyles (JLOAF), joint line orientation angle by middle knee joint space (JLOAM), joint line orientation angle by tibial plateau (JLOAT), Mikulicz joint line angle (MJLA) and medial proximal tibial angle (MPTA), as well as KJLO-related frontal deformity parameters including joint line convergence angle (JLCA), knee ankle joint angle (KAJA) and hip-knee-ankle angle (HKA). Influences of bipedal distance in double-leg standing and osteoarthritis grade on the above measurements were analysed. Measurement reliability was evaluated by intraclass correlation coefficient.

Results

From single-leg to double-leg standing radiographs MPTA and KAJA did not change significantly, whereas the other measurements showed significant changes: JLOAF, JLOAM and JLOAT decreased 0.88°, 1.24° and 1.77°, MJLA and JLCA decreased 0.63° and 0.85°, and HKA increased 1.11° ($p<0.05$). Bipedal distance in double-leg standing radiographs moderately correlated with JLOAF, JLOAM and JLOAT (r_p = -0.555, -0.574 and -0.549). Osteoarthritis grade moderately correlated with JLCA in single-leg and double-leg standing radiographs (r_s =0.518 and 0.471). All measurements had at least good reliability.

Conclusion

In long-standing radiographs, measurements of JLOAF, JLOAM, JLOAT, MJLA, JLCA and HKA are all influenced by single-leg/double-leg standing; JLOAF, JLOAM and JLOAT are also affected by bipedal distance in double-leg standing; and JLCA is affected by osteoarthritis grade. Knee joint obliquity as assessed by MPTA measurement is independent of single-leg/double-leg standing, bipedal distance or osteoarthritis grade, and has excellent measurement reliability. We therefore propose MPTA as the preferable KJLO measurement method for clinical practice and future research.

Introduction

High tibial osteotomy is an effective treatment option for symptomatic medial knee osteoarthritis with tibial varus deformity [1]. However, a postoperative suspected excessive knee joint line obliquity (KJLO) can be introduced in the frontal plane after this surgical treatment, which seems to result in inferior clinical outcomes [2-4].

Five KJLO measurement methods are described in literature, including joint line orientation angle by femoral condyles (JLOAF), joint line orientation angle by middle knee joint space (JLOAM), joint line orientation angle by tibial plateau (JLOAT), Mikulicz joint line angle (MJLA) and medial proximal tibial angle (MPTA), of which the JLOAT is the most frequently used [3-9]. Also, three different frontal deformity parameters, including joint line convergence angle (JLCA), knee ankle joint angle (KAJA) and hip-knee-ankle angle (HKA), are related to a postoperative suspected excessive KJLO in high tibial osteotomy, and as such important measurement entities [9-11]. Anteroposterior long radiographs with single-leg and double-leg standing are performed to assess both KJLO and the three KJLO-related frontal deformity parameters, with great variability in the bipedal distance used in the double-leg standing radiographs [5, 9-13]. The medial knee osteoarthritis severity grade differs in patients when assessing the KJLO and KJLO-related frontal deformity parameters [3, 14, 15].

How radiographic techniques and osteoarthritis grade influence the measurements of KJLO and KJLO-related frontal deformity is not fully understood. To the best of our knowledge, there is no published consensus on which KJLO measurement method should be used. Preferable KJLO measurement methods need to be identified for clinical usage and research purposes.

The aim of the present study is to investigate the influences of long single-leg and double-leg standing radiographs, bipedal distance in double-leg standing, and osteoarthritis grade on the measurements of KJLO and KJLO-related frontal deformity, and to propose preferable KJLO measurement methods.

Methods

Study design

Patient database from a published study was reviewed [16]. This database included 298 patients with symptomatic medial knee osteoarthritis and varus lower limb alignment, who were indicated for a high tibial osteotomy. From this database we included 130 patients who had both a preoperative anteroposterior long single-leg as well as a double-leg standing radiograph.

The patient selection process is depicted in **Figure 1**. Based on pilot study results, to detect a 1.66° mean measurement difference in JLOAT between the single-leg and the double-leg standing radiograph with a standard deviation of 2.73, a power of 95% and an alpha of 0.05, at least 38 patients were needed (G*power software, version 3.1.9.7). We randomly selected 40 patients (31 men and 9 women) with 80 anteroposterior long-standing radiographs.

The design and reporting of this study followed the STROBE (*Strengthening* the Reporting of *Observational Studies in Epidemiology*) checklist for cross-sectional studies [17]. This study was approved by the ethics committee of our hospital (MEC no. 2022-005).

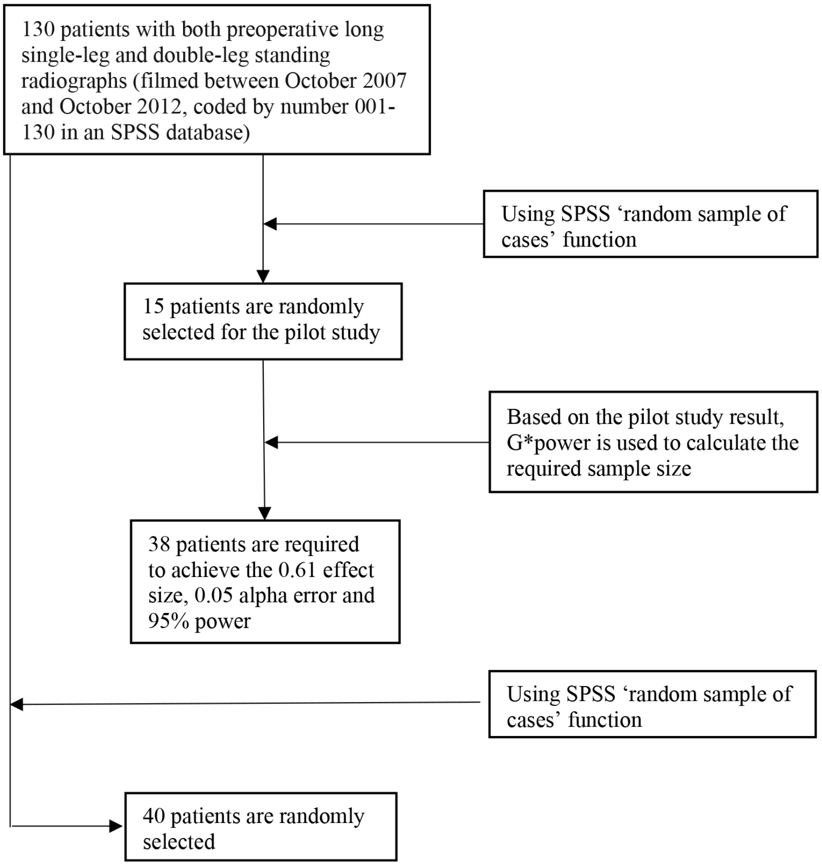

Figure 1. Flowchart of patient selection process

Long-standing radiographs

Anteroposterior long-standing radiographs were performed as follows: (1) single-leg standing: the patient stood barefoot on the affected leg, the affected knee in full extension and patella facing forward. The contralateral flexed knee was supported by a small box. The X-ray central beam targeted the affected knee centre and was perpendicular to the cassette at a distance of 1.5 metres from the tube. (2) double-leg standing: the patient stood barefoot on double legs, both knees in full extension and patella facing forward. The X-ray central beam was targeted between the knees and was perpendicular to the cassette at a distance of 1.5 meters from the tube.

Radiographic measurements

Picture Archiving and Communication System (PACS) software (Vue PACS, Philips, N.V.) was used for radiographic measurements. The minimum measurement differences that this software could determine were 0.01° for angle parameters and 0.01cm for distance parameters.

Medial knee osteoarthritis grade was evaluated by the Kellgren-Lawrence classification [18]. Two orthopaedic surgeons obtained the preoperative osteoarthritis grade in anteroposterior short-standing radiographs with the knee in full extension using paired-reading and sequence-known method [16].

Measurements were performed as illustrated in the anteroposterior long single-leg standing radiograph **(Figure 2)** and double-leg standing radiograph **(Figure 3)** from the same patient, following these procedures:

(1) JLOAF: The angle between the tangential line of the femoral condyles and the ground line [5]. This angle represented the KJLO. (**Figures 2A** and **3A**)
(2) JLOAM: The angle between the line that connected the midpoints of the medial and lateral knee joint space and the ground line [4]. This angle represented the KJLO. (**Figures 2B** and **3B**)
(3) JLOAT: The angle between the tangential line of the tibial plateau and the ground line [6]. This angle represented the KJLO. (**Figures 2C** and **3C**)
(4) JLCA: The angle between the tangential line of the femoral condyles and the tangential line of the tibial plateau [19, 20]. This angle represented the knee intra-articular deformity. (**Figures 2D** and **3D**)
(5) MJLA: The medial angle between the bisector line of the JLCA and the lower limb weight-bearing line (Mikulicz line) [7]. This angle represented the KJLO. (**Figures 2D** and **3D**)
(6) MPTA: The medial angle between the tangential line of the tibial plateau and the tibial mechanical axis [19]. This angle represented the KJLO. (**Figures 2E** and **3E**)

(7) KAJA: The angle between the tangential line of the tibial plateau and the tangential line of the distal tibial articular surface [10]. This angle represented the deformity relation between the knee and ankle joints. (**Figures 2F** and **3F**)
(8) HKA: The medial angle between the femoral mechanical axis and the tibial mechanical axis [21]. This angle represented the global deformity of the lower limb. (**Figures 2G** and **3G**)
(9) Intertalar distance (ITD): The distance between the centres of both talar domes, representing the bipedal distance [22]. (**Figure 3G**)

For the measurements of JLOAF, JLOAM, JLOAT and KAJA, a positive value (+) indicated a medial opening angle and a negative value (-) indicated a lateral opening angle.

The above measurements were performed independently by two observers (TX and RWB), each observer blinded to the other observer's measurements. All measurements were performed twice at a three-week interval. Intraobserver and interobserver reliability was assessed using the intraclass correlation coefficient (ICC).

Preferable KJLO measurement method

A preferable KJLO measurement method should have (1) adequate measurement stability: this measurement method was not influenced by the long single-leg or double-leg standing radiographs used, the bipedal distance used in the double-leg standing radiograph, or the knee osteoarthritis grade; and (2) adequate measurement reliability: this measurement method had at least good intraobserver and interobserver reliability (ICCs $\geq$ 0.75).

Statistical analysis

All statistical analyses were conducted using SPSS software (version 25, IBM Corporation, NY, USA). Descriptive statistics were used to present demographic data of patients, like gender and age. The distribution of continuous data was checked by Shapiro-Wilk test and Q-Q plots. Normally distributed data were described by mean ± standard deviation. Paired t-tests were used to compare the KJLO and KJLO-related measurement data between the single-leg and double-leg standing radiographs. Pearson correlation coefficients were calculated to determine the correlations between the bipedal distance in the double-leg standing radiographs and the KJLO and KJLO-related measurement data. Spearman correlation coefficients were calculated to determine the correlations between the osteoarthritis grade and the KJLO and KJLO-related measurement data. ICCs (two-way mixed, absolute agreement) were calculated to determine intraobserver and interobserver measurement reliability [23]. A p-value <0.05 was considered statistically significant.

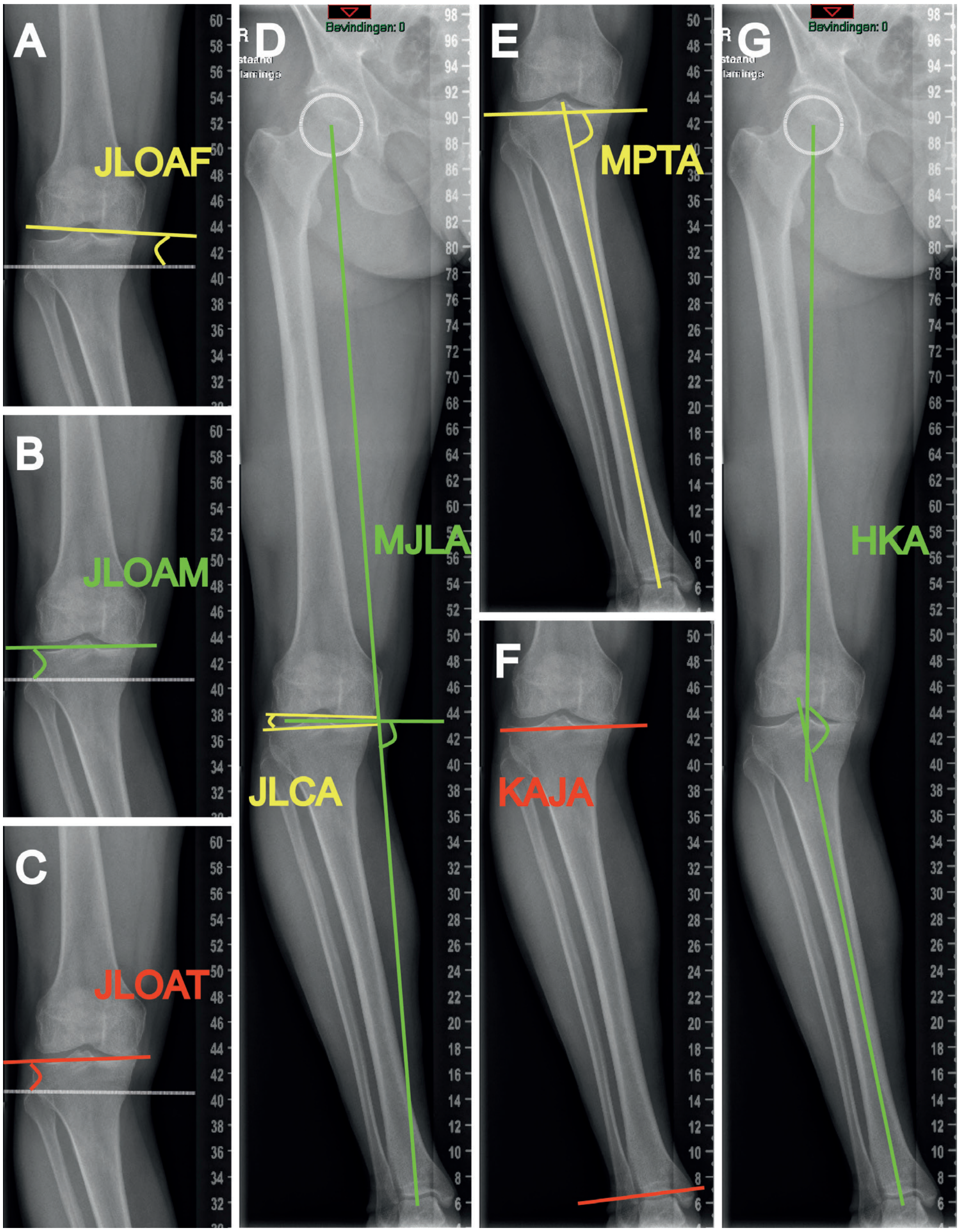

Figure 2. Measurements in anteroposterior long single-leg standing radiograph
Abbreviations: JLOAF, joint line orientation angle with knee joint orientation line of the femoral condyles; JLOAM, joint line orientation angle with knee joint orientation line of the middle knee joint space; JLOAT, joint line orientation angle with knee joint orientation line of the tibial plateau; JLCA, joint line convergence angle; MJLA, Mikulicz joint line angle; MPTA, medial proximal tibial angle; KAJA, knee ankle joint angle; HKA, hip-knee-ankle angle.
Note: In this patient example, JLOAF, JLOAM, JLOAT, JLCA, MJLA, MPTA, KAJA and HKA are measured as -3.37°, 0.20°, 2.06°, 5.32°, 84.86°, 80.96°, -4.52° and 166.57°, respectively.

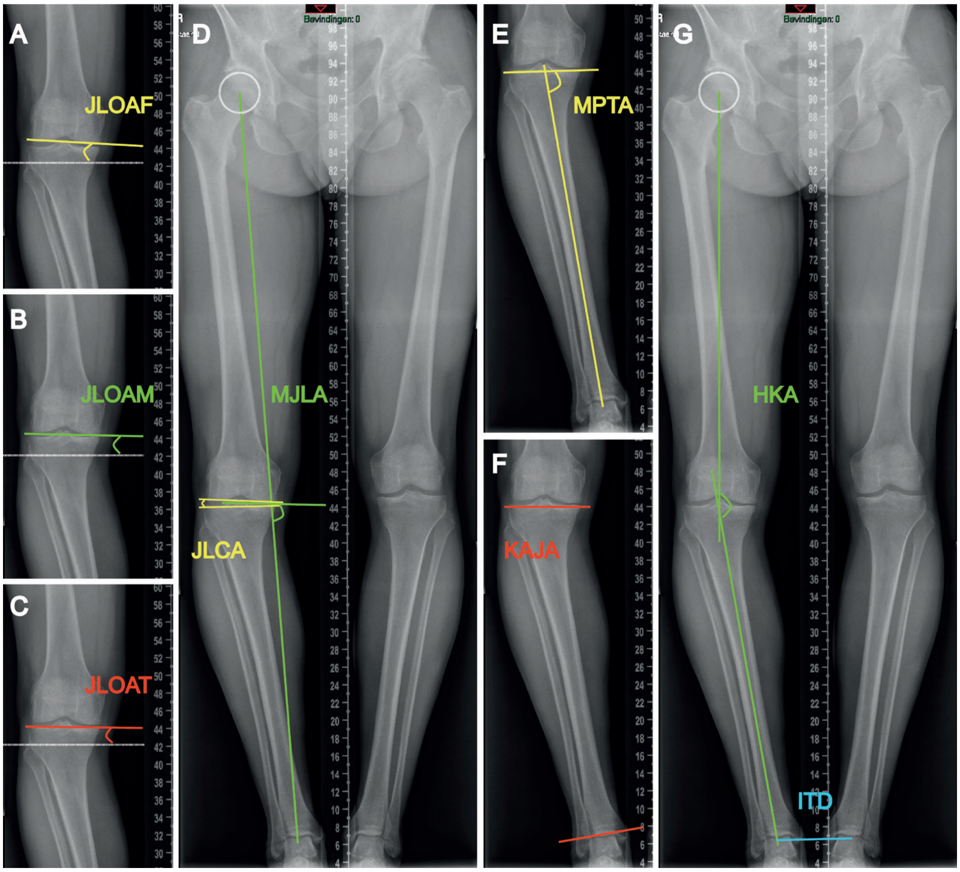

Figure 3. Measurements in anteroposterior long double-leg standing radiograph
Abbreviations: JLOAF, joint line orientation angle with knee joint orientation line of the femoral condyles; JLOAM, joint line orientation angle with knee joint orientation line of the middle knee joint space; JLOAT, joint line orientation angle with knee joint orientation line of the tibial plateau; JLCA, joint line convergence angle; MJLA, Mikulicz joint line angle; MPTA, medial proximal tibial angle; KAJA, knee ankle joint angle; HKA, hip-knee-ankle angle; ITD, intertalar distance.
Note: This radiograph is from the same patient as in **Figure 2**; JLOAF, JLOAM, JLOAT, JLCA, MJLA, MPTA, KAJA, HKA and ITD are measured as -3.81°, -1.48°, -0.58°, 2.39°, 83.66°, 80.69°, -4.73°, 169.03° and 8.42cm, respectively.

Measurement reliability and correlation magnitude

Measurement reliability was graded in accordance with Koo's guideline [23]. The ICCs <0.50, 0.50-0.75, 0.75-0.90, and >0.90 indicated poor, moderate, good, and excellent reliability, respectively. The interpretation of a correlation magnitude was in accordance with Schober's tutorial [24]. Correlation coefficient values of 0.00-0.10, 0.10-0.39, 0.40-0.69, 0.70-0.89, and 0.90-1.00 indicated negligible, weak, moderate, strong, and very strong magnitude, respectively.

Results

Patient characteristics

Patients' age at filming was 49.1±8.3 years (range 24-65). The osteoarthritis grades of the medial knee compartment were Kellgren-Lawrence grade I in 13 knees, grade II in 18 knees, and grade III in 9 knees. Bipedal distance in the long double-leg standing radiographs was 13.89±4.07cm.

Single-leg versus double-leg standing

The KJLO measurements and KJLO-related frontal deformity parameters performed on the single-leg and double-leg standing radiographs are described in **Table 1**. Mean JLOAF differed by 0.88° on long single-leg compared to double-leg standing radiographs, mean JLOAM differed by 1.24°, mean JLOAT by 1.77° , mean MJLA by 0.63°, mean JLCA by 0.85°, and mean HKA differed by 1.11°.

Table 1 Single-leg versus double-leg standing radiograph

	Single-leg standing radiograph		Double-leg standing radiograph		Measurement difference		P-value
Radiological parameters	mean	standard deviation	mean	standard deviation	mean	95% confidence interval	
JLOAF	-1.11°	2.41	-2.00°	2.15	0.88°	0.17° to 1.60°	0.016*
JLOAM	0.76°	2.28	-0.48°	2.00	1.24°	0.52° to 1.95°	0.001*
JLOAT	2.61°	2.60	0.85°	2.20	1.77°	1.12° to 2.41°	<0.001*
MJLA	88.20°	1.75	87.57°	1.80	0.63°	0.37° to 0.88°	<0.001*
MPTA	86.42°	2.49	86.13°	2.55	0.29°	-0.06° to 0.64°	0.1
JLCA	3.49°	1.50	2.64°	1.27	0.85°	0.57° to 1.13°	<0.001*
KAJA	-1.15°	3.59	-1.06°	3.73	-0.09°	-0.63° to 0.46°	0.752
HKA	173.03°	3.07	174.14°	2.94	-1.11°	-1.38° to -0.84°	<0.001*

Statistical significance*
Abbreviations: JLOAF, joint line orientation angle by femoral condyles; JLOAM, joint line orientation angle by middle knee joint space; JLOAT, joint line orientation angle by tibial plateau; MJLA, Mikulicz joint line angle; MPTA, medial proximal tibial angle; JLCA, joint line convergence angle; KAJA, knee ankle joint angle; HKA, hip-knee-ankle angle.

Bipedal distance

The bipedal distance (measured as ITD) in the double-leg standing radiographs and the correlations with the KJLO measurements and KJLO-related frontal deformity parameters are presented in **Table 2**. There were moderate negative correlations between ITD and JLOAF, JLOAM and JLOAT.

Osteoarthritis grade

Osteoarthritis grade (Kellgren-Lawrence I, II, III) and the correlations with the KJLO measurements and KJLO-related frontal deformity parameters are presented in **Table 2**. In single-leg standing radiographs, osteoarthritis grade had weak positive correlation with JLOAT and weak negative correlation with HKA. In double-leg standing radiographs, osteoarthritis grade had weak positive correlations with JLOAT and MJLA and weak negative correlations with JLOAF and HKA. Osteoarthritis grade correlated moderately positively with JLCA in single-leg standing radiographs and in double-leg standing radiographs.

Measurement reliability

Intraobserver and interobserver reliability is described in **Table 3**. All measurements had at least good measurement reliability, with measurements JLOAF, JLOAT, MPTA, HKA and ITD having excellent intraobserver and interobserver reliability.

Table 2 Bipedal distance and osteoarthritis grade

	Bipedal distance		**Osteoarthritis grade**			
	Double-leg standing radiograph		**Single-leg standing radiograph**		**Double-leg standing radiograph**	
Radiological parameters	Coefficient (rp)	p-value	Coefficient (rs)	p-value	Coefficient (rs)	p-value
JLOAF	-0.555	<0.001*	-0.012	0.942	-0.146	0.368
JLOAM	-0.574	<0.001*	0.091	0.575	0.034	0.835
JLOAT	-0.549	<0.001*	0.181	0.264	0.122	0.454
MJLA	-0.002	0.992	0.060	0.714	0.105	0.519
MPTA	0.019	0.908	-0.077	0.637	-0.004	0.980
JLCA	0.062	0.702	0.518	<0.001*	0.471	0.002*
KAJA	0.036	0.826	-0.001	0.994	-0.013	0.937
HKA	0.017	0.915	-0.326	0.040*	-0.316	0.047*

Statistical significance*

Abbreviations: rp, Pearson correlation coefficient; rs, Spearman correlation coefficient; JLOAF, joint line orientation angle by femoral condyles; JLOAM, joint line orientation angle by middle knee joint space; JLOAT, joint line orientation angle by tibial plateau; MJLA, Mikulicz joint line angle; MPTA, medial proximal tibial angle; JLCA, joint line convergence angle; KAJA, knee ankle joint angle; HKA, hip-knee-ankle angle.

Note: Bipedal distance is evaluated by intertalar distance, osteoarthritis grade (I, II, III) is evaluated by Kellgren-Lawrence classification.

Table 3 Measurement reliability

	Intraobserver ICCs	**Interobserver ICCs**
Single-leg standing radiograph		
JLOAF	0.96-0.99 (excellent)	0.93-0.98 (excellent)
JLOAM	0.96-0.99 (excellent)	0.93-0.99 (excellent)
JLOAT	0.97-0.99 (excellent)	0.91-0.98 (excellent)
MJLA	0.94-0.98 (excellent)	0.92-0.98 (excellent)
MPTA	0.96-0.99 (excellent)	0.95-0.99 (excellent)
JLCA	0.92-0.98 (excellent)	0.85-0.96 (good-to-excellent)
KAJA	0.85-0.96 (good to excellent)	0.84-0.95 (good-to-excellent)

Table 3 Continued

	Intraobserver ICCs	Interobserver ICCs
HKA	0.99-1 (excellent)	0.95-0.99 (excellent)
Double-leg standing radiograph		
JLOAF	0.95-0.99 (excellent)	0.91-0.97 (excellent)
JLOAM	0.94-0.98 (excellent)	0.89-0.97 (good-to-excellent)
JLOAT	0.95-0.99 (excellent)	0.93-0.98 (excellent)
MJLA	0.93-0.98 (excellent)	0.88-0.97 (good-to-excellent)
MPTA	0.96-0.99 (excellent)	0.95-0.99 (excellent)
JLCA	0.92-0.98 (excellent)	0.85-0.95 (good-to-excellent)
KAJA	0.90-0.98 (good to excellent)	0.85-0.95 (good-to-excellent)
HKA	0.94-0.98 (excellent)	0.96-0.99 (excellent)
ITD	1 (excellent)	0.99-1 (excellent)

Abbreviations: ICCs, intraclass correlation coefficients; JLOAF, joint line orientation angle by femoral condyles; JLOAM, joint line orientation angle by middle knee joint space; JLOAT, joint line orientation angle by tibial plateau; MJLA, Mikulicz joint line angle; MPTA, medial proximal tibial angle; JLCA, joint line convergence angle; KAJA, knee ankle joint angle; HKA, hip-knee-ankle angle; ITD, intertalar distance.
Note: The ICCs are graded on 95% confidence interval. ICCs <0.50, 0.50-0.75, 0.75-0.90, and >0.90 indicated poor, moderate, good, and excellent reliability, respectively. [23]

Discussion

The main finding of this study is that there is a significant difference in determining KJLO using JLOAF, JLOAM, JLOAT and MJLA between single-leg and double-leg standing radiographs, which is influenced by degree of loading and decreases in the double-leg standing radiograph. An increase in bipedal distance in double-leg standing radiographs results in lower KJLO using JLOAF, JLOAM and JLOAT, and a higher medial knee osteoarthritis grade correlates moderately with a more varus-aligned JLCA.

Among the five KJLO measurement methods and the three KJLO-related frontal deformity parameters, MPTA and KAJA were not influenced by the long single-leg or double-leg standing radiographs used. This is because the measurements of MPTA and KAJA depend on the tibial geometry, which should remain unchanged with the degree of weight-loading adjustment. Our finding on the influences of single-leg and double-leg standing on JLCA and HKA is consistent with previous research, even though there are differences: the present study finds a difference in JLCA of 0.85° and a difference in HKA of 1.11° when determined on single-leg and double-leg standing radiographs in patients with medial knee osteoarthritis (Kellgren-Lawrence I, II, III) and varus alignment, whereas Yazdanpanah et al. [25] report a difference in JLCA of 0.42° JLCA and in HKA of 0.76° in patients with knee osteoarthritis and varus/valgus alignment, and Bardot et al. [26] report a difference in JLCA of 0.8° and in HKA of 1.92° in patients with medial knee osteoarthritis (Ahlbäck grades I, II) and tibial-originating varus deformity.

An increase in bipedal distance results in lower JLOAF, JLOAM and JLOAT in long double-leg standing radiographs. Previous research assessed the JLOAT measurement in long double-leg standing radiographs of patients who underwent total knee replacement, and a change of 3.7° JLOAT per 10-cm bipedal distance was reported [22]. Referencing the ground line during the measurement procedure may be the reason why JLOAF, JLOAM and JLOAT are all affected by bipedal distance in double-leg standing radiographs. Hence for studies that measure JLOAF, JLOAM and JLOAT in double-leg standing radiographs, a feet-together position or a footplate should be used to fix the bipedal distance [19]. The bipedal distance in the double-leg standing radiographs should at least be reported: JLOAM and JLOAT have been used to determine the acceptable KJLO upper limits in other studies [2, 8, 27], but the determined upper limit values may not be accurate as the bipedal distance used at filming was not described in these studies.

Medial knee osteoarthritis grade does not affect KJLO measurements but does influence the KJLO-related frontal deformity parameter of JLCA. Our finding indicates that a higher medial knee osteoarthritis grade (Kellgren-Lawrence I, II, III) moderately relates to a higher magnitude of knee intra-articular varus deformity illustrated by a higher JLCA degree. Also, the present study finds a weak correlation between medial knee osteoarthritis grade and the global deformity parameter of HKA, in contrast to a study on the correlation magnitude: Brouwer et al. [28] assessed the HKA measurement in long double-leg standing radiographs of patients with medial knee osteoarthritis (Ahlbäck grades I, II, III), and reported a strong correlation between osteoarthritis grade and HKA ($r=0.75$). There are differences between the present and previous studies, including patient numbers, osteoarthritis grade classification system used, and whether or not lateral fluoroscopy is used to ensure a 100% anteroposterior projection, which may affect the correlation magnitude of osteoarthritis grade and HKA.

Although all measurements have shown at least good reliability, the reliability of KAJA appears inferior to those radiographic parameters with both excellent intraobserver and interobserver reliability. As a novel radiographic parameter, KAJA is used much less frequently than the other parameters by our observers in daily clinical practice. A reasonable speculation is that a lack of observers' past measurement experience may negatively influence the determined measurement reliability of this novel radiographic parameter.

According to the predefined criteria, MPTA should be the preferable KJLO measurement method, as it has both adequate measurement stability and reliability. JLOAF, JLOAM, JLOAT and MJLA lack measurement stability, which restricts comparison of KJLO measurement results between studies using long single-leg and double-leg standing radiographs. The lack of measurement stability in JLOAF, JLOAM and JLOAT also hampers the acceptable KJLO upper-limit determination in studies using nonstandardised bipedal distance in double-leg standing radiographs. In addition to the predefined criteria, based on our current measurement experience we find that the measurement procedure of MJLA is more complicated and time-consuming than the other four KJLO measurement methods, which also limits the usage of MJLA.

To predict a postoperative suspected excessive KJLO, using KAJA could have more advantages than JLCA and HKA. This is because KAJA can be performed regardless of the long single-leg or double-leg standing radiographs used. Also, KAJA is not affected by osteoarthritis grade. When measuring JLCA and HKA, the long-standing radiograph used should be well-described.

The strength of this study is that the outcome helps fill the knowledge gap on how to assess KJLO and its related frontal deformity using long-standing radiographs. Choosing a measurement method without adequate stability may explain the conflicting evidence on the relation between KJLO and clinical outcomes in literature [2, 9]. We therefore propose a preferable KJLO measurement method that can be used to determine the actual relation between KJLO and clinical outcomes.

As a limitation, although all anteroposterior long-standing radiographs were made with knee in full extension and patella in forward position, the lateral fluoroscopic control that secures a 100% anteroposterior image without rotation was not applied. As a consequence, some rotation variations could be present at filming, which may affect the radiographic measurements in this study.

Conclusion

In long-standing radiographs, measurements of JLOAF, JLOAM, JLOAT, MJLA, JLCA and HKA are all influenced by single-leg/double-leg standing; JLOAF, JLOAM and JLOAT are also affected by bipedal distance in double-leg standing; and JLCA is affected by osteoarthritis grade. Knee joint obliquity as assessed by MPTA measurement is independent of single-leg/double-leg standing, bipedal distance or osteoarthritis grade, and has excellent measurement reliability. We therefore propose MPTA as the preferable KJLO measurement method for clinical practice and future research.

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Part II

Consequences of increased knee joint line obliquity after high tibial osteotomy

Chapter 4

Clinical relevance of joint line obliquity after high tibial osteotomy for medial knee osteoarthritis remains controversial: a systematic review

Tianshun Xie
Reinoud W. Brouwer
Inge van den Akker-Scheek
Hugo C. van der Veen

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Abstract

Purpose

To systematically review the literature on the association between knee joint line obliquity (KJLO) and clinical outcome after high tibial osteotomy (HTO) for medial knee osteoarthritis and summarize the KJLO cut-off value used when studying this association.

Methods

A systematic search was conducted in three databases (PubMed, Embase, and Web of Science) on September 2022, updated on February 2023. Eligible studies describing postoperative KJLO in relation to clinical outcome after HTO for medial knee osteoarthritis were included. Nonpatient studies and conference abstracts without full-text were excluded. Two independent reviewers assessed title, abstract and full-text based on the inclusion and exclusion criteria. The modified Downs and Black checklist was used to assess the methodological quality of each included study.

Results

Of the seventeen studies included, three had good methodological quality, thirteen fair quality, and one had poor quality. Conflicting findings were shown on the associations between postoperative KJLO and patient-reported outcome, medial knee cartilage regeneration, and 10-year surgical survival in sixteen studies. Three good-quality studies found no significant differences in lateral knee cartilage degeneration between postoperative medial proximal tibial angle > 95° and < 95°. Joint line orientation angles by the proximal tibia of 4° and 6°, joint line orientation angle by the middle knee joint space of 5°, medial proximal tibial angles of 95° and 98°, and Mikulicz joint line angle of 94° were KJLO cut-off values used in the included studies.

Conclusion

Based on current evidence, the actual association between postoperative KJLO and clinical consequences after HTO for medial knee osteoarthritis cannot be ascertained. The clinical relevance of joint line obliquity remains controversial.

4

Introduction

As a bony correction technique performed at the proximal tibia, HTO can result in knee joint line obliquity (KJLO) increase, particularly when there is a large correction [1-3]. Different KJLO measurement methods of joint line orientation angle by the femoral condyles (JLOAF), joint line orientation angle by the middle knee joint space (JLOAM), joint line orientation angle by the tibial plateau (JLOAT), medial proximal tibial angle (MPTA), and Mikulicz joint line angle (MJLA) are described in literature **(Figure 1)** [1-4].

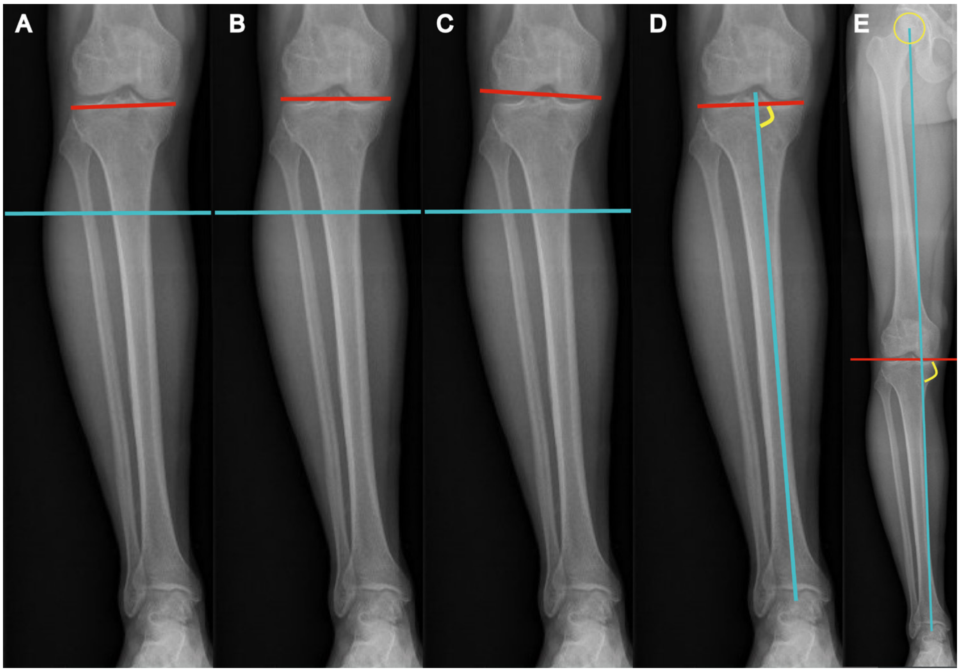

Figure 1. KJLO measurement methods illustrated on anteroposterior long-standing radiograph
A Joint line orientation angle by the tibial plateau (JLOAT) [16]: angle between the proximal tibial line and the ground line; **B** Joint line orientation angle by the middle knee joint space (JLOAM) [2]: angle between the middle knee joint space line and the ground line; **C** Joint line orientation angle by the femoral condyles (JLOAF) [1]: angle between the distal femoral line and the ground line; **D** Medial proximal tibial angle (MPTA) [4]: medial angle between the proximal tibial line and the tibial mechanical axis; **E** Mikulicz joint line angle (MJLA) [4]: medial angle between the middle knee joint space line and the weight-bearing line.

To the best of our knowledge, there is no published consensus on whether to take a suspected excessive postoperative KJLO into consideration during osteotomy planning. Some studies suggest a double-level osteotomy when there is a predicted excessive postoperative KJLO during HTO planning, which involves a postoperative MPTA > 95° [5-7] or a postoperative JLOAT > 6° [8]. Another study suggests that HTO is still justifiable despite a predicted slightly excessive postoperative KJLO [9]. A review of current evidence is therefore necessary, with a focus on associations between postoperative KJLO and patient-reported outcome, status of knee ligament and cartilage, radiological outcomes, surgical survival, and outcome of gait analysis or physical function after HTO. The aim of this paper is to systematically review the literature on the association between KJLO and clinical outcome after HTO for medial knee osteoarthritis and summarize the KJLO cut-off value used when studying this association. We hypothesize that an increase of KJLO after HTO has adverse influences on clinical outcome.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline [10]. The protocol of this review was preregistered in the PROSPERO registry with no. CRD42022359034.

Search strategy

A "PEO" method was used to develop the search strategy for this systematic review [11]. The population (P) was defined as patients who underwent HTO for medial knee osteoarthritis. Exposure (E) was defined as postoperative knee joint line obliquity. Outcome (O) was defined as the association between postoperative KJLO and certain clinical outcomes that include the score on a patient-reported outcome measure, assessment of knee cartilage and ligament status, radiological outcome, outcome of gait analysis or physical function, and surgical survival (revision to knee arthroplasty).

Search strategies used in three databases, PubMed, Embase, and Web of Science, are presented in **Table 1**. Articles were searched from the databases' inception to 14 September 2022, with an updated search on 9 February 2023 for additional articles. No language restriction was used during the search.

Eligibility criteria

Eligible clinical study designs were randomized controlled trials and observational studies including cohort studies, comparative studies, case-control studies and case series (≥10 cases). Clinical studies were included in this review when KJLO was measured and the clinical outcome in relation to this KJLO was reported. Nonpatient studies and conference abstracts without full-text were excluded.

Table 1. Search Strategy

Database	Search String
PubMed	("Osteoarthritis, Knee"[Mesh] OR tibia* [tiab] OR knee [tiab]) AND ("Osteotomy"[Mesh] OR osteotom*[tiab]) AND (joint line obliquit* [tiab] OR joint line orientat* [tiab]) AND (outcom* [tiab] OR scor* [tiab] measur* [tiab] OR funct* [tiab] OR test* [tiab] OR exam* OR ligament* [tiab] OR cartilage [tiab] OR musc* [tiab] OR gait [tiab] OR surviv* [tiab] OR fail* [tiab] OR revis* [tiab] OR radiograph* [tiab] OR radilolog* [tiab] OR parameter [tiab])
Embase	("knee osteoarthritis"/exp OR "tibia*":ab,ti,kw OR knee:ab,ti,kw) AND ("osteotomy"/exp OR "osteotom*":ab,ti,kw) AND ("joint line obliquit*":ab,ti,kw OR "joint line orientat*":ab,ti,kw) AND ("outcom*":ab,ti,kw OR "scor*":ab,ti,kw OR "measur*":ab,ti,kw OR "funct*":ab,ti,kw OR "test*":ab,ti,kw OR "exam*":ab,ti,kw OR "ligament*":ab,ti,kw OR "cartilage*":ab,ti,kw OR "musc*":ab,ti,kw OR "gait*":ab,ti,kw OR "surviv*":ab,ti,kw OR "fail*":ab,ti,kw OR "revis*":ab,ti,kw OR "radiograph*":ab,ti,kw OR "radiolog*":ab,ti,kw OR "parameter":ab,ti,kw)
Web of Science	TS= ("knee" OR "tibia*") AND TS= "osteotom*" AND TS= ("joint line obliquit*" OR "joint line orientat*") AND TS= ("outcom*" OR "scor*" OR "measur*" OR "funct*" OR "test*" OR "exam*" OR "ligament*" OR "cartilage" OR "musc*" OR "gait" OR "surviv*" OR "fail*" OR "revis*" OR "radiograph*" OR "radiolog*" OR "parameter")

Identification of eligible studies

Endnote software (version 20, Clarivate) was used to exclude duplicates. Based on the predefined eligible criteria, two reviewers (TX and HV) independently screened the studies through three ordered rounds: first titles, then abstracts, and last full-texts. Disagreement between two reviewers was resolved by discussion. If no consensus was achieved, a third reviewer was consulted (IA).

Data extraction

One reviewer (TX) extracted the following data from included studies: publication year, study location, study design, included knees, mean patient age, mean follow-up time, HTO technique used, KJLO change after HTO, KJLO cut-off value used, and KJLO-related clinical outcome.

Methodological quality

The modified Downs and Black checklist was used to assess the methodological quality of each included study, with an assessment of study reporting, external and internal validity, and statistical power of patient sample size [12, 13]. Methodological quality was graded by the overall score obtained: excellent (26-28), good (20-25), fair (15-19), and poor (≤ 14) [14, 15]. Two independent reviewers evaluated the methodological quality (TX and HV). Disagreements between the two reviewers were solved by discussion, and a third reviewer was consulted when necessary (IA).

Results

The article selection procedure based on the PRISMA guideline is presented in **Figure 2**. A total of seventeen clinical observational studies were included: thirteen cohort studies, three case series, and one case-control study. Fifteen studies performed medial opening wedge HTO, and two studies performed lateral closing wedge HTO. Article publication years and study locations are specified in **Figure 3**. The extracted information is depicted in **Table 2**.

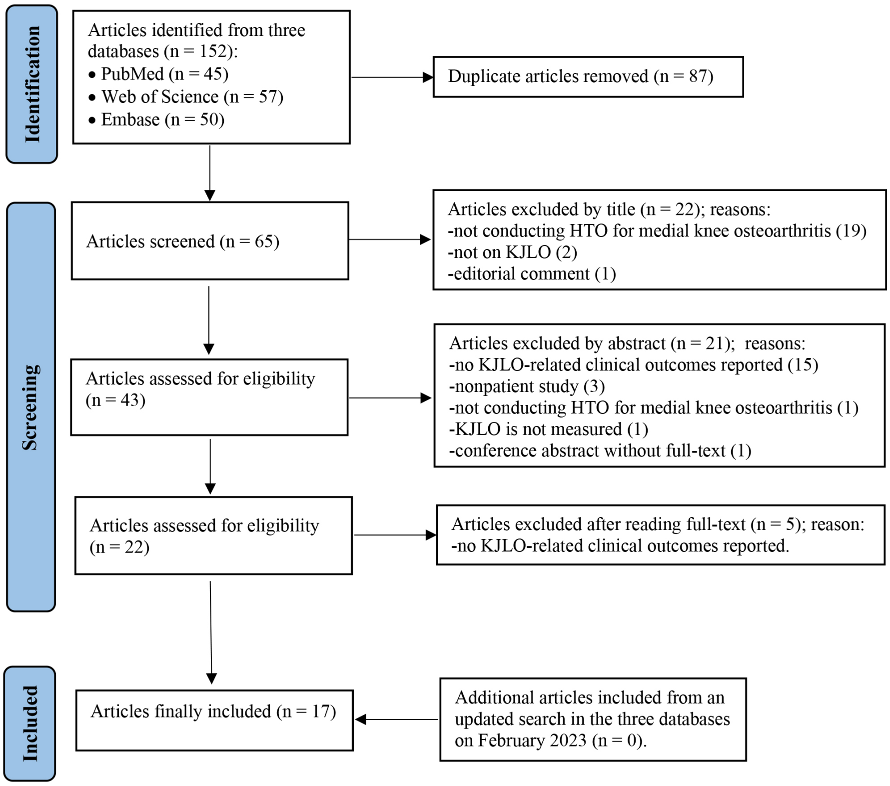

Figure 2. PRISMA flowchart

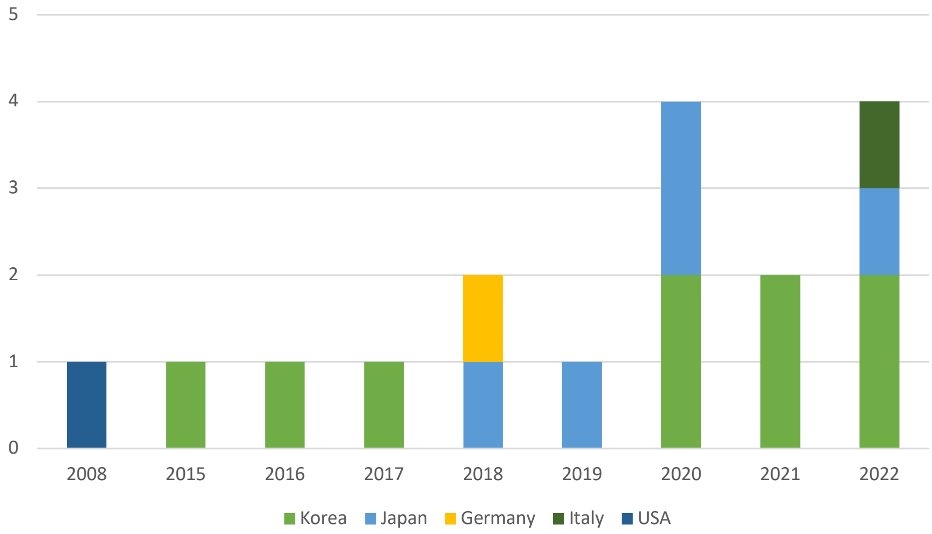

Figure 3. Publication Years and Study Locations

Quality assessment of the included studies

The methodological quality of each included study is presented in **Table 3** [1-4, 6, 8, 9, 16-25]. Three studies were rated as good quality, thirteen as fair quality, and one study as poor quality.

Assessment tools

Patient-reported outcome was assessed by nine different tools in fourteen studies [1, 2, 4, 6, 8, 9, 16, 18, 19, 21-25] (**Table 4**). Knee cartilage was assessed arthroscopically in four studies [1, 9, 17, 22] and by medial joint space width (mJSW) in one study [8].

Table 2. Summary of findings (17 articles)

Author, year (location)	Study design/ Included knees	Patient age/ Follow-up time (means, years)	HTO technique (patient groups)	KJLO change after HTO (means)	KJLO cut-off value used and association between KJLO and clinical outcome after HTO
Babis et al., 2008 (USA) [3]	Case series/36	53.0 / 10.0	LCW HTO	JLOAT (4.17°)	JLOAT postop < 4° is one of the criteria for patients to achieve 10-year surgical survival.
Lee KM et al., 2015 (Korea) [2]	Case control/50	53.0 / 1.0	MOW HTO	JLOAM (4.1°, 0.3°–4.4°)	JLOAM postop is negligibly related to WOMAC and SF-36 (r<0.10).
Oh et al., 2016 (Korea) [16]	Cohort/69	54.4 / 2.5	MOW HTO (JLOAT postop *-4°–4°*, < -4° or > 4°)	JLOAT (2.1°, -0.7°–1.34°)	Between-group: no significant difference in KSS.
Kim CW et al., 2017 (Korea) [17]	Cohort/62	52.3 / (> 2.0)	MOW HTO	JLOAM (-0.4°–3.2°)	JLOAM postop > 5° is one risk factor for inferior medial knee cartilage regeneration.
Akamatsu et al., 2018 (Japan) [1]	Cohort/86	65.3 / 2.0	MOW HTO (MPTA postop > *95°*, ≤ 95°)	JLOAF (*5.0°, 0.7°–5.7°*), (3.4°, -0.1°–3.2°) MPTA (*12.5°, 84.7°–97.5°*), (8.5°, 84.6°–93.2°)	MPTA postop > 95°: inferior KSS (range of motion, alignment) and KOOS (sports and recreation). Between-group: no significant difference in KOOS (pain, symptoms, activities of daily living, quality of life), Lysholm score, lateral knee cartilage degeneration, and medial knee cartilage regeneration.
Schuster et al., 2018 (Germany) [18]	Cohort/79	50.9 / 10.0	MOW HTO (MPTA postop > *95°*, ≤ 95°)	MPTA (84.9°–93.2°)	MPTA postop > 95°: inferior IKDC score. Between-group: no significant difference in surgical survival rate at 10 years.
Goshima et al., 2019 (Japan) [9]	Cohort/94	63.2 / 6.1	MOW HTO (MPTA postop ≥ *95°*, < 95°)	JLOAT (3.7°, -2.3°–1.4°) MPTA (10.4°, 84.1°–94.5°)	Between-group: no significant difference in JOAS, OKS, KOOS, and lateral knee cartilage degeneration and medial knee cartilage regeneration.

Table 2. Continued

Author, year (location)	Study design/ Included knees	Patient age/ Follow-up time (means, years)	HTO technique (patient groups)	KJLO change after HTO (means)	KJLO cut-off value used and association between KJLO and clinical outcome after HTO
Goto N et al., 2020 (Japan) [19]	Cohort/105	61.0 / 10.2	LCW HTO (MPTA postop ≥ *98*°, ≤ 95°)	MPTA postop (96.6°)	Between-group: no significant difference in KSS.
Kim JE et al., 2020 (Korea) [20]	Case series/72	57.1 / 1.6	MOW HTO	JLOAT (0.79°–2.72°)	JLOAT increase is related to anterior cruciate ligament deterioration (odds ratio 1.6).
Kubota et al., 2020 (Japan) [21]	Cohort/68	60.3 / 2.5	MOW HTO	JLOAT (1.1°–2.6°)	JLOAT postop is weakly correlated to KOOS (pain, symptom, activities of daily living, sports and recreation, quality of life) (r = -0.31, -0.23, -0.30, -0.28, -0.21), physical performance of single-leg standing (r = -0.16), isometric muscle strength (quadriceps) (r = -0.12), and negligibly correlated with KSS, physical performance of timed up-and-go, isometric muscle strength (hamstrings) (r < 0.10).
Song et al., 2020 (Korea) [8]	Cohort/109	58.6 / 4.6	MOW HTO	Not mentioned	JLOAT postop ≥ 4° is a significant predictor of inferior KSS. JLOAT postop ≥ 6° is a significant predictor of inferior KSS and medial joint space narrowing .
Kim GW et al., 2021 (Korea) [22]	Cohort/62	(*56.1*, 57.2) / (> 4.0)	MOW HTO (MPTA postop > *95*°, ≤ 95°)	MPTA (*86.8°–96.1°*, 85.8°–90.8°)	MPTA postop > 95°: more patient cases with lateral compartment pain symptom. Between-group: no significant difference in WOMAC, KSS, HSSKS, and lateral knee cartilage degeneration.
Lee SJ et al., 2021 (Korea) [23]	Cohort/87	59.7 / 3.0	MOW HTO	JLOAT (2.10°–3.32°)	JLOAT postop is negligibly related to IKDC score (r < 0.10).
Kawashima et al., (2022 (Japan) [24]	Case series/39	58.3 / 2.5	MOW HTO	JLOAT (3.2°, -0.5°–2.8°)	JLOAT increase is weakly related to KOOS (pain) (r = -0.12).
Kim JS et al., 2022 (Korea) [6]	Cohort/135	(*57.8*, 55.4, **56.5**, 57.5) / 5.6	MOW HTO (MPTA postop *85°– 90°*, 90°– 93°, **93°–95°**, 95°– 102°)	JLOAT (*1.42°*, 1.78°, **1.23°**, 4.08°) MPTA (*5.81°*, 7.31°, **9.05°**, 11.41°)	MPTA postop > 95°: inferior KSS (function) and SF-36. Between-group: no significant difference in WOMAC.

Table 2. Continued

Author, year (location)	Study design/ Included knees	Patient age/ Follow-up time (means, years)	HTO technique (patient groups)	KJLO change after HTO (means)	KJLO cut-off value used and association between KJLO and clinical outcome after HTO
Rosso et al., 2022 (Italy) [4]	Cohort/92	53.5 / 10.8	MOW HTO	MJLA (88.3°–90.6°), MPTA (85.1°–91.5°)	MJLA postop ≥ 94° versus < 94° or MPTA postop ≥ 95° versus <95°: no significant difference in WOMAC and KSS.
Sohn et al., 2022 (Korea) [25]	Cohort/133	56.7 / 1.0	MOW HTO (MPTA postop > *95°*, ≤ *95°*)	JLOAT (*2.9°, 3.5°–6.0°*), (3.0°, 0.7°–3.7°) MPTA (*10.6°, 85.2°–95.8°*), (8.1°, 83.2°–91.3°)	Between-group: no significant difference in WOMAC and KSS.

a *Postoperative (postop); Knee joint line obliquity (KJLO); Medial opening wedge high tibial osteotomy (MOW HTO); Lateral closing wedge high tibial osteotomy (LCW HTO); Medial proximal tibial angle (MPTA); Mikulicz joint line angle (MJLA).*
b *For joint line orientation angles (JLOAF, JLOAM, JLOAT), a positive value (+) indicates a medial opening angle, a negative value (-) indicates a lateral opening angle.*
c *The design of the included study is determined in accordance with the tutorials of Marthes et al.* [53] *and Dekkers et al.* [54].
d *The correlation magnitude is graded by the tutorial of Schroter et al.* [55].
e *P-value <0.05 is considered statistically significant.*
f *Italicized or bolded figures correspond to the same groups in a study.*

Table 3. Methodological quality of included studies by modified Downs and Black checklist

Authors, year	Reporting (top score=11)	External validity (top score=3)	Internal validity (bias) (top score=7)	Internal validity (confounding) (top score=6)	Power (top score=1)	Overall score (top score=28)	Methodological quality grade
Babis et al., 2008 [3]	6	1	4	1	0	12	Poor
Lee KM et al., 2015 [2]	9	2	4	2	1	18	Fair
Oh et al., 2016 [16]	9	2	4	3	1	19	Fair
Kim CW et al., 2017 [17]	8	2	4	3	0	17	Fair
Akamatsu et al., 2018 [1]	10	2	5	4	1	22	Good
Schuster et al., 2018 [18]	8	2	4	2	0	16	Fair
Goshima et al., 2019 [9]	9	2	6	3	1	21	Good
Goto N et al., 2020 [19]	8	1	5	2	0	16	Fair
Kim JE et al., 2020 [20]	8	2	4	3	0	17	Fair
Kubota et al., 2020 [21]	7	2	4	2	0	15	Fair
Song et al., 2020 [8]	9	2	4	2	0	17	Fair
Kim GW et al., 2021 [22]	10	2	6	4	1	23	Good
Lee SJ et al., 2021 [23]	8	2	4	2	0	16	Fair
Kawashima et al., 2022 [24]	8	2	4	3	0	17	Fair
Kim JS et al., 2022 [6]	8	2	5	3	1	19	Fair
Rosso et al., 2022 [4]	10	2	4	3	0	19	Fair
Sohn et al., 2022 [25]	9	2	3	3	0	17	Fair

a *Methodological quality was graded by the overall score: excellent (26-28), good (20-25), fair (15-19), poor (≤14)* [14, 15]

4

Table 4. Tools used for assessing patient-reported outcome

Tools	Used by included studies	Types	Description
Knee Society Score (KSS) [56, 57]	Oh et al., 2016 (old) [16]; Akamatsu et al., 2018 (old) [1]; Goto et al., 2020 (new) [19]; Kubota et al., 2020 (new) [21]; Song et al., 2020 (new) [8]; Kim GW et al., 2021 (old) [22]; Kim JS et al., 2022 (old) [6]; Rosso et al., 2022 (old) [4]; Sohn et al., 2022 (not mentioned) [25].	Knee-specific	Old KSS version: presented in 1989 and updated in 1993 by Dr Insall to assess functional capabilities after knee arthroplasty, including knee score and functional score. New KSS version: presented in 2011 by Dr Scuderi, adding objective components including patient treatment expectations, patient satisfaction, and knee activity level to the old version.
Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [58]	Lee KM et al., 2015 [2]; Kim GW et al., 2021 [22]; Kim JS et al., 2022 [6]; Rosso et al., 2022 [4]; Sohn et al., 2022 [25].	Disease-specific	WOMAC: widely used to assess hip and knee osteoarthritis, including subscales for pain, stiffness, and physical function.
Knee injury and Osteoarthritis Outcome Score (KOOS) [59]	Akamatsu et al., 2018 [1]; Goshima et al., 2019 [9]; Kubota et al., 2020 [21]; Kawashima et al., 2022 [24].	Knee-specific	KOOS: used as an extension of WOMAC, adding new items to WOMAC subscales of pain and stiffness as well as adding two new subscales (sports and recreation, quality of life) to assess knee injury.
International Knee Document Committee (IKDC) subject knee form [60]	Lee SJ et al., 2021 [23]; Schuster et al., 2018 [18].	Knee-specific	IKDC: developed for outcome measures in patients with knee impairments from ligament/meniscus injury, cartilage lesion and patellofemoral osteoarthritis, including symptoms, sports activity, knee function, and daily living activity assessment.
Short-Form 36 (SF-36) [61]	Lee KM et al., 2015 [2]; Kim JS et al., 2022 [6].	Generic	SF-36: a 36-item form widely used to assess health-related quality of life, including both physical and psychological outcome measures.
Hospital for Special Surgery Knee Score (HSSKS) [62]	Kim GW et al., 2021 [22]	Knee-specific	HSSKS: designed to assess knee symptoms and function after knee arthroplasty.
Japanese Orthopaedic Association Score (JOAS) [63]	Goshima et al., 2019 [9]	Knee-specific	JOAS: used to assess knee function after knee surgery, including pain, function, range of motion, deformity degree, and activities of daily living.
Lysholm Score [64]	Akamatsu et al., 2018 [1]	Knee-specific	Lysholm score: designed for outcome measures in patients after knee ligament injuries.
Oxford Knee Score (OKS) [65]	Goshima et al., 2019 [9]	Knee-specific	OKS: designed for outcome measures in patients after knee arthroplasty with 12 simple questions, including pain, symptoms, and assessment of daily functioning.

Patient-reported outcome

Of the eight included studies assessing the association between postoperative MPTA and postoperative patient-reported outcome, one good-quality study showed inferior Knee injury and Osteoarthritis Outcome Score (KOOS) (sports and recreation) [1], and two fair-quality studies showed inferior Knee Society Score (KSS) (function), Short-Form 36 (SF-36), and International Knee Document Committee (IKDC) scores [6, 18] when postoperative MPTA was > 95°. Two good-quality studies and two fair-quality studies presented no significant differences in KOOS, KSS, Western Ontario and McMaster Universities Osteoarthritis Index score, Japanese Orthopaedic Association Score, Oxford Knee Score, and Hospital for Special Surgery Knee Score between postoperative MPTA > 95° and < 95° [4, 9, 22, 25], and one fair-quality study presented no significant difference in KSS between postoperative MPTA ≥ 98° and ≤ 95° [19].

Out of five fair-quality included studies assessing the association between postoperative JLOAT and postoperative patient-reported outcome, one study showed that postoperative JLOAT ≥ 4° and ≥ 6° were both significant predictors for inferior KSS [8]; another study presented no significant difference in KSS between postoperative JLOAT > 4° and < 4° [16]. A third study stated that postoperative JLOAT was weakly negatively correlated with KOOS and negligibly correlated with KSS [21]; a fourth study showed negligible correlation between postoperative JLOAT and IKDC score [23]. The last of these studies showed weak negative correlation between JLOAT increase post-HTO and postoperative KOOS (pain) [24].

Knee Cartilage

Three good-quality studies showed no significant difference arthroscopically in medial knee cartilage regeneration and lateral knee cartilage degeneration post-HTO between postoperative MPTA > 95° and < 95° [1, 9, 22]. One fair-quality study showed arthroscopically that postoperative JLOAM > 5° was one of the risk factors leading to inferior medial knee cartilage regeneration [17]. Another fair-quality study showed that postoperative JLOAT ≥ 6° was a significant predictor of mJSW narrowing, as assessed by a Rosenberg view X-ray [8].

Surgical survival

One fair-quality study showed no significant difference in 10-year surgical survival rate between postoperative MPTA > 95° and ≤ 95° [18]. One poor-quality study showed that a postoperative JLOAT < 4° was one of the criteria for achieving 10-year surgical survival after HTO [3].

Discussion

The most important finding of this review is that there is conflicting evidence on the associations between postoperative KJLO and patient-reported outcome, knee cartilage regeneration, and 10-year surgical survival. Six different KJLO cut-off values are used when studying these associations. Only three of the seventeen included studies meet the criteria of good methodological quality.

The evidence about the association between postoperative KJLO and patient-reported outcome after HTO is conflicting, due to the presence of both supportive and opposite findings on whether a suspected excessive postoperative KJLO is significantly related to an inferior patient-reported outcome. Regarding the supportive findings [1, 6, 8, 18], the patient-reported outcome difference between suspected excessive postoperative KJLO and normal postoperative KJLO also exceeds the published minimal clinically important difference of the assessment tool used [26-30]. A possible explanation for the current conflicting findings could be that most included studies do not properly match the covariates that can affect postoperative patient-reported outcomes when comparing between suspected excessive postoperative KJLO and normal postoperative KJLO patient groups. This can involve covariates such as patient age, gender, body mass index, preoperative patient-reported outcome, degree of preoperative varus alignment, amount of correction, and postoperative follow-up time [31-34]. In one study the between-group covariate matching is incorporated into the study design using the propensity score-matching method [22], yet some important covariates such as preoperative patient-reported outcome and amount of correction are not used for propensity score-matching. Some supportive findings should be re-interpreted: Kubota et al. [21] concluded there was a significant correlation between postoperative KJLO and postoperative KOOS (pain, activity daily living, sports and recreation), as the p-value was < 0.05; however, the correlation coefficient magnitude between postoperative KJLO and the postoperative subscales can be classified as weak, which should be the main outcome rather than whether the correlation is significant or not. Future research should have a better consideration of the covariates that can affect postoperative patient-reported outcome.

The association between postoperative KJLO and medial knee cartilage regeneration after HTO is conflicting, and postoperative KJLO seems not to affect lateral knee cartilage deterioration. A finite element analysis study reported that excessive KJLO (MPTA > 95°) could result in a rapid increase of shear stress in the knee joint [7]. In vitro research shows that abnormal shear stress could induce inflammation and apoptosis of chondrocytes [35-37], decreasing chondrocyte viability [38]; this may negatively influence cartilage status. However, the above finite element analysis and in vitro findings can only be partially confirmed in clinical research. When comparing between patients with postoperative

MPTA > 95° and < 95°, there is no significant difference arthroscopically in medial knee cartilage regeneration and lateral knee cartilage degeneration at mean follow-ups at 1/1.5 years [1, 9, 22]. However, JLOAM > 5° is one of the arthroscopic risk factors for inferior medial knee cartilage regeneration at mean follow-up of 1.9 years, along with the other risk factors which include preoperative severe knee osteoarthritis and a medial knee cartilage bipolar lesion [17]. This conflicting finding may be due to the difference in KJLO measurement method and cut-off value used, as well as the time interval between HTO and follow-up arthroscopy, where a longer time interval benefits medial cartilage regeneration [1, 39]. Also, the difference of lateral knee cartilage degeneration between excessive and normal postoperative KJLO may be evident in a long-term follow-up [1, 9, 22]. Furthermore, a previous study used mJSW on X-ray to assess medial knee cartilage and concluded that JLOAT ≥ 6° was a significant predictor of mJSW narrowing after HTO [8]. However, what the mJSW truly represents remains controversial in recent studies: One study reported that mJSW correlated moderately with knee cartilage thickness on magnetic resonance imaging (MRI) [40], whereas another study reported that mJSW change after HTO reflected the weight-bearing line ratio change on X-ray instead of cartilage regeneration arthroscopically [41]. It is therefore better to use MRI or arthroscopy than mJSW to assess knee cartilage status.

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The evidence for the association between suspected excessive postoperative KJLO and long-term surgical survival (revision to knee arthroplasty) after HTO is conflicting. To achieve 10-year surgical survival after HTO, one study stated that patients should have postoperative JLOAT < 4°, postoperative 0–6° valgus alignment, and adequate medial knee loading [3]. Another study found no significant difference in 10-year surgical survival rate between postoperative MPTA > 95° and ≤ 95° patient groups [18]; however, whether between-group covariates were taken into account is not specified. Covariates of patient age, knee cartilage condition, preoperative knee osteoarthritis severity, and postoperative alignment could all affect long-term surgical survival after HTO [42, 43], which may further influence such between-group surgical survival comparisons and the conclusions. Furthermore, although longer operation time has already been described for total knee arthroplasty following HTO than primary arthroplasty [44], an excessive KJLO after HTO might further increase technical challenges when there is a need of conversion to total knee arthroplasty, such as difficulties in restoring soft tissue and ligament balance, joint line height, and mechanics and kinematics of tibiofemoral and patellofemoral joints. In some cases, a stemmed augmented tibial component may be required. Computer assisted three-dimensional planning and simulation may help overcome these difficulties.

There is limited clinical evidence that a KJLO increase after HTO negatively influences the anterior cruciate ligament (ACL), as shown by MRI and arthroscopy in one fair-quality study [20]. Possibly explaining this finding, a previous cadaver study reported that KJLO increase is significantly related to femorotibial subluxation [45]; Ogawa et al. [46, 47] discussed that an abnormal femorotibial subluxation might escalate ligament tension, which might result in ACL deterioration. Not only KJLO increases but also the post-HTO posterior tibial slope increase is found to be related to ACL deterioration [20]. The tibial slope may play a more prominent role than KJLO on ACL status by influencing the ligament strain and laxity in the sagittal plane [48]. Future research could focus on how much KJLO increase is acceptable after HTO.

There is limited clinical evidence that postoperative KJLO is only weakly/negligibly correlated with postoperative physical performance (single-leg standing/timed up-and-go) and isometric muscle strength (quadriceps/hamstrings) after HTO. As discussed by Kubota et al. [21], the two physical performance tests used are too easy for patients to accomplish after HTO, which might be a reason for the weak/negligible correlation determined. A high-demand physical performance test focusing on medial knee loading might result in a better correlation. A previous study reported that postoperative KJLO can affect knee adduction moment after total knee arthroplasty [49], where the knee adduction moment during gait indicates the medial knee contact pressure [50]. Moreover, each HTO-operated patient can present a difference in preoperative KJLO, correction magnitude for targeted alignment, and preoperative physical performance and muscle strength. The influence of KJLO increase after HTO on physical performance test outcomes that determine knee loading should be investigated in future research.
As mentioned in the Introduction concerning the excessive KJLO problem after HTO, double-level osteotomy is suggested when there is a predicted postoperative MPTA > 95° or JLOAT > 6° [5-8]. Yet again, whether a postoperative MPTA > 95° is associated with inferior clinical outcome after HTO remains uncertain. Also, the proposed 6° JLOAT might not be accurately measured, as the JLOAT measurement can be affected by single-leg and double-leg standing as well as by the bipedal distance used at filming [51, 52]; the patient's standing position is not well described in the study that proposes a JLOAT of 6° as acceptable KJLO upper limit [8]. According to the present review's findings, no postoperative KJLO cut-off value is sufficiently supported for clinical usage.

A limitation is that, due to the large variabilities in KJLO measurement methods, KJLO cut-off values, and clinical outcome assessment tools used in the included studies, a meta-analysis could not be performed. Also, there is a lack of the literature regarding the clinical effects of KJLO after double-level osteotomy and varus-producing HTO.

The strength of this systematic review lies in its investigation of the association between postoperative KJLO and clinical outcome, providing a summary of current knowledge for orthopaedic surgeons who perform HTO procedures and are concerned about postoperative KJLO. This review revealed the need of unified KJLO measurement methods and adequate covariate control for future research when assessing the association between postoperative KJLO measurements and clinical outcome.

Conclusion

Due to the conflicting and limited evidence, the actual association between postoperative KJLO and clinical consequences after HTO for medial knee osteoarthritis cannot be ascertained. The clinical relevance of KJLO after HTO remains controversial.

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Chapter 5

Joint line obliquity after lateral closing-wedge high tibial osteotomy does not adversely affect clinical and radiological outcome: a 5-year follow-up study

Tianshun Xie
Maarten R. Huizinga
Inge van den Akker-Scheek
Hugo C. van der Veen
Reinoud W. Brouwer

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Abstract

Purpose

To analyze the association between change in knee joint line obliquity (KJLO) and patient-reported outcome, radiological progression of osteoarthritis, and surgical survival after lateral closing-wedge high tibial osteotomy (HTO).

Methods

A cohort of 180 patients treated in one single hospital with lateral closing-wedge HTO was examined. KJLO was defined by the medial proximal tibial angle (MPTA). To assess the association between KJLO and patient-reported outcome, radiological progression of osteoarthritis, and surgical survival, patient groups were defined: I, postoperative MPTA <95.0°; II, postoperative MPTA ≥95.0°; A, MPTA change <8.0°; B, MPTA change ≥8.0°. Propensity score matching was used for between-group (I and II, A and B) covariates matching, including age, gender, preoperative lower limb alignment, preoperative medial joint space width (mJSW), preoperative Western Ontario and McMaster Universities osteoarthritis Index (WOMAC) score, wedge size, and postoperative follow-up time. Patient-reported outcome was assessed by the WOMAC questionnaire, radiological progression of osteoarthritis by mJSW and Kellgren-Lawrence (KL) grade progression (≥1) preoperatively and at follow-ups (>2 years). Failure was defined as revision HTO or conversion to knee arthroplasty.

Results

After propensity score matching, groups I and II contained 58 pairs of patients and groups A and B contained 50 pairs. There were no significant differences in postoperative WOMAC score or surgical failure rate between groups I and II or between groups A and B (p>0.05). However, the postoperative mJSW was significantly lower in group I than group II (3.2±1.6mm vs 3.9±1.8mm; p=0.018) and in group A than group B (3.0±1.7mm vs 3.7±1.5mm; p=0.040). KL grade progression rate was significantly higher in group I than group II (53.4% vs 29.3%; p=0.008) and in group A than group B (56.0% vs 28.0%; p=0.005).

Conclusion

Increased KJLO (postoperative MPTA ≥95.0°) or MPTA change≥8.0° after lateral closing-wedge HTO does not adversely affect patient-reported outcome, radiological progression of osteoarthritis, or surgical survival at an average 5-year follow-up.

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Introduction

High tibial osteotomy (HTO) realigns the weight-bearing axis in the lower limb, providing a treatment option for medial knee osteoarthritis associated with varus alignment [1]. Two essential techniques are typically used: medial opening-wedge and lateral closing-wedge HTO [2]. However, every HTO creates a change in knee joint line obliquity (KJLO), and the medial proximal tibial angle (MPTA) can be used to describe the KJLO [3-5].

There is controversial evidence on the association between postoperative KJLO and patient-reported outcomes following medial opening-wedge HTO. Some studies suggest inferior postoperative patient-reported outcomes with an excessive postoperative KJLO [4, 6, 7], and other studies have found no significant difference in postoperative patient-reported outcomes between excessive and normal postoperative KJLO [5, 8, 9]. Additionally, limited research has explored this relationship after a lateral closing-wedge HTO.

Understanding the link between the change in KJLO and patient-reported outcome, radiological progression of osteoarthritis, and surgical survival is necessary when selecting the appropriate knee osteotomy to treat varus medial knee osteoarthritis. Some studies suggest a double-level osteotomy when a valgus-producing HTO is predicted to result in a postoperative MPTA exceeding 95° [4, 10]. However, this recommendation may not be warranted given the current controversy surrounding the association between postoperative KJLO and patient-reported outcomes. There is limited evidence on the associations between postoperative KJLO and radiological progression of osteoarthritis and surgical survival after HTO, highlighting the need for further research in this area.
The purpose of this study is to analyze the associations between change in KJLO and patient-reported outcome, radiological progression of osteoarthritis, and surgical survival after lateral closing-wedge HTO. Our hypothesis is that patients with excessive postoperative KJLO after lateral closing-wedge HTO will present poorer patient-reported outcomes and higher rates of radiological osteoarthritis progression and surgical failure compared to those with normal postoperative KJLO.

Methods

Study design

A secondary analysis of patient data from another paper was conducted [11], screening 298 patients undergoing lateral closing-wedge HTO to treat symptomatic medial knee osteoarthritis with varus alignment. Patients were excluded if they (1) did not complete the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire at postoperative follow-ups (>2 years), (2) did not have preoperative or postoperative anteroposterior long-standing radiographs, or (3) had a postoperative anteroposterior long-standing radiograph filmed, but the film time was not within 6-18 months after HTO. After applying these exclusion criteria, a total of 180 patients were included in the analyses.

This study design followed the statement of STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) for cohort studies [12] and was approved by the ethics committee of our hospital (MEC no. 2022-005).

Lateral closing-wedge HTO

The lateral closing-wedge HTO was performed by a single experienced knee surgeon (RWB), in accordance with the procedure described by Huizinga et al. [11] and van Raaij et al. [13]. The procedure involved making an incision from the tibial tuberosity to the posterior aspect of the fibular head, exposing and snaring the common peroneal nerve, resecting the anterior part of the proximal fibular head, and removing the tibial wedge using a calibrated saw guide (Allopro instrument; Zimmer, Winterthur, Switzerland). Lower limb alignment was then corrected, and the osteotomy was fixated with two staples, accompanied by an anterior compartment fasciotomy. The preoperative planning only focused on the hip-knee-ankle angle (HKA) with the goal of achieving a 4-degree valgus alignment [14]. The mechanical lateral distal femoral angle (mLDFA) and MPTA were not considered in the surgical planning for determining the osteotomy type.

Patient-reported outcome

Patient-reported outcome was evaluated by the WOMAC score including three subscales (pain, stiffness, physical function) [15]. The WOMAC is a disease-specific questionnaire, commonly used to assess pain, stiffness, and physical function in knee osteoarthritis patients and in patients after knee surgery [16, 17]. The WOMAC score was completed preoperatively and at postoperative follow-ups (>2 years).

Radiological measurements

Radiological measurements are illustrated in **Figure 1**. The KJLO was defined by the medial proximal tibial angle (MPTA), which is the medial angle between the line tangential to the tibial plateau surface and the tibial mechanical axis [5]. Medial joint space width (mJSW) was measured by the minimum interbone distance between the medial tibial plateau and the medial femoral condyle [18]. HKA was measured by the angle between the femoral mechanical axis and the tibial mechanical axis [19]. The mLDFA was measured by the lateral angle between the tangential line of the femoral condyles and the femoral mechanical axis [20]. Joint line convergence angle (JLCA) was measured by the angle between the tangential line of the femoral condyles and the tangential line of the tibial plateau [20]. Wedge size was obtained by targeting the lower limb mechanical axis at one-third of the lateral knee compartment (4° valgus HKA). The Kellgren and Lawrence (KL) classification was used to grade knee osteoarthritis severity, with four ordinal grades: 1 (doubtful), 2 (mild), 3 (moderate), 4 (severe) [21, 22]. The mJSW and the KL grade progression (≥1) were used to evaluate radiological progression of medial knee osteoarthritis [23].

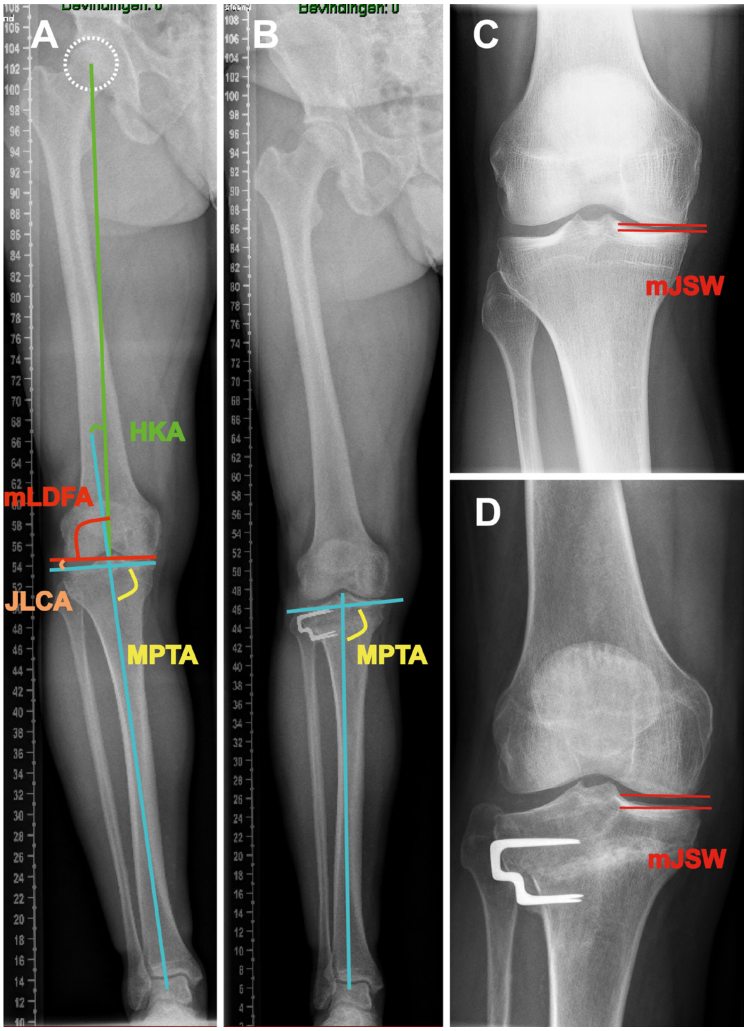

Figure 1. Illustration of radiological measurements
Note: HKA, hip-knee-ankle angle; MPTA, medial proximal tibial angle; mLDFA, mechanical lateral distal femoral angle; JLCA, joint line convergence angle; mJSW, medial joint space width.

Anteroposterior double-leg standing radiographs were used to assess MPTA, HKA, mLDFA, JLCA and wedge size, and anteroposterior short knee standing radiographs were used to assess mJSW and KL grade. Patients were positioned with full knee extension and patellar forward during filming. Preoperative and postoperative MPTA, preoperative and postoperative mLDFA, preoperative and postoperative JLCA, and postoperative HKA were measured (TX), and their reliabilities were assessed by two observers (TX, RWB) in 40 patient cases from that patient database, with a three-week interval. The intraobserver and interobserver intraclass correlation coefficients of MPTA, mLDFA, JLCA and HKA were at least good (>0.75) [24, 25]. Preoperative HKA and wedge size were obtained during planning of lateral closing-wedge HTO (MH). The preoperative and postoperative mJSW and KL grade were obtained by two orthopaedic surgeons who were blinded to the patient's clinical status using paired reading and sequence-known method [11]. The picture archiving and communication system (Philips Vue, N.V.) was used for radiological measurement, with a minimal determination of 0.01° angle and 0.1 mm distance.

Surgical Failure

Surgical failure was defined as the need for revision HTO or conversion to knee arthroplasty by the time of postoperative follow-up.

Patient grouping and propensity score matching

Included patients were categorized into two groups based on MPTA cut-off points of postoperative 95° and change of 8°, respectively. These cut-off points were determined from previous biomechanical research, indicating significant shear stress increase and contact stress redistribution beyond these values [10, 26]. Group I: postoperative MPTA <95.0°; II: postoperative MPTA ≥95.0°. Group A: MPTA change<8.0°; B: MPTA change≥8.0°. The propensity score matching (PSM) method was used to match the covariates between groups I and II and between groups A and B. The present study defined covariates as patient age at surgery, gender, preoperative HKA, preoperative mJSW, preoperative WOMAC (pain, stiffness, and physical function subscores, and total score), wedge size, and postoperative follow-up time [27-30].

Sample size calculation

The minimal clinically important difference of WOMAC (a total score difference of 16.1 points) was used to calculate the required sample size [17]. Forty-four patients were needed in each patient group to obtain an effect size of 0.80, an alpha of 0.05, and a power of 0.95 as determined by the Mann-Whitney U test (G*Power software version 3.1.9.7).

Statistical analysis

SPSS software (version 25) was used for statistical analysis. Distribution of continuous data was checked using the Shapiro-Wilk test and Q-Q plot. PSM was performed with a match tolerance of 0.02. Pearson chi-square tests were used for between-group comparison of gender and KL grade progression (≥1). Fisher's exact test was used for between-group comparison of surgical revision rates. Independent t-tests were used for between-group comparison of parametric continuous data (postoperative mJSW and mJSW change), and Mann-Whitney U tests for between-group comparison of non-parametric continuous data (age at surgery, preoperative and postoperative HKA, preoperative and postoperative MPTA, preoperative and postoperative mLDFA, preoperative and postoperative JLCA, preoperative and postoperative WOMAC scores, wedge size, and postoperative follow-up time) and ordinal data (preoperative and postoperative KL grade). The WOMAC score was transformed to a 0-100-point scale where 0 indicates the best possible outcome. A $p<0.05$ was considered statistically significant.

Results

Patient selection process is depicted in **Figure 2**. The baseline characteristic of included patients is presented in **Table 1**. Of the 180 patients included, postoperative MPTA ranges from 86.1° to 103.1° and MPTA change ranges from 1.4° to 15.3°.

After PSM, 58 pairs of patients were in groups I (postoperative MPTA <95.0°) and II (postoperative MPTA ≥95.0°), and 50 pairs were in groups A (MPTA change <8.0°) and B (MPTA change ≥8.0°). The covariates were matched between groups I and II (**Table 2**) and between groups A and B (**Table 3**). Comparison of patient-reported outcome, radiological progression of osteoarthritis, and surgical failure rate between groups I and II and between groups A and B are presented in **Table 4**.

There were no significant differences in postoperative WOMAC or surgical failure rate between groups I and II or between groups A and B. Postoperative mJSW was significantly lower in group I than group II, and in group A than group B. Rate of KL grade progression (≥1) was significantly higher in group I than group II, and in group A than group B.

Table 1. Baseline characteristics before propensity score matching

Patient baseline characteristics	
Total number of patients	180
Age at surgery, years	51.5±7.6 (24 to 69)
Gender, Male/Female, n (%)	122/58 (68% / 32%)
Operated side, Left/Right, n (%)	94/86 (52% / 48%)
Preoperative hip-knee-ankle angle, degrees	5.5±2.4 (1 to 14)
Preoperative medial proximal tibial angle, degrees	87.3±2.3 (79 to 92)
Wedge size, degrees	9.5±2.1 (3 to 6)

Note: Data are shown as mean ± standard deviation (range) unless indicated otherwise.

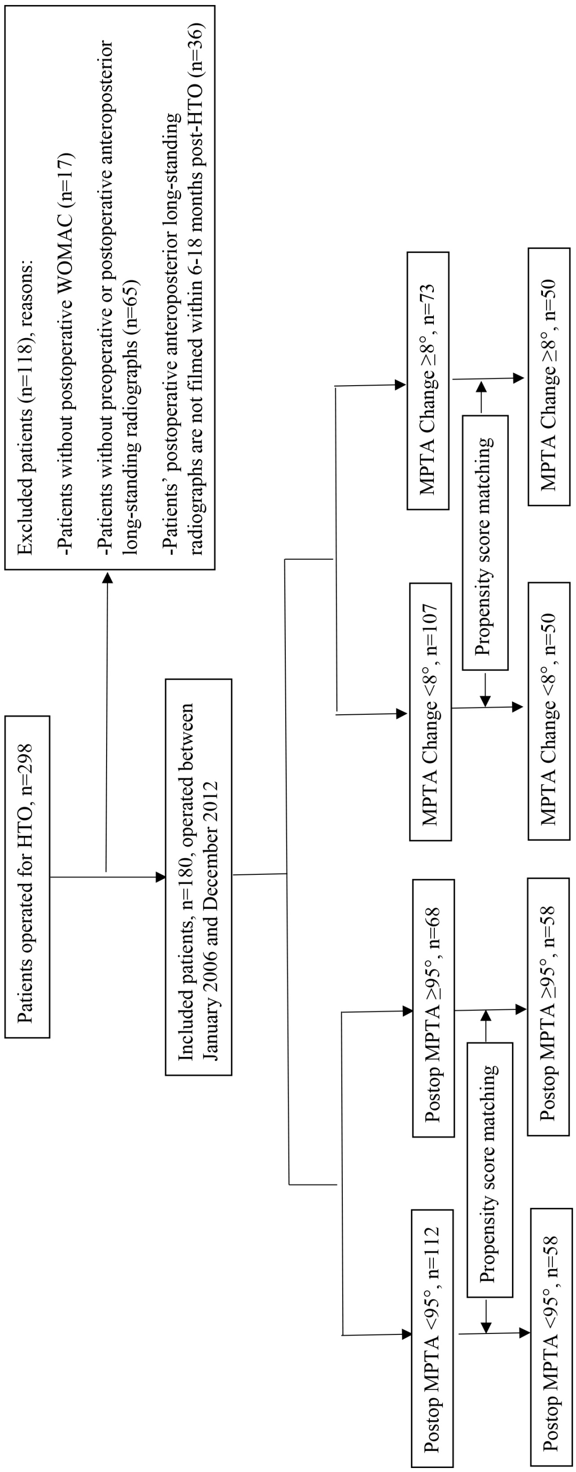

Figure 2. Patient selection process

Table 2. Propensity score matching between groups I and II

Covariates	Before propensity score matching			After propensity score matching		
	Group I (Postoperative MPTA <95°)	Group II (Postoperative MPTA ≥95°)	P-value	Group I (Postoperative MPTA <95°)	Group II (Postoperative MPTA ≥95°)	P-value
Age at surgery, years	51.0±7.8	52.2±7.3	0.344 M	52.3±7.8	52.0±7.6	0.875 M
Gender (M/F)	79/33	43/25	0.310 C	40/18	41/17	0.840 C
Preoperative HKA, degrees	5.4±2.4	5.7±2.5	0.305 M	5.6±2.2	5.5±2.5	0.819 M
Preoperative mJSW, mm	3.5±1.5	3.3±1.6	0.353 I	3.4±1.5	3.5±1.6	0.747 I
Preoperative WOMAC Pain subscore	52.1±16.3	57.2±15.9	0.025* M	55.5±16.5	55.5±16.3	0.863 M
Preoperative WOMAC Stiffness subscore	48.8±20.7	52.4±17.3	0.176 M	50.4±22.8	51.1±17.1	0.826 M
Preoperative WOMAC Physical function subscore	46.8±17.1	51.3±17.2	0.076 M	50.6±18.1	49.4±17.2	0.623 M
Preoperative WOMAC Total score	48.1±16.2	52.6±15.9	0.069 M	51.6±17.3	50.8±16.0	0.689 M
Wedge size, degrees	9.2±2.0	9.9±2.2	0.058 M	9.6±1.9	9.7±2.2	0.995 M
Postoperative follow-up time, years	5.1±1.8	5.2±1.8	0.827 M	5.4±1.8	5.2±1.8	0.490 M

Note: Data are shown as mean ± standard deviation.
MPTA, medial proximal tibial angle; HKA, hip-knee-ankle angle; mJSW, medial joint space width; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
M Mann-Whitney U test; I Independent t-test; C Pearson chi-square test. *Statistical significance.

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Table 3. Propensity score matching between groups A and B

Covariates	Before propensity score matching			After propensity score matching		
	Group A (MPTA Change <8°)	Group B (MPTA Change ≥8°)	P-value	Group A (MPTA Change <8°)	Group B (MPTA Change ≥8°)	P-value
Age at surgery, years	51.3±7.9	51.7±7.2	0.911 M	51.4±6.8	51.8±6.7	0.959 M
Gender (M/F)	73/34	49/24	0.877 C	34/16	32/18	0.673 C
Preoperative HKA, degrees	4.7±2.0	6.7±2.4	<0.001* M	5.7±1.6	5.6±1.7	0.653 M
Preoperative mJSW, mm	3.6±1.5	3.3±1.5	0.150 I	3.2±1.6	3.3±1.3	0.740 I
Preoperative WOMAC Pain subscore	54.3±14.9	53.8±18.2	0.858 M	55.1±14.8	54.9±20.1	0.862 M
Preoperative WOMAC Stiffness subscore	51.2±19.0	48.6±20.3	0.425 M	51.3±19.1	51.0±20.5	0.955 M
Preoperative WOMAC Physical function subscore	48.9±16.6	47.9±18.2	0.700 M	50.0±17.3	50.2±19.2	0.953 M
Preoperative WOMAC Total score	50.2±15.5	49.2±17.3	0.596 M	51.1±16.0	51.2±18.6	0.896 M
Wedge size, degrees	8.7±1.8	10.6±2.0	<0.001* M	9.7±1.6	9.6±1.5	0.713 M
Postoperative follow-up time, years	5.3±1.8	4.9±1.7	0.123 M	5.3±1.8	4.9±1.8	0.311 M

Note: Data are shown as mean ± standard deviation.
MPTA, medial proximal tibial angle; HKA, hip-knee-ankle angle; mJSW, medial joint space width; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
M Mann-Whitney U test; I Independent t-test; C Pearson chi-square test. * Statistical significance.

Table 4. Between-group comparison after propensity score matching

Measurements and outcomes	Group Ⅰ (Postoperative MPTA <95°)	Group Ⅱ (Postoperative MPTA ≥95°)	P-value	Group A (MPTA Change <8°)	Group B (MPTA Change ≥8°)	P-value
Postoperative HKA, degrees	-1.4±3.2	-5.2±2.1	<0.001* M	-0.8±3.2	-4.9±2.4	<0.001* M
Preoperative mLDFA, degrees	88.6±1.9	89.8±1.8	<0.001* M	89.0±1.9	89.1±2.5	0.454 M
Postoperative mLDFA, degrees	88.6±2.0	89.4±1.7	0.088 M	88.9±2.1	88.8±2.2	0.901 M
Preoperative JLCA, degrees	2.9±1.3	3.0±1.5	0.763 M	3.3±1.5	3.0±1.5	0.438 M
Postoperative JLCA, degrees	2.6±1.4	2.4±1.5	0.534 M	2.9±1.6	2.5±1.3	0.279 M
Preoperative MPTA, degrees	86.6±2.2	88.4±2.0	<0.001* M	87.3±2.1	87.0±2.5	0.343 M
Postoperative MPTA, degrees	92.5±2.0	97.2±1.9	<0.001* M	92.4±2.4	96.4±2.7	<0.001* M
MPTA Change, degrees	5.8±2.8	8.8±2.2	<0.001* M	5.1±1.8	9.4±1.1	<0.001* M
Postoperative WOMAC Pain subscore	24.9±18.5	20.2±20.0	0.103 M	26.0±18.7	19.9±17.3	0.078 M
Postoperative WOMAC Stiffness subscore	30.4±22.0	27.6±21.3	0.554 M	31.5±21.9	30.8±22.3	0.785 M
Postoperative WOMAC Physical function subscore	25.0±20.0	19.2±17.2	0.123 M	25.3±19.4	21.6±18.8	0.381 M
Postoperative WOMAC Total Score	25.4±19.1	20.1±17.4	0.103 M	25.9±18.7	22.0±18.2	0.284 M
Postoperative mJSW, mm	3.2±1.6	3.9±1.8	0.018* I	3.0±1.7	3.7±1.5	0.040* I
mJSW Change, mm	-0.2±1.1	0.4±1.3	0.005* I	-0.2±1.4	0.4±1.1	0.025* I
Preoperative KL grades 1/2/3/4, n (%)	18/32/7/1 (31.0/55.2/12.1/1.7)	27/18/11/2 (46.6/31.0/19.0/3.4)	0.462 M	13/27/8/2 (26.0/54.0/16.0/4.0)	17/23/10/0 (34.0/46.0/20.0/0.0)	0.499 M
Postoperative KL grades 1/2/3/4, n (%)	7/24/25/2 (12.1/41.4/43.1/3.4)	17/23/14/4 (29.3/39.7/24.1/6.9)	0.041* M	6/14/25/5 (12.0/28.0/50.0/10.0)	9/25/15/1 (18.0/50.0/30.0/2.0)	0.007* M

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Table 4. Continued

Measurements and outcomes	Group I (Postoperative MPTA <95°)	Group II (Postoperative MPTA ≥95°)	P-value	Group A (MPTA Change <8°)	Group B (MPTA Change ≥8°)	P-value
KL grade progression (≥1), n (%)	31 (53.4)	17 (29.3)	0.008* C	28 (56.0)	14 (28.0)	0.005* C
Surgical failure, n(%)	2 (3.4)	0 (0)	0.496 F	2 (4.0)	0 (0)	0.495 F

Notes: Data are shown as mean ± standard deviation; Measurement change = postoperative measurement – preoperative measurement.

The two patients who had surgical failure are the same individuals in both groups I and A: one had revision to lateral closing-wedge HTO due to reoccurrence of painful varus malalignment at 4.7 years postoperative follow-up, the other had conversion to total knee arthroplasty due to reoccurrence of medial knee pain (morbid obesity patient, BMI 51) at 4.3 years postoperative follow-up.

MPTA, medial proximal tibial angle; HKA, hip-knee-ankle angle; mLDFA, mechanical lateral distal femoral angle; JLCA, joint line convergence angle; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; mJSW, medial joint space width; KL, Kellgren-Lawrence.

A positive value of the HKA indicates a varus alignment, while a negative value indicates a valgus alignment.
M Mann-Whitney U test; I Independent t-test; C Pearson chi-square test; F Fisher's exact test is used if >20% of the expected frequencies < 5. * Statistically significant.

Discussion

The most important finding is that an increased KJLO (postoperative MPTA ≥95.0°) or MPTA change ≥8.0° does not have a negative impact on patient-reported outcome and surgical survival after an average follow-up of 5 years. Furthermore, this increase appears to slow down radiological progression of medial knee osteoarthritis. These findings reject our hypothesis.

It was previously investigated that increased KJLO causes unfavourable biomechanical changes. A finite element analysis study reported that MPTA >95° can result in a rapid shear stress rise at the tibial plateau surface [10]. According to the result of a 10-case cadaveric study, a significant increase of contact stress at the medial spine and lateral meniscus is observed when there is an 8° KJLO increase in lateral direction (from 1° to 9° laterally) at both 0° and 20° knee flexion [26]. However, these biomechanical changes did not negatively influence the clinical and radiological results in our patient group 5 years after lateral closing-wedge HTO. A possible explanation is that these biomechanical changes may not be the primary determinants of the clinical and radiological outcomes, and the follow-up length we used may not be long enough to fully observe the effects on these outcomes.

Besides MPTA, other angles are used to assess KJLO, such as joint line orientation angles and the Mikulicz joint line angle [5, 6, 31, 32]. In the present study, MPTA was used, as it is independent of factors such as osteoarthritis grade, single-leg/double-leg standing position, and stance width during radiograph filming, making it the preferred choice over the other angles [25].

The present study demonstrates that the increased KJLO does not affect patient-reported outcome. This finding aligns with previous studies that used similar but different questionnaires with varying follow-up lengths post-HTO, finding no significant differences in outcomes when comparing patients with postoperative MPTA <95° and >95°: Sohn et al. [9] used WOMAC and the knee society score (KSS) with 1-year follow-up; Kim GW et al. [33] used the WOMAC, KSS, and Hospital for Special Surgery knee-rating score with >4 years follow-up; Goshima et al. [8] used the Japanese the orthopaedic association score, Oxford knee score, and Knee injury and Osteoarthritis Outcome Score (KOOS) with mean postoperative follow-up of 6.1 years; and Rosso et al. [5] used the WOMAC and KSS with mean follow-up of 10 years. By contrast, other studies report inferior outcomes that surpass the minimal clinically important difference of the questionnaire when postoperative MPTA >95°, including Akamatsu et al. [6] with KSS and KOOS at 2-year follow-up, Kim JS et al. [4] with KSS and Short-Form 36 at a mean follow-up of 5.6 years, and Schuster et al. [7] with the International Knee Document Committee subjective knee score at a mean follow-up of 10 years. The present study distinguishes itself by the use of the PSM method to match covariates one-on-one, with a consideration of various covariates that may affect patient-reported outcome measures. Moreover, these studies all investigate medial opening-wedge HTO, whereas the present study analyses lateral closing-wedge HTO. There are biomechanical differences between postoperative medial opening-wedge and lateral closing-wedge HTOs, such as knee-loading distribution [34], which might contribute to the reported variations in postoperative patient-reported outcome measures.

Patients with increased KJLO appear to maintain the mJSW at follow-ups. It has been reported that mJSW can continuously increase up to 3 years post-HTO [35]. However, the clinical interpretation of mJSW is still under debate. Some suggest it reflects the thickness of the medial knee cartilage [18, 36] or the status of the medial meniscus [37, 38]. The mJSW narrowing is often used to evaluate medial knee osteoarthritis progression [23, 39], whereas post-HTO changes in mJSW may be linked to the weight-bearing line ratio [40, 41]. A lateral closing-wedge HTO causes lateral defect laxity due to a decrease in the height of the lateral tibial plateau. This defect laxity, along with the postoperative valgus alignment, contributes to the increased KJLO. One possible explanation for our results is that patient with a higher increase in KJLO has a more valgus postoperative HKA, along with more significant tibial bony valgisation and increased lateral defect laxity following a lateral closing-wedge HTO, which in turn results in a larger opening of the medial knee compartment. Limited evidence is published on the association between MPTA and mJSW. One study reported that 1° MPTA decrease can significantly increase the odds of mJSW narrowing by 21% in medial knee osteoarthritis patients with a 2-year follow-up [42]; another reported no significant difference in postoperative MPTA (92.7° vs 91.9°) between patients with increased mJSW and decreased mJSW (0.8 mm vs -0.5 mm) three years following medial opening-wedge HTO [35]. A medial opening-wedge HTO can increase medial collateral ligament strain, potentially affecting mJSW if no release technique is used [43-45]. By contrast, a lateral closing-wedge HTO has minimal impact on the medial collateral ligament [45]. Future studies should investigate the long-term impact of increased KJLO on lateral cartilage and meniscus status post-HTO.

The absence of mJSW narrowing in patients with increased KJLO, as observed in our study, may explain their lower rate of KL grade progression in the medial knee compartment. However, it is important to note that the evaluation of KL grade and mJSW is based on radiographs, which is not an ideal imaging modality for assessing osteoarthritis progression and cartilage thickness. Hence, future studies using magnetic resonance imaging (MRI) or arthroscopy after a long-term follow-up post-HTO are warranted to confirm these findings.

Another important finding of our study is that KJLO increase does not affect surgical failure rate after HTO. Only one other study compared the rate of revision to knee arthroplasty between postoperative MPTA ≤95° and >95° following medial opening-wedge HTO, finding no significant difference over an average 10-year follow-up [7]. Another study found that a postoperative MPTA ≥95° can help prevent recurrent varus malalignment following a valgus-producing HTO, as observed at short-term follow-up of 1 year [46]. Likewise, in the present study, surgical failure in one of the two revised patients with MPTA <95° was due to the reoccurrence of painful varus malalignment. Future studies may explore the impact of increased KJLO on conversion to total knee arthroplasty following a failed HTO, including surgical complexity and choice of tibial component.

To achieve a targeted alignment and prevent under-correction after a valgus-producing HTO, a large postoperative KJLO may be predicted during surgical planning, but lowering it down to the normal range (MPTA, 85°-90°) can be challenging [20]. Based on the present finding, 95° MPTA may not be a strict cut-off point that indicates a double-level osteotomy, and a MPTA change >8° post-HTO also appears tolerable. Notably, our results do not imply that the postoperative KJLO can be entirely disregarded during HTO planning, as an increase in KJLO can have other negative impacts on gait pattern and knee kinematics [47, 48].

The strength of this study lies in its contribution towards filling the knowledge gap regarding the influences of KJLO on outcomes after a lateral closing-wedge HTO. We used a reliable KJLO measurement method and utilized the PSM method to minimize the influence of unmatched covariates on comparing outcomes. Besides the postoperative KJLO, we also examined the effects of KJLO change.

As a retrospective study, limitations include insufficient assessment of the effects of increased KJLO on knee cartilage and meniscus status. Since mJSW is an indirect indicator for assessing medial knee cartilage and meniscus status, and given the controversy surrounding what it actually represents, MRI or arthroscopy would be more suitable modalities for this assessment. Also, obesity might have negative effects on outcomes and can lead to early HTO failure; however, the data of patient body mass index at surgery was incomplete and could not be used in the analyses.

Conclusion

Increased KJLO (postoperative MPTA ≥95.0°) or MPTA change ≥8.0° after lateral closing-wedge HTO does not adversely affect patient-reported outcome, radiological progression of osteoarthritis, or surgical survival at an average 5-year follow-up. The decision to choose a double-level osteotomy over HTO should not be exclusively based on a predicted increase in KJLO (postoperative MPTA≥95.0°) at planning.

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Chapter 6

Increased joint line obliquity after lateral closing-wedge high tibial osteotomy does not influence survivorship

Tianshun Xie
Astrid J. de Vries
Hugo C. van der Veen
Reinoud W. Brouwer

This Chapter has been submitted

Abstract

Background

Although high tibial osteotomy (HTO) emerges as a powerful intervention for treating symptomatic medial osteoarthritis and varus malalignment, it results in an increase in knee joint line obliquity (KJLO) in the frontal plane. Limited current evidence hinders understanding the impact of increased KJLO on HTO survivorship.

Purpose

To investigate the influence of KJLO and other potential risk factors on the survivorship of lateral closing-wedge HTO.

Methods

Patients with symptomatic medial knee osteoarthritis and varus malalignment operated by lateral closing-wedge HTO at a single hospital were screened with a minimum follow-up of 5 years. HTO survival rate was assessed by Kaplan-Meier survival analysis. The influence of postoperative increased KJLO (medial proximal tibial angle, MPTA ≥ 95°), age (≥55 years), gender (female), preoperative malalignment (hip-knee-ankle angle, HKA ≥10° varus), postoperative untargeted alignment (HKA <2° or >6° valgus), and preoperative osteoarthritis severity (Kellgren-Lawrence grade ≥ III) on survivorship of HTO was evaluated by Cox regression analysis. A failure of HTO was defined as a conversion to total knee arthroplasty.

Results

410 patients (463 knees) were included, with a mean follow-up of 13.0 years (range: 5.0 to 18.1 years) and a mean survival time of 11.2 years (range: 1.2 to 18.1 years). HTO survival rates at postoperative 5, 10, and 15 years were 91%, 78%, and 60%, respectively. Multivariate Cox regression showed that female gender (hazard ratio = 2.0; $p<0.001$) and postoperative untargeted alignment (HKA <2° or >6° valgus) (hazard ratio = 1.6; $p = 0.003$) were risk factors for a conversion to total knee arthroplasty.

Conclusion

Increased postoperative KJLO (MPTA ≥ 95°) has no significant influence on the survivorship of lateral closing-wedge HTO. Males demonstrate superior survival outcomes than females, and it is important to achieve a targeted postoperative alignment (HKA 2°-6° valgus) for ensuring favourable HTO survivorship.

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Introduction

High tibial osteotomy (HTO) proves to be a powerful intervention for managing patients with symptomatic medial knee osteoarthritis by realigning lower limb malalignment [1]. Despite initial efficacy, the enduring effectiveness of HTO experiences a gradual decline over time [2]. In cases where HTO fails, a total knee arthroplasty (TKA) presents itself as an alternative treatment option [3].

An increased knee joint line obliquity (KJLO) has raised concerns following a valgus-producing HTO, potentially leading to biomechanical consequences of increased shear stress and an abnormal redistribution of contact stress within the knee joint [4, 5]. The medial proximal tibial angle (MPTA) has been identified as a preferable method for assessing KJLO due to its demonstrated measurement stability and reliability [6]. An MPTA exceeding 95° postoperatively is generally considered as an excessively increased KJLO after HTO [4]. The actual impact of postoperative increased KJLO on HTO survivorship remains a topic of debate, with limited and controversial evidence published to date [7].

Pape et al. [8] outlined the ideal indication for a valgus-producing HTO: patients with medial uni-compartmental osteoarthritis, aged younger than 55 years old, and a preoperative varus malalignment less than 10°. Hui et al. [9] reported poorer HTO survival with higher TKA transition risk for patients aged over 50 years compared to those below 50. Hence, it is intriguing to explore the potential impact of age and preoperative varus malignment on the survivorship of HTO, utilizing specified cut-off values. Moreover, as a hip-knee-ankle angle (HKA) within the range of valgus 2°-6° has been considered as the targeted alignment for lateral closing-wedge HTO [10-12], investigating the potential impact of a correction falling outside this targeted alignment range on the survival rate of HTO holds clinical significance, addressing a notable knowledge gap. Additionally, an advanced preoperative medial knee osteoarthritis grade (≥ III) has been reported to be associated with an increased risk of a conversion to TKA after HTO by previous research [13]. Furthermore, a previous study suggested a higher risk of TKA conversion in females after HTO [14], while others found no gender difference [13, 15], making the role of gender controversial in this context.

The primary purpose of this study is to investigate the influence of increased postoperative KJLO (MPTA ≥ 95°) on the survivorship of lateral closing-wedge HTO. The secondary purpose is to examine the effects of age, gender, perioperative HKA, and preoperative osteoarthritis severity on the survivorship. We hypothesize that an excessively increased postoperative KJLO has a negative influence on survivorship of lateral closing-wedge HTO.

Materials and methods

Study design

This retrospective cohort study was conducted within one major teaching hospital located in the northern part of the Netherlands. The study design adhered to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guideline [16]. This study has been approved by the local ethical committee (MEC nr. 2023-105).

Patients

Patients with symptomatic medial knee osteoarthritis and varus malalignment operated by lateral closing-wedge HTO at a single hospital were screened. The HTO was performed between January 1, 2003, and August 3, 2018. The medical records and radiographs of these patients were reviewed. Last follow-ups were conducted via outpatient clinic visits (part of usual care) or either via mails or telephone calls in 2023. All HTOs were performed by experienced knee surgeons in our orthopaedics department.

Inclusion and exclusion criteria

Patients were eligible for inclusion if they met the following criteria: (1) had undergone lateral closing-wedge HTO for treating symptomatic medial knee osteoarthritis with varus malalignment, and (2) had anteroposterior long-standing and short-standing radiographs, as well as lateral radiographs, taken before and after HTO, and (3) had a follow-up duration ≥ 5 years after HTO.

Patients were excluded if they: (1) had undergone osteotomy for medial knee osteoarthritis other than lateral closing-wedge HTO, such as medial opening-wedge HTO, combined-wedge HTO, or double-level osteotomy, or (2) had congenital deformity, a history of lower limb fractures or trauma surgery that could affect the radiological measurements, or (3) were deceased, refused to participate in this cohort study, or were lost to our last follow-ups due to non-response to mails or telephone calls.

Surgical technique

A lateral closing-wedge HTO was performed as described by van Raaij et al. [17]. After a transverse incision and safeguarding the common peroneal nerve, the anterior proximal tibia-fibular syndesmosis was resected and the tibial wedge was removed using a calibrated guide. The osteotomy was stabilized with two staples, accompanied by a fasciotomy of the anterior compartment. The correction target was to attain a 4-degree valgus alignment after HTO [18].

Radiological measurements

Anteroposterior long-standing radiographs were used to measure MPTA and HKA

(Figure 1), while anteroposterior short knee standing radiographs were used to assess Kellgren-Lawrence (KL) grades. The knee was positioned in full extension and patellar facing forward during filming.

KJLO was assessed by the MPTA, which was the medial angle between mechanical axis of the tibia and the tangential line of the tibial plateau [6]. HKA was the angle formed by the mechanical axes of the femur and tibia [19]. In this study, a positive value signified a varus alignment, while a negative value indicated a valgus alignment. Excellent intra- and inter- observer measurement reliabilities (intraclass correlation coefficients >0.9) were observed in both MPTA and HKA [6]. KL grades were employed to assess medial knee osteoarthritis severity before HTO, with four ordinal grades: I for doubtful, II for mild, III for moderate, and IV for severe [20].

Grouping and definition

Eligible patients were categorized based on different factors, including postoperative KJLO (MPTA<95°, ≥95°), age at HTO (<55, ≥55 years), gender (male, female), preoperative malalignment (HKA<10° varus, HKA≥10° varus), postoperative alignment (HKA 2°-6° valgus, HKA <2° or >6° valgus), and preoperative osteoarthritis severity (KL grade <III, ≥III).

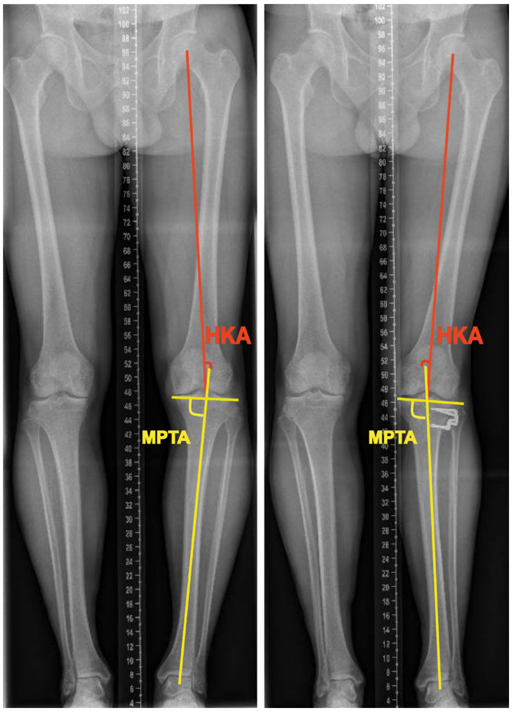

Figure 1. Illustration of radiological parameters
HKA Hip-knee-ankle angle; *MPTA* Medial proximal tibial angle.

A HTO failure was defined as a conversion to TKA. The HTO survival time was calculated as the duration from date of HTO to either the date of a conversion to TKA or the last follow-up date. The postoperative complications were defined as adverse events or unintended outcomes associated with HTO.

Statistical analysis
SPSS software (version 25) was used for statistical analysis. Distribution of continuous data was checked with the Shapiro-Wilk test and Q-Q plot. The univariate and multivariate Cox regression were used to generate hazards ratio (HR) and their corresponding 95% confidence intervals for potential risk factors, including postoperative KJLO (MPTA<95°, ≥95°), age (<55, ≥55), gender (male, female), preoperative alignment (HKA<10° varus, HKA ≥10° varus), postoperative alignment (HKA 2°- 6° valgus, HKA<2° or >6° valgus), and preoperative osteoarthritis severity (KL grade <III, ≥III). The Kaplan-Meier analysis was used for determining the survival rate at 5, 10, and 15 years, postoperatively. Continuous data were reported as mean ± standard deviation, and categorical data were presented as numbers and frequencies. A p-value less than 0.05 signified statistical significance.

Results

The patient selection process is illustrated in **Figure 2**. After applying the predefined inclusion and exclusion criteria, a total of 410 patients with 463 knees were included. Patient baseline characteristics were described in **Table 1**. The mean patient age at the time of HTO was 52.1±7.5 years old. At the last follow-up, a total of 159 knees (34%) received a conversion to TKA. The mean HTO survival time was 11.2±4.1 years, ranging from 1.2 to 18.1 years. The follow-up length after HTO was 13.0±3.2 years, ranging from 5.0 to 18.1 years. The HTO survivorship assessed by Kaplan-Meier analysis is shown in **Figure 3,** with survival rates of 91.1%, 77.9%, and 59.7% at 5, 10, and 15 years, respectively. The complication rate following HTO is 3.3%, as presented in **Table 2**.

The influences of potential risk factors on HTO survivorship analysed by univariate and multivariate Cox regression model is shown in **Table 3**.

In both univariate and multivariate Cox regression, the postoperative increased KJLO (MPTA ≥95°) was not associated with a conversion to TKA following HTO (p>0.05), whereas the female gender (HR=1.9 and 2.0, respectively; p<0.001) and postoperative untargeted alignment (HKA<2° or >6° valgus) (HR=1.7 and 1.6, respectively; p<0.01) were significant risk factors for a conversion to TKA following HTO.

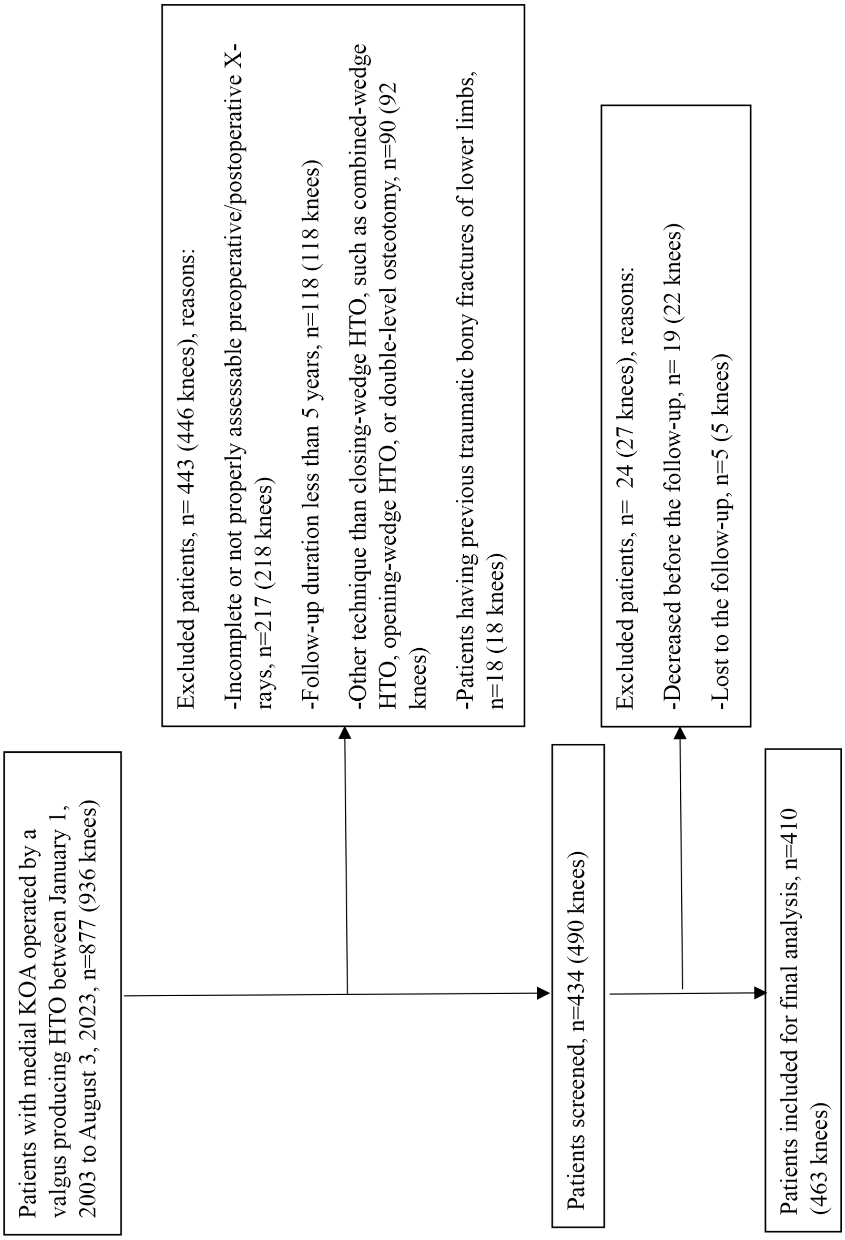

Figure 2. Flowchart of patient selection process

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Table 1. Patient characteristics before and after HTO

Included Knees	463
Age at HTO, years	52.1±7.5
Gender, male/female, n (%)	298 (64)/165 (36)
Operated side, left/right, n (%)	238 (51)/225 (49)
Preoperative HKA, degrees	5.1±2.5
Postoperative HKA, degrees	-2.4±3.5
Preoperative MPTA, degrees	86.9±2.2
Postoperative MPTA, degrees	94.0±3.3
Preoperative KL grades (I/ II/ III/ IV) (%)	18/382/58/5 (4/82/13/1)

a Data are shown as mean±standard deviation (range) unless indicated otherwise.
[b] *HTO,* high tibial osteotomy*; HKA,* hip-knee-ankle angle*; MPTA,* medial proximal tibial angle*; KL,* Kellgren-Lawrence*; TKA,* total knee arthroplasty.

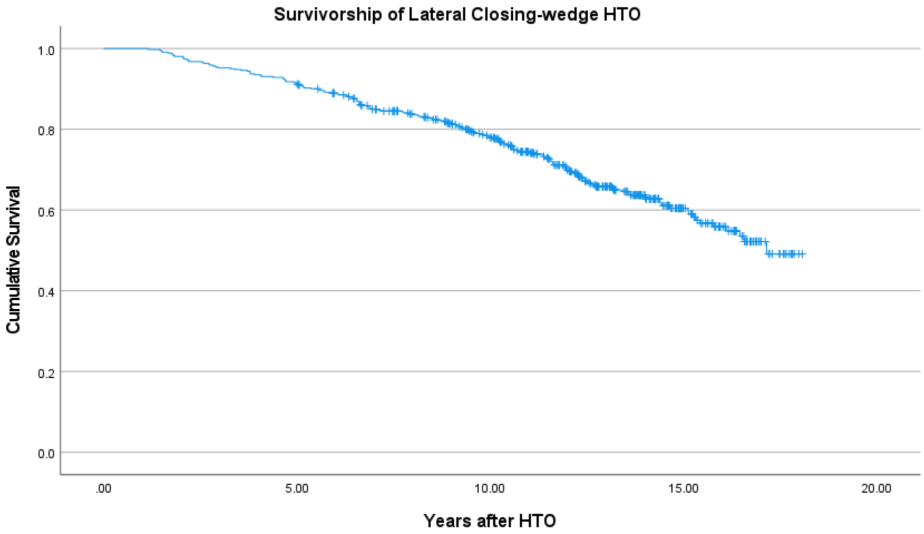

Figure 3. Kaplan-Meier survival analysis for 463 patients following lateral closing-wedge high tibial osteotomy (HTO)

Table 2. Complications after HTO

Complication	Number of cases (percentage)
Re-surgery for recurrent of varus malalignment	9 (1.9%)
Non-union	2 (0.4%)
Delayed union	2 (0.4%)
Deep Venous Thrombosis	2 (0.4%)
Compartment syndrome	1 (0.2%)
Total	16 (3.3%)

a A re-surgery denotes either a reoperated high tibial osteotomy (HTO) or conversion to total knee arthroplasty.

Table 3. Influences of factors on a conversion to TKA after HTO using univariate and multivariate Cox regression

Factors	Category	Number	5-year Survival (%)	10-year Survival (%)	15-year Survival (%)	Hazard ratio		95% confidence interval of hazard ratio		p-value	
						Univariate regression	Multivariate regression	Univariate regression	Multivariate regression	Univariate regression	Multivariate regression
Postoperative MPTA, degrees	<95	285	90.2	76.9	56.2	0.8	0.8	0.5-1.1	0.6-1.1	0.111	0.148
	≥95	178	92.7	79.6	64.2						
Age at HTO, years	<55	268	92.2	80.9	61.1	1.2	1.3	0.9-1.6	0.9-1.7	0.250	0.158
	≥55	195	89.7	73.9	55.7						
Gender	Male	298	94.6	82.7	65.9	1.9	2.0	1.4-2.6	1.5-2.8	<0.001*	<0.001*
	Female	165	84.8	69.6	46.8						
Preoperative HKA, degrees	<10 varus	449	91.1	78.2	60.8	1.9	2.0	0.9-3.8	1.0-4.1	0.087	0.065
	≥10 varus	14	85.7	70.7	34.4						
Postoperative HKA, degrees	2-6 valgus	229	95.6	83.1	68.3	1.7	1.6	1.3-2.4	1.2-2.3	<0.001*	0.003*
	<2 valgus or >6 valgus	234	86.3	72.9	51.3						
Preoperative KL grade	< III	400	92.0	78.9	61.2	1.5	1.4	1.0-2.3	0.9-2.2	0.059	0.099
	≥ III	63	85.7	69.9	48.1						

a *HTO*, high tibial osteotomy; *TKA*, total knee arthroplasty; *HKA*, hip-knee-ankle angle; *MPTA*, medial proximal tibial angle; *KL*, Kellgren-Lawrence.
b The hazard ratio is calculated relative to the first category in each variable.

In both univariate and multivariate Cox regression, age at HTO (≥55), preoperative malalignment (HKA≥10° varus), and preoperative medial knee osteoarthritis severity (KL grade ≥ III) were not associated with a conversion to TKA following HTO ($p>0.05$).

Discussion

The most important finding of this study is that an excessively increased postoperative KJLO (MPTA≥95°) does not influence the survivorship of lateral closing-wedge HTO. Female gender and postoperative untargeted alignment (HKA<2° or >6° valgus) were significant risk factors associated with a conversion to TKA following HTO. The present finding rejects our hypothesis that an excessively increased KJLO has a negatively influence on survivorship of lateral closing-wedge HTO.

Although an excessively increased KJLO following HTO has been related to abnormal biomechanical effects such as shear stress increase and contact loading redistribution [4, 5], this increased KJLO does not affect the survivorship of a lateral closing-wedge HTO. Babis et al. [21] found that a postoperative KJLO (measured by joint line orientation angle) below 4° was associated with an improved 10-year survival rate of lateral closing-wedge HTO in 10 knees. However, this joint line orientation angle is influenced by the filming technique used (single-leg/double-leg standing, feet distance), which is proven not to be an ideal method for assessing KJLO [6]. Schuster et al. [22] found no significant difference in 10-year survival rate of medial opening-wedge HTO, when comparing between postop-MPTA≤95° and >95° (64 versus 15 patients). Xie et al. [19] found no significant difference in 5-year survival rate of lateral closing-wedge HTO, when comparing postop-MPTA<95° and ≥95° (58 patients in each group). However, the above studies were constrained by their inclusion of a limited number of patients and the absence of a regression model for survival analysis. Furthermore, it is important to recognize biomechanical differences between closing-wedge and opening-wedge HTOs [23], as the former creating lateral defect laxity that may affect HTO survival [19]. Notably, while previous KJLO studies mostly focus on medial opening-wedge HTO [7], our study highlights no influence of increased KJLO on survival after lateral closing-wedge HTO.

The present study demonstrates that female gender and an untargeted postoperative alignment (HKA<2° or >6° valgus) are risk factors associated with deteriorated survivorship of lateral closing-wedge HTO. Our finding aligns with the discovery of van Raaij et al. [14], indicating that female patients undergoing lateral closing-wedge HTO exhibit inferior survival rates compared to their male counterparts (100 cases, mean follow-up of 12 years). The observed between-gender difference may be attributed to hormonal variations, with higher testosterone levels in males potentially enhancing muscle strength and overall joint stability, resulting in improved post-HTO survival. Whereas Efe et al. [13] (199 cases, mean follow-up of 10 years) and Michaela et al. [15] (134 cases, mean follow-up of 12 years) did not identify a survival difference between males and females in HTO. Jin et al. [24] identified that a postoperative HKA <0°, indicating an under-correction, was associated with HTO failure necessitating conversion to TKA. Both our study and Jin et al. [24]'s study underscore the importance of achieving a targeted postoperative valgus alignment in HTO.

Our study found that the age ≥55, preoperative HKA ≥10° varus, and preoperative KL grade ≥ III were not significantly associated with HTO survival. This finding aligns with Michaela et al.'s conclusion [15], suggesting that the preoperative HKA varus degree is not associated with survival of lateral closing-wedge HTO. This implies that HTO prioritizes correcting varus alignment for a specific postoperative alignment, emphasizing the critical role of successful correction over the initial varus degree. However, it is important to note that our study has an imbalance in patient numbers between groups, with 454 patients in preoperative HKA <10° group and only 15 patients in the ≥10° group. This imbalance may affect the statistical power during the comparison. Contrary to the present finding, Efe et al. [13] identified high preoperative osteoarthritis severity (KL grade ≥ III) as a risk factor for lateral closing-wedge HTO failure (199 cases, mean follow-up of 10 years). There are differences in KL grade distribution in present study (I/II/III/IV, 4/82/13/1%) and Efe et al. [13] study (I/II/III, 49/48/3%). In Efe et al.'s study [13], half of the patients have doubtful osteoarthritis (KL grade I), and none had severe osteoarthritis. The differences in KL grade distribution may explain variations in the relationship between KL grade and HTO survivorship in our study versus Efe et al.'s study [13]. Furthermore, our findings do not align with the recommended indications proposed by Pape et al. [8], as we did not observe improved long-term survivorship with age younger than 55 years old and preoperative varus malalignment less than 10°. The age and preoperative varus malalignment degree may not be stringent criteria for defining the ideal indications in HTO. Future HTOs might adopt a more inclusive set of indications.

Lateral closing-wedge HTO demonstrated favourable survivorship outcomes. Efe et al. [13] reported a survival rate of 93%, 84%, and 68% at 5, 10, and 15 years; Michaela et al. [15] found survival rates of 94%, 80%, and 66% at 5, 10, and 15 years. The present finding showed survival rates marginally lower than those reported in the aforementioned studies, with rates of 91%, 78%, and 60% at 5, 10, and 15 years, respectively. These results highlight lateral closing-wedge HTO as a potent and enduring surgical technique for medial knee osteoarthritis with varus malalignment, maintaining a sustained effectiveness in around 80% operated patients at 10 years.

A surgical intervention (re-HTO or conversion to TKA) for recurrent of varus malalignment within the 5 years after lateral closing-wedge HTO is the most common complication (1.9%) in the present study. In Hui et al.'s study [9], deep venous thromboses (2%) and pulmonary emboli (1%) were reported as the most common complications in the 394 cases after a lateral closing-wedge HTO. In Howells et al.'s study [25], delayed union (3%), superficial wound infection (2%), common peroneal nerve palsy (1%), and pulmonary emboli (1%) were complications in 95 cases after a lateral closing-wedge HTO. The present study observed a deep venous thrombosis rate of 0.4%, signifying a lower incidence within the study cohort than Hui et al. [9] and Howells et al. [25]. Additionally, zero cases of peroneal nerve palsy were observed in our included patients. This is achieved by carefully exposing and protecting the peroneal nerve while leaving the fascia of this compartment open. Moreover, although our correction aimed for a 4-degree valgus alignment, there are instances where under-correction has been noted. The reoccurrence of varus malalignment may be attributed to this under-correction.

This cohort study stands out as the first to employ the Cox regression model in assessing the influence of KJLO on HTO survival rates. It boasts the largest patient sample among current published studies, encompassing 463 HTO-operated knees. Additionally, this study benefits from a significant follow-up duration, averaging 13 years (ranging from 5 to 18 years).

This study has a limitation as the body mass index (BMI) data for our included patients is incomplete, precluding a comprehensive analysis. The potential influence of BMI overweight on the survival of HTO remains a significant consideration [9, 25].

Conclusion

Increased KJLO after HTO (MPTA ≥ 95°) has no impact on the survivorship of HTO at 5, 10, and 15-year follow-up intervals. Our finding suggests that males exhibit superior survival outcomes than females after HTO, and emphasizes the importance of a targeted postoperative alignment (HKA 2°-6° valgus) for ensuring favourable long-term survivorship.

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Part III

Total knee arthroplasty after high tibial osteotomy

Chapter 7

Total knee arthroplasty following lateral closing-wedge high tibial osteotomy versus primary total knee arthroplasty: a propensity score matching study

Tianshun Xie
Astrid J. de Vries
Hugo C. van der Veen
Reinoud W. Brouwer

This Chapter has been submitted

Abstract

Background

The disparity in patient-reported outcomes between total knee arthroplasty (TKA) following high tibial osteotomy (HTO) and primary TKA has yet to be fully comprehended. This study aims to compare the patient-reported outcomes, radiological parameters and complication rates between TKA following HTO and primary TKA.

Methods

Sixty-five patients who underwent TKA following lateral closing-wedge HTO were compared to a matched group of primary TKA at postoperative 6-month and 1-year. Between-group confounders of age, gender, smoking status, Body Mass index, preoperative Numeric Rating Scale (NRS) pain in rest, Knee injury and Osteoarthritis Outcome Score-Physical function Shortform (KOOS-PS), EuroQol five-dimensional (EQ-5D) overall health score, and Oxford Knee Score (OKS) were balanced by propensity score matching. Patient-reported outcome measures were NRS pain in rest, KOOS-PS, EQ-5D overall health score, and OKS. Radiological parameters were femorotibial angle, medial proximal tibial angle, anatomical lateral distal femoral angle, posterior tibial slope, and patellar height assessed by Insall-Salvati ratio. The complication rates of TKA were compared between the two groups. The HTO survival time, the choice of staple removal before or during TKA in patients who underwent TKA following HTO patients, and the rate of patellar resurfacing were assessed. The p-value < 0.0125 indicates statistical significance after Bonferroni correction.

Results

After propensity score matching, no significant between-group differences in the patient-reported outcome measures, radiographical parameters and complication rates were found ($p>0.0125$). In the TKA following HTO group, with an average HTO survival time of 8.7 years, staples were removed before TKA in 46 patients (71%) and during TKA in 19 patients, and 11 cases (17%) had patella resurfacing. In the primary TKA group, 15 cases (23%) had patella resurfacing.

Conclusion

The short-term assessment of TKA following HTO indicates outcomes similar to primary TKA. A previous HTO does not impact the early results of subsequent TKA, suggesting that the previous HTO has minimal influence on TKA outcomes.

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Introduction

High tibial osteotomy (HTO) has proven to be an effective technique for addressing medial knee osteoarthritis and delivering good clinical outcomes, with 10-year survival rates ranging from 64 to 97.6% and 20-year survival rates ranging from 46 to 85.1% [1]. However, it is important to acknowledge that its efficacy may deteriorate with time [2]. In cases where HTO has failed or in the presence of advanced symptomatic knee osteoarthritis, a total knee arthroplasty (TKA) is performed as the subsequent treatment [3].

Past research has highlighted the technical complexities involved in performing TKA following a previous HTO [4-6], such as the soft tissue balancing and the amount of bone resection at the proximal tibia. Ongoing discussions revolve around whether TKA following HTO yields differing outcomes compared to primary TKA [7-10]. As a result, determining whether a previous HTO can encompass the consequences of TKA may impact the surgeon's choice for a HTO.

Although previous studies have explored this research topic, there are constraints in comparing clinical results between TKA following HTO and primary TKA [4]. Previous studies mostly relied on the Knee Society Score (KSS) questionnaire [6, 7, 9-15], primarily assessed from the physician's viewpoint [16, 17]. Using questionnaires that consider the patients' perspectives is necessary [18, 19]. Previous studies compared patient-reported outcomes (e.g., Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Hospital for Special Surgery (HSS) score) between TKA following HTO and primary TKA with follow-ups ranging from 2 to 13 years, but they did not match preoperative patient-reported outcomes between groups before the comparison [9, 15]. Moreover, the above studies employed a retrospective design with variable postoperative follow-up durations for assessing questionnaire outcomes. To address the ongoing controversy, a study with diverse patient-reported outcome questionnaires, well-matched preoperative patient-reported outcomes, and standardized follow-up durations is needed. Furthermore, the assessment of radiological parameters plays a critical role in confirming the intended alignment post-TKA, and early complication assessment is paramount for ensuring patient safety. Consequently, a comparative analysis of patient-reported outcomes, radiological parameters and complications between TKA following HTO and primary TKA is warranted.

The primary objective of this study is to compare patient-reported outcomes at 6-month and 1-year postoperatively between two groups: patients with TKA following lateral closing-wedge HTO and those with primary TKA. The secondary objectives include comparing radiological parameters and complication rates between these two groups. The hypothesis is that patients with TKA following lateral closing-wedge HTO will present inferior patient-reported outcomes compared to patients with a primary TKA.

Materials and Methods

Study design

This cohort study was conducted at a leading tertiary hospital in the northern Netherlands, and the patients' electronic medical records and radiographs were checked. The present study followed the statement of STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) for cohort studies [20]. The ethical committee of our hospital approved this study (MEC no. 2023-105).

Patients

One-hundred-six patients who had TKA following lateral closing-wedge HTO between January 1, 2016 and December 31, 2022 were screened. Patients were included if they completed the routinely administered questionnaires of Numeric Rating Scale (NRS) pain in rest [21], Knee injury and Osteoarthritis Outcome Score-Physical function Shortform (KOOS-PS) [22], EuroQol 5 Dimension (EQ-5D) overall health score [23], and Oxford Knee Score (OKS) [24] at preoperative, postoperative 6-month and postoperative 1-year, following the LROI (Dutch Arthroplasty Register) protocol. Patients were excluded if they had a previous HTO other than a lateral closing-wedge approach, such as medial opening-wedge HTO, combined wedge osteotomy, or double-level osteotomy.

Three-hundred-one patients who had primary TKA without previous HTO or unicompartmental knee arthroplasty between January 1, 2019 and December 31, 2022, and completed the above questionnaires at preoperative, postoperative 6-month and postoperative 1-year, were included for matching.

Surgical treatment

The surgical technique used for the lateral closing-wedge HTO was performed as described previously [25]: a transverse incision was executed, with careful preservation of the peroneal nerve. The procedure included the resection of the anterior proximal tibiofemoral syndesmosis, removal of the tibial wedge, and fixation using two staples, followed by a concluding fasciotomy of the anterior compartment. The preoperative planning aimed for a 4° valgus lower limb mechanical axis following HTO [26]. The shift of the lower limb mechanical axis from varus to valgus following a lateral closing-wedge HTO is depicted in **Figure 1**.

TKA was performed following the standard procedure [27]: the surgical procedure commenced with a midline skin incision, which was succeeded by a medial parapatellar arthrotomy of the joint capsule. In cases of moderate-to-severe patellofemoral osteoarthritis identified, patellar resurfacing was carried out. In this study, both cruciate-retaining or posterior-stabilized TKA implants were used.

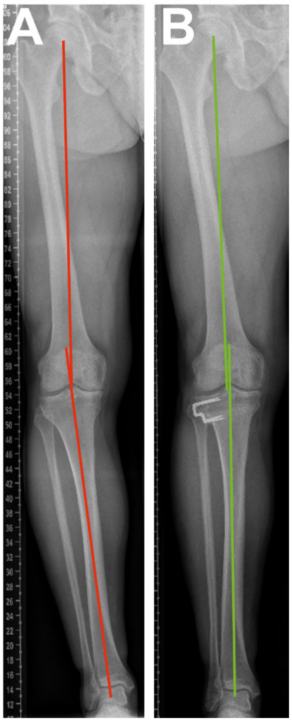

Figure 1. Radiographs taken before and after lateral closing-wedge HTO
HTO High tibial osteotomy. **A:** Varus mechanical axis before HTO; **B:** Valgus mechanical axis after HTO.

Patient-reported outcomes

Four questionnaires, NRS pain in rest, KOOS-PS, EQ-5D overall health score and OKS, were routinely administered at three separate time points: preoperative, postoperative 6-month, and postoperative 1-year, following the LROI (Dutch arthroplasty register) protocol.

(1) NRS pain in rest [21]: this scale was a generic tool employed to grade pain levels, ranging from 0 to 10, where 1-3 corresponded to mild pain, 4-6 indicated moderate pain, and 7-10 signified severe pain.

(2) KOOS-PS [22]: this was a condensed version of KOOS, with scores converted to a 100-point scale. This questionnaire comprises seven items for assessing physical function in knee osteoarthritis. In this study, a score of 0 indicated the highest

level of physical function as no difficulty.

(3) EQ-5D overall health score [23]: this assessment was employed to evaluate overall health, with scores ranging from 0 to 100. A score of 0 indicated the poorest overall health, while a score of 100 reflected optimal health.

(4) OKS [24]: this was utilized to measure pain and function following TKA, ranging from 0 to 48. This questionnaire comprises twelve items. A score of 48 signified the highest level of physical function.

Radiological Parameters

Radiological parameters, encompassing frontal and sagittal alignments, were assessed. The anteroposterior short-knee standing radiograph was used for measuring knee osteoarthritis grade, and frontal alignments of femoral-tibial angle (FTA), medial proximal tibial angle (MPTA), and anatomical lateral distal femoral angle (aLDFA). The lateral short-knee standing radiograph with 30-degree flexion was used for assessing posterior tibial slope (PTS) and patella height. The radiological parameters are illustrated in **Figure 2**.

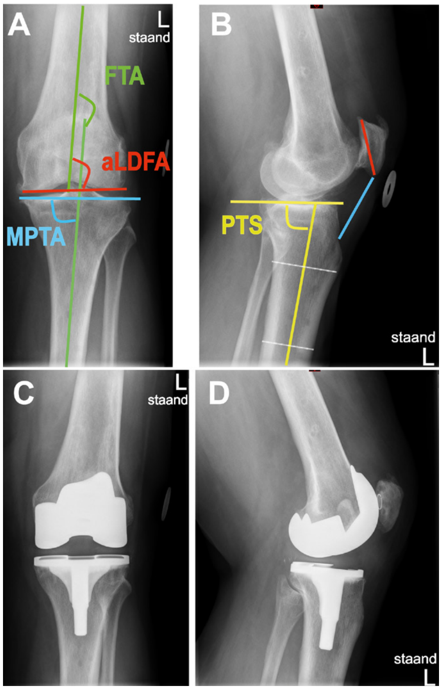

Figure 2. Illustration of radiological measurements
A: *FTA* Femorotibial angle; *aLDFA* anatomical lateral distal femoral angle; *MPTA* medial proximal tibial angle; **B:** *PTS* posterior tibial slope; Patellar height via Insall-Salvati method: ratio of blue-line to red-line; **C and D:** Total knee arthroplasty with Genesis II Posterior Stabilized implant and patellar resurfacing.

Kellgren&Lawrence grade [28]: this consisted of four ordinal grades for assessing knee osteoarthritis severity: I (indicating doubtful), II (mild), III (moderate), and IV (severe). Patellar height: assessed by the Insall-Salvati method [29], which was defined as the ratio of the patellar tendon length to the maximum length of patella in the sagittal plane. The normal range of this ratio was from 0.8 to 1.2.

PTS [30]: the posterior angle between the anatomic axis of the proximal tibia and the tangential line of the medial tibial plateau in the sagittal plane.

FTA [31]: the lateral angle between the distal femoral anatomic axis and proximal tibial anatomic axis in the frontal plane. The normal range for this angle was from 174° to 178°.

MPTA [32, 33]: the medial angle between the anatomical line of proximal tibia and the tangential line of the tibial plateau in the frontal plane. The normal value was 87°, ranging 85°-90°. This angle is also used for assessing knee joint line obliquity [34].

aLDFA [32, 33]: the lateral angle between the distal femoral anatomic axis and the tangential line of the femoral condyles in the frontal plane. The normal value was 81°, ranging 79°-83°.

Other outcomes

TKA complications in this study were defined as adverse issues arising from TKA that necessitates medical intervention, such as surgical site infection, pulmonary embolism or deep venous thrombosis etc. [35], which were extracted from medical records. In the TKA following HTO group, the HTO survival time was calculated as the duration from the time of HTO to the conversion to TKA in years, and the choice of staple removal before or during TKA in patients who underwent TKA following HTO patients were assessed. The rate of patellar resurfacing during TKA was assessed in each group.

Propensity score matching

Age [36], gender [37], smoking status [38], and Body Mass index (BMI) at the time of TKA [39] are all factors that impact patient-reported outcomes after TKA. These factors, along with preoperative patient-reported outcome measures including NRS pain in rest, KOOS-PS, EQ-5D overall health score and OKS, were considered confounding variables in this study. They were one-on-one matched between patients undergoing TKA following HTO and those undergoing primary TKA.

Statistical analysis

SPSS software (version 25) was used for statistical analysis. Propensity score matching method was used with a matching tolerance of 0.02. Distribution of continuous data was checked using Shapiro-Wilk test and Q-Q plot. The independent t tests were used for between-group comparison of parametric continuous data (age at TKA), and Mann-Witney U tests were used for between-group comparison of non-parametric continuous data (BMI at TKA, patient-reported outcome measures, and radiological results). Pearson chi-square tests were used for between-group comparison of gender, smoking status at TKA, and Kellgren&Lawrence grade before TKA. Fisher's exact tests were used for between-group comparison of TKA complication rate. Continuous data were reported as mean ± standard deviation, and categorical data were presented as numbers and frequencies. The p-value <0.0125 (0.05/4) indicated statistical significance after Bonferroni correction. Based on an effect size of 0.8, a significant level (alpha) of 0.0125, and a study power of 95% determined by the Mann-Whitney U test, a sample size of 58 patients per group was indicated by G*Power software.

Results

The patient selection process is shown in **Figure 3**. Confounding variables before and after the propensity score matching are presented in **Table 1**. Three types of primary TKA cemented implants were utilized: GENESIS II Posterior-Stabilized (Smith and Nephew, Memphis, USA), GENESIS II Cruciate-Retaining, and NexGen Legacy® Posterior Stabilized Flex (Zimmer, Warsaw, USA). In TKA following HTO group, the distribution of the above implants was 60/2/2, while in primary TKA, it was 56/6/3. In the TKA following HTO group, one patient received a stemmed tibial component (Legion; Smith and Nephew, Memphis, USA).

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A comparison of patient-reported outcomes, radiological results and complication rates between TKA following HTO and primary TKA after propensity score matching is depicted in **Table 2**. No statistically significant between-group differences in the patient-reported outcome measures (NRS pain in rest, KOOS-PS, EQ-5D overall health score and OKS), radiographical parameters (postoperative patellar height, PTS, FTA, MPTA, aLDFA) and complication rates were found (p>0.0125).

The average HTO survival time in this group was 8.7 years, ranging from 1.1 to 15.1 years. In the TKA following HTO group, staples had already been removed in 46 patients (71%) before the TKA; in 19 patients, staple removal occurred during the TKA in one procedure through the midline incision. In the TKA following HTO group, 11 cases (17%) had patella resurfacing; in the primary TKA group, 15 cases (23%) had patella resurfacing.

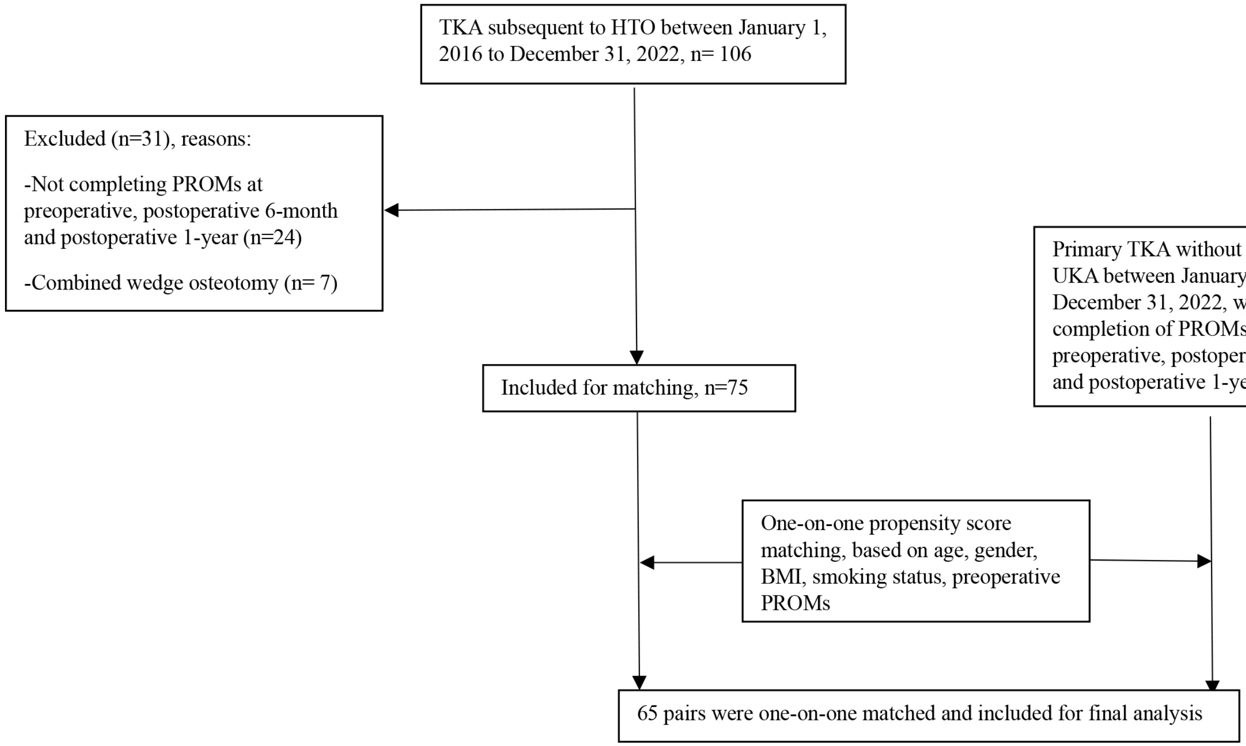

Figure 3. Patient selection process
TKA Total knee arthroplasty; *HTO* High tibial osteotomy; *UKA* uni-compartmental knee arthroplasty; *BMI* Body Mass Index; *PROMs* Patient-reported outcome measures
The PROMs are Numeric Rating Scale pain in rest, Knee injury and Osteoarthritis Outcome Score-Physical function Shortform (KOOS-PS), EuroQol 5 Dimension overall health score, and Oxford Knee Score.

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Table 1. Propensity score matching between groups TKA following HTO and Primary TKA

	Before Propensity Score Matching			After Propensity Score Matching		
Confounding variables	**TKA-HTO**	**Primary TKA**	**P-value**	**TKA-HTO**	**Primary TKA**	**P-value**
Number of knees, N	75	301		65	65	
Age at surgery, years	61.8±6.4	70.6±8.5	<0.001b*	62.6±6.0	62.9±6.0	0.782 b
Gender, male/female	45/30	112/189	<0.001c*	36/29	41/24	0.372 c
Smoking status, Y/N	11/64	14/287	0.002 c*	6/59	5/60	0.753 c
BMI, kg/m2	31.7±5.3	30.1±5.1	0.008 a*	31.4±5.3	31.8±5.6	0.718 a
Preoperative NRS pain in rest score	5.6±2.5	4.8±2.4	0.013 a*	5.6±2.5	5.3±2.1	0.461 a
Preoperative KOOS-PS score	44.4±13.8	46.1±13.3	0.266 a	43.8±13.6	44.5±14.2	0.963 a
Preoperative EQ-5D overall health score	69.0±20.5	66.9±17.2	0.056 a	68.4±20.4	66.1±19.8	0.288 a
Preoperative OKS	24.1±8.6	22.8±8.1	0.198 a	24.7±8.8	23.8±8.2	0.531 a

Continuous data are shown as mean ± standard deviation. Categorical data were presented as numbers and frequencies.
TKA Total knee arthroplasty; *HTO* High tibial osteotomy; *BMI* Body Mass Index; *NRS* Numeric Rating Scale; *KOOS-PS* Knee injury and Osteoarthritis Outcome Score-Physical function Short-form; *EQ-5D* EuroQol-5 dimension; *OKS* Oxford Knee Score.
* Statistical significance
a Mann-Whitney U test
b Independent t-test
c Pearson chi-square test

Table 2. Between-group comparison after propensity score matching

Outcomes	**TKA following HTO (n=65)**	**Primary TKA (n=65)**	**P-value**
Preoperative Kellgren&Lawrence grade (III/IV)	24/41, 37%/63%	20/45, 31%/69%	0.458 c
Preoperative patellar height (N, normality/abnormality)	58/7, 89%/11% +	58/7, 89%/11% ǂ	1.0 c
Postoperative patellar height (N, normality/ abnormality)	58/7, 89%/11% +	59/6, 91%/9% ǂ	0.770 c
Preoperative PTS, degrees	87.2±5.4	84.9±4.7	<0.001a*
Postoperative PTS, degrees	88.4±2.0	89.3±2.1	0.017 a*
Preoperative FTA, degrees	176.1±5.1	177.5±6.6	0.080 a
Postoperative FTA, degrees	175.0±3.0	175.9±2.3	0.056 a
Preoperative MPTA, degrees	91.1±4.1	86.7±2.4	<0.001a*
Postoperative MPTA, degrees	88.2±2.1	87.5±1.6	0.075 a
Preoperative aLDFA, degrees	82.5±2.0	82.0±2.4	0.192 a
Postoperative aLDFA, degrees	83.4±2.0	83.6±2.3	0.301 a
Postoperative NRS pain in rest 6-month, score	2.2±2.2	2.2±2.4	0.768 a
Postoperative NRS pain in rest 1-year, score	2.0±2.4	1.9±2.3	0.934 a
Postoperative KOOS-PS 6-month, score	29.1±13.0	31.6±14.9	0.347 a
Postoperative KOOS-PS 1-year, score	29.1±12.5	28.0±14.8	0.651 a
Postoperative EQ-5D health score 6-month, score	77.5±15.0	74.3±18.8	0.456 a
Postoperative EQ-5D health score 1-year, score	77.2±14.7	78.6±14.5	0.605 a
Postoperative OKS 6-month, score	35.6±8.2	31.9±10.2	0.039 a*
Postoperative OKS 1-year, score	37.2±8.4	36.3±9.8	0.819 a
Complication rate	0%	1.5% ⊥	1.0 d

Continuous data are shown as mean ± standard deviation. Categorical data were presented as numbers and frequencies. The Insall-Salvati ratio defines patellar height: 0.8-1.2 (normal), >1.2 (alta), <0.8 (baja).

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TKA Total knee arthroplasty; *HTO* High tibial osteotomy; *MPTA* medial proximal tibial angle; *FTA* femorotibial angle; *aLDFA* anatomical lateral distal femoral angle; *PTS* posterior tibial slope; *NRS* Numeric Rating Scale; *KOOS-PS* Knee injury and Osteoarthritis Outcome Score-Physical function Short-form; *EQ-5D* EuroQol-5 dimension; *OKS* Oxford Knee Score.

* Statistical significance
a Mann-Whitney U test
b Independent t-test
c Pearson chi-square test
d Fisher's exact test
┼ Before TKA following HTO, seven patellar alta; After TKA following HTO, five alta, two baja.
╪ Before primary TKA, six patellar alta, one baja; After primary TKA, five alta, one baja.
┴ One had periprosthetic joint infection.

Discussion

The most important finding of the present study is that the patient-reported outcomes are similar between the TKA following HTO and primary TKA groups at short-term follow-ups, along with resembling between-group radiological parameters and complication rates. This finding rejects our hypothesis that patients with a TKA following HTO have inferior patient-reported outcomes compared to patients with a primary TKA.

The present study demonstrates no statistically and clinically significant disparity in postoperative patient-reported outcomes between TKA following HTO and primary TKA. This finding is consistent with previous studies when comparing patient-reported outcomes between TKA following lateral closing-wedge HTO and primary TKA: Bae et al. [9] reported no significant between-group difference in WOMAC score with a follow-up ranging from 2 to 13 years; Kazakos et al. [15] reported no significant difference in HSS with a follow-up ranging from 3 to 8 years. Other previous studies frequently used the KSS questionnaire, and no significant between-group differences in TKA following lateral closing-wedge HTO and primary TKA have been found in studies by Amendola et al. [11] and Meding et al. [6] with a follow-up ranging from 3 to 22 years. Whereas Efe et al. [7] reported a significantly lower knee score of Knee Society Score (KSS) in TKA following lateral closing-wedge HTO compared to primary TKA (4-10 years follow-up), and Erak et al. [8] found higher pain levels and a significantly lower knee score of KSS in TKA following medial opening-wedge HTO compared to primary TKA (2-8 years follow-up). However, previous studies were limited by their retrospective designs and variable follow-up durations. Moreover, the evaluation of KSS is predominantly conducted from an objective standpoint by physicians, rather than relying on patient-reported assessments [16, 17]. In present study, besides no statistical significance, the between-group difference in the patient-reported outcome measures also falls below the published threshold for minimal clinically important significance [40-42]. Furthermore, most previous studies compared TKA following lateral closing-wedge HTO and primary TKA; there is a need for future research to focus more on the TKA following medial opening-wedge HTO.

Patients appear to exhibit similar radiological parameters in TKA following lateral closing-wedge HTO and primary TKA. The Insall-Salvati ratio is a common metric for assessing patellar height. Kazakos et al. [15] observed a significantly higher incidence of patella baja in the TKA following HTO patients than primary TKA, while Efe et al. [7] and Bae et al. [9] found no significant differences in patellar height between TKA following HTO and primary TKA. The present study showed no significant between-group difference in the incidence of abnormal patellar height, and both the TKA following HTO and primary TKA groups exhibit higher incidences of patellar alta than patellar baja following surgery. This is likely linked to the pre-existing patellar alta prior to the TKA procedures. Although the present study shows a 0.9° PTS difference between TKA following HTO and primary TKA, this disparity may be possibly explained by the measurement bias, also it lacks statistical significance and falls below the established minimal clinically significant threshold of 1.5° PTS [43]. Moreover, the TKA following HTO group exhibited a higher preoperative MPTA compared to the primary TKA group, with no significant differences in the remaining alignment parameters. This may be attributed to an observed increase in knee joint line obliquity following a valgus-producing HTO. Further research is needed to explore any lasting disparities in radiological results, including the positions of prothesis components.

Our study found no significant difference in complication rates between TKA-HTO and primary TKA. A meta-analysis showed that there was no significant difference in complication rates between TKA following HTO group and primary TKA [44], while another meta-analysis indicated a higher infection rate in TKA following HTO group compared to primary TKA [3]. Altered knee anatomy and surgical scar tissue might offer a possible explanation for the previous observations of a higher increase in infection rates among cases with a history of HTO. In our study, there was only one infection case among all analysed patients, occurring in the primary TKA group, with no significant difference in the between-group comparison of infection or complication rates. A larger patient sample may be necessary to discern the difference in complication rates between these two groups in future studies.

The present study showed a higher use of posterior-stabilized implants over cruciate-retaining ones, likely due to challenges in achieving proper tensioning of the posterior cruciate ligament in cruciate-retaining total knee arthroplasty after previous high tibial osteotomy [45]. Notably, Chen et al. [45] reported similar clinical outcomes between cruciate-retaining and posterior-stabilized implants in cases of TKA following HTO. Hence, we did not equalize the between-group distribution of implant types (cruciate-retaining and posterior-stabilized) in this study. In one case of TKA following HTO in our study, a stemmed tibial component (Legion) was chosen considering the patient's bone quality and overweight status.

The strength of the present study is its use of one-on-one matching, taking into account a total of eight confounding variables to mitigate their influence, thereby enhancing the robustness and validation of the evidence. Moreover, the study adopted a design with standardized follow-up length at 6-month and 1-year postoperatively. Furthermore, we employed the Bonferroni correction on the p-value to mitigate the risk of the inflation of significance, enhancing the rigor of the comparison.

A limitation of the present study was the absence of anteroposterior long-standing radiographs for patients, necessitating the use of short-knee radiographs for assessing lower limb alignment. Consequently, the femoral-tibial angle based on the anatomical axes may not serve as a reliable indicator for evaluating lower limb alignment [46]. Additionally, it is important to highlight that the study's conclusions were derived from a relatively short follow-up period, underscoring the necessity for future studies with extended follow-up durations.

Conclusions

The short-term assessment of TKA following HTO indicates outcomes similar to primary TKA. A previous HTO does not impact the early results of subsequent TKA, suggesting that the previous HTO has minimal influence on TKA outcomes.

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Chapter 8

General discussion and future perspectives

This thesis focused on clinical aspects related to increased knee joint line obliquity (KJLO) after lateral closing-wedge high tibial osteotomy (HTO), encompassing how to measure KJLO and investigating the influence of increased KJLO on the patient-reported outcomes, radiological progression of osteoarthritis, and survival of HTO. Moreover, patients undergoing a conversion to total knee arthroplasty (TKA) following HTO were compared with patients after primary TKA patients, focusing on patient-reported outcomes, radiological parameters and complication rates. In this chapter, the outcomes of each objective mentioned in the general introduction are summarized below. In alignment with the thesis outline, this chapter discusses the overall findings and provides insights into future research directions and clinical implications.

Part I – How to measure knee joint line obliquity

A valgus-producing HTO corrects the proximal tibia by removing a bony wedge, realigning the lower limb weight bearing line and altering the proximal tibial geometry; however, this procedure introduces a change of knee joint line in the frontal plane [1]. Chapters 2 and 3 addressed the first objective outlined in the general introduction, which focused on the methodology for measuring KJLO.

Chapter 2 outlined an overview of the current methods utilized for evaluating KJLO in HTO via a scoping review. This review identified five distinct methods employed for assessing KJLO on anteroposterior long-standing radiographs in published literature. The findings of this review indicated the need for a preferred method with sufficient measurement stability and reliability. This would not only enable better comparison of results across different studies but would also facilitate in reaching consensus on acceptable KJLO limits.

Chapter 3 comprehensively examined these five distinct methods by evaluating their measurement stability and reliability in a cross-sectional study design [2]. Meeting the criteria of both adequate measurement stability and reliability, the medial proximal tibial angle (MPTA) seems to be the preferred method for measuring KJLO. As compared to the other four methods, MPTA measurement is not influenced by variations in radiographs and bipedal distance.

A preferred KJLO measurement method with adequate measurement stability and reliability is highly necessary for clinical use. Regarding the filming protocol for anteroposterior long-standing radiographs employed in KJLO measurement [2], there is no consensus on whether to adopt a single leg or double legs position. Additionally, maintaining control over bipedal distance during double legs filming poses a challenge, necessitating the use of supplementary aids for precise foot placement, such as using a foot plate. In cases where patients exhibit a valgus leg resulting from lateral knee compartment osteoarthritis or due to a valgus-producing HTO aimed at treating medial knee osteoarthritis, achieving a bipedal stance by aligning both malleoli together may even be impossible. Moreover, a distinction exists in the loading between the double legs standing position (approximately 50% loading per leg) and the single leg standing position (experiencing over 90% loading) [3]. Furthermore, single leg standing radiographs reveal greater malalignment, particularly in cases of collateral laxity, compared to double legs stance [2]. Although it has been reported that single leg standing radiographs are considered to better represent dynamic gait situations than double legs standing, the latter is easier to film and allows for a comparison with the contralateral side [3-5]. Although maintaining the knee in full extension with patella positioned forward is commonly used for an effective control of rotation during filming [6], caution should be exercised as patella forward positioning, especially in patients with lateralized patella and valgus legs, may lead to an overestimation of the patient's valgus condition. 100% anteroposterior projection can be ensured with lateral fluoroscopic control by superimposing the dorsal aspect of the femoral condyles [7]. Due to the fact that there is no consensus about the optimal filming protocol, there is a pressing need for a measurement method for KJLO that remains unaffected by variations in anteroposterior long-standing radiographs and bipedal distance during filming.

This thesis showed that the MPTA stands out as the preferred method for measuring KJLO [2]. In previous literature, the assessment of KJLO commonly involves measuring the angle between the knee joint line, often represented by the proximal tangential line of the tibial plateau, and a reference line formerly designated as the ground line, denoted as the joint line orientation angle by tibial plateau (JLOAT) [2]. However, angles formed by the ground line can be influenced by the single/double legs standing or bipedal distance in double legs standing used during filming, limiting the practical application of JLOAT and other angles formed in relation to the ground line [2]. The MPTA, derived from the tangential line of the tibial plateau and the tibial mechanical axis, relies solely on tibial bony geometry, remaining unaffected by filming position. This angle also serves as a reliable indicator for assessing tibial deformity and the correction magnitude of HTO, making it our preferred method for assessing KJLO [1]. According to our scoping review (chapter 2), only three out of the thirty eligible studies employed the MPTA to measure KJLO. As a result, I advocate a wider use of MPTA as the preferred KJLO measurement method in both clinical practice and future studies. This will facilitate the comparisons of KJLO results across different hospitals and studies using different filming protocols, enhancing the determination of the clinical consequences of increased KJLO after HTO.

Part II – Consequences of increased knee joint line obliquity after high tibial osteotomy

Chapters 4, 5, and 6 addressed the second objective of this thesis, which involved investigating the influence of increased KJLO after HTO on patient-reported outcomes, radiological progression of osteoarthritis, and survivorship of HTO.

Chapter 4 was a systematic review conducted with a search up to February 2023. This review delved into the clinical relevance of increased KJLO after HTO for medial knee osteoarthritis, as well as summarized the currently utilized KJLO threshold values. I concluded that the clinical relevance of increased KJLO after HTO is controversial and somewhat limited, and JLOAT (4° and 6°), joint line orientation angle by middle knee joint space (5°), MPTA (95° and 98°), and Mikulicz joint line angle (94°) were the used KJLO upper limits [8]. Since the last search was conducted one year ago when writing this general discussion, I did an updated search in January 2024, which yielded only one new eligible article meeting our predefined criteria, authored by us (chapter 5) [9].

Chapter 5 described a cohort study investigating influence of KJLO after lateral closing-wedge HTO, which adopted the MPTA as the method for measuring KJLO and used propensity score matching to control the cofounding variables. Chapter 5 found that an increased postoperative KJLO (MPTA≥95°) or KJLO change (MPTA change≥8°) does not influence patient-reported outcomes, as measured by the Western Ontario and McMaster Universities Osteoarthritis Index score (WOMAC), nor radiological progression of osteoarthritis, as measured by medial joint space width narrowing and Kellgren-Lawrence (KL) grade at mid-term follow-up (5 years) [9].

Chapter 6 investigated the influence of increased postoperative KJLO (MPTA≥95°), alongside other critical factors, on the survival of lateral closing-wedge HTO, with a mean follow-up of 13 years in 463 patients after HTO. A conversion to TKA was regarded as the critical endpoint of HTO. We found that increased postoperative KJLO (MPTA≥ 95°) had no significant influence, but female gender and postoperative untargeted alignment (HKA<2° or >6° valgus) were identified as risk factors for a conversion from a lateral closing-wedge HTO to TKA.

Research on the KJLO topic initiated in 2008 and experienced a notable upswing since 2020, indicating the increasing popularity of this topic in the past few years [8]. Despite the uprising publication number on this topic, there still exists controversy and limited evidence on the clinical consequences of increased KJLO after HTO. This may be attributed to the variety of KJLO measurement methods used, a lack of sufficient control over confounding variables, as well as a limited number of patients included. Regarding the first, I suggest implementing MPTA for KJLO measurement, intended for use by knee surgeons, orthopaedic research groups, and potentially establishing it as a consensus within international orthopaedic associations. Furthermore, in assessing the clinical consequences of increased KJLO after HTO, common practice involves comparing groups with increased KJLO to those maintaining acceptable KJLO; to enhance the reliability of these comparisons by minimizing the impact of confounding variables, I recommend implementing propensity score matching.

There is a lack of evidence regarding KJLO studies focused on lateral closing-wedge HTO in comparison to medial opening-wedge HTO. This is likely because the medial opening-wedge HTO has been increasingly favoured over the past two decades, offering benefits such as preserving the proximal tibiofibular joint integrity and preventing peroneal nerve injuries [10]. Yet, the benefits of lateral closing-wedge HTO should not be overlooked, as it may exert less impact on leg length in comparison to medial opening-wedge HTO, particularly in situations requiring substantial correction [11]. Furthermore, through a lateral closing-wedge approach, a defect laxity is created by resecting bone from the lateral side and depressing the lateral plateau [9]. This differs biomechanically from the medial opening-wedge HTO, where the medial plateau is elevated by creating an opening wedge from the medial side, coupled with a release of the medial collateral ligament. Consequently, an increased KJLO may have varying consequences for a specific HTO technique. My findings urge the need of well-designed studies for examining the relationship between increased KJLO and clinical outcomes within the framework of a lateral closing-wedge HTO.

In the context of surgical indications for HTO, our KJLO studies diverge from the criteria established in certain preceding research [9, 12]. Our preoperative surgical planning did not consider the origin of bony deformity; instead, we focused solely on assessing preoperative varus alignment through the hip-knee-ankle angle (HKA). Our target correction aimed for a 4° valgus HKA, aligning with a 62%-66% weight bearing ratio associated with a correction targeted range of 2°-6° valgus HKA [13, 14], known as the Fujisawa point [15]. Moreover, we performed HTO across various medial knee osteoarthritis severities, including cases with KL grade III or IV (moderate or severe), although the predominant focus remained on grade I or II (doubtful or mild) patients [9]. Whereas Ollivier et al. [12] performed HTO in patients with symptomatic medial knee osteoarthritis of Ahlbäck grade I or II (approximately corresponding to KL grade I or II), where the deformity originated from the tibia (preoperative MPTA<85°, normal range 85°-90°), and femur geometry was normal, characterized within the mechanical lateral distal femoral angle range of 85°-90°. When applying our indication with preoperative planning based on the HKA, postoperative outcomes revealed good patient satisfaction, marked improvement in outcomes, including a reduction in the progression of medial knee osteoarthritis, as well as decreased pain and improved knee function [16]. One possible explanation of the positive postoperative outcomes with our HTO indication criteria is that attaining a properly realigned valgus HKA is of paramount importance in influencing the clinical outcomes of HTO, rather than focusing on whether to correct the bony deformity at its origin. This is attributed to the fact that the primary purpose of HTO is to establish a valgus alignment in the lower limb, thereby redistributing knee loading and addressing medial knee osteoarthritis [17, 18].

While an increased KJLO beyond MPTA 95° has shown no negative influence on the patient-reported outcomes, radiological progression of knee osteoarthritis (chapter 5), and survival rates of lateral closing-wedge HTO (chapter 6), caution may still be warranted for a high postoperative KJLO. The alteration of knee joint geometry associated with an increased KJLO prompts concerns about other potential influences, such as on gait mechanics and overall mobility, given the absence of published evidence on these aspects. Considering that the effectiveness of HTO may diminish over time [19], potentially necessitating a TKA, the altered geometry introduced by an increased KJLO could pose technical challenges for a subsequent TKA. These challenges may encompass considerations related to alignment, bone reshaping, and soft tissue balance [20]. For example, an extreme KJLO after a valgus producing HTO may necessitate the utilization of a lateral augmented stemmed tibial component in a subsequent TKA.

There seems to be a gender-based difference in the long-term survival of lateral closing-wedge HTO. This might be caused by hormonal factors; the impact of estrogen levels in females on bone quality and the bony healing process is common knowledge. I found that males exhibit a more favourable HTO survival rate than females (no significant difference in postop-KJLO), a trend consistent with the results of Van Raaij et al [21]; however, my finding does not align with a widely accepted pattern, with some other studies indicating that gender may not exert a significant influence on HTO survival [22, 23]. Future investigation may be necessary to explore the theoretical foundations explaining how gender influences the survival of HTO. Conclusively, our findings suggest that males might be more favourable candidates than females for lateral closing-wedge HTO.

It is crucial to achieve the specified range of 2°-6° valgus HKA (targeted at 4° valgus) after lateral closing-wedge HTO. This targeted HKA range was used by previous studies [14, 24, 25]. To the best of our knowledge, our study is the first to explore the influence of this targeted HKA range (2°-6° valgus) on HTO survival. This targeted alignment not only ensures superior survival rate compared to deviations from the specified range but also reinforces the viability and effectiveness of adhering to this specific target. One plausible interpretation of the aforementioned finding could be that achieving a targeted alignment post-HTO proves advantageous for optimizing biomechanics. This is achieved by redistributing the load within the knee joint, thereby unloading the medial compartment affected by medial knee osteoarthritis [26, 27].

It is worth noting that our study aims for a 4° valgus HKA to reach the Fujisawa point, whereas some other studies employ a planning strategy with the mechanical axis passing through the knee at the lateral tibial spine, around 1.6° valgus HKA [15]. Lee et al. [15] found that the Fujisawa point group and the lateral tibial spine point group (24/65 knees in each group, mean follow-up 1.7 years) showed similar results in patient-reported outcomes and arthroscopic cartilage grading for medial femoral condyle, trochlea and patella. They suggested that both targeted points are viable options in HTO planning. However, it is important to highlight that their conclusion is derived from a single study with a small number of patients and a short follow-up. Moreover, it is essential to consider the severity of medial knee osteoarthritis and cartilage status of the lateral knee compartment when determining the optimal correction degree in HTO. Therefore, further research with a larger patient cohort and an extended follow-up period is necessary to establish a solid conclusion, making a meaningful comparison between targeting at lateral tibial spine point and Fujisawa point.

The decision to perform HTO may not be impeded by the presence of advanced preoperative medial knee osteoarthritis severity. Although Lee et al. [28] did not recommend HTO for knee osteoarthritis beyond Ahlbäck grade III (approximately corresponding to KL grade III), my study demonstrates similar survival outcome (mean postoperative follow-up 13 years) in lateral closing-wedge HTO for patients with preoperative medial knee osteoarthritis severity KL grades III or IV (moderate or severe) and KL grades I or II (doubtful or mild). As a result, it may not be necessary to impose restrictions solely based on a specific preoperative knee osteoarthritis grade when deciding on HTO. The decision for HTO should be highly individualized, with surgeons assessing each patient's unique condition, involving a thorough evaluation of patients' preoperative malalignment, clinical symptoms, and overall health status.

Part III – Total knee arthroplasty after high tibial osteotomy

Chapter 7 addressed the third objective of this thesis, evaluating differences in patient-reported outcomes, postoperative radiological parameters, and complication rates between patients after primary TKA with prior HTO and patients after primary TKA without prior HTO. Our finding suggests that a prior HTO procedure does not significantly influence the patient-reported outcomes of TKA in the short-term 1-year follow-up.

Although there appears to be consistent outcomes of TKA, irrespective of a prior HTO, challenges and complexities arise when dealing with TKA in patients who have undergone a prior HTO. These include addressing the altered alignment resulting from the HTO realignment and managing soft tissue balance, which may contribute to an elevated risk of future revision surgeries for these patients [29]. Hence, when undertaking a conversion from HTO to TKA, knee surgeons need thoughtful preoperative planning, encompassing decisions on TKA implant selection, potential use of augments, and possible consideration of customized components to address anticipated technical difficulties.

While an HTO is a potent technique for addressing medial knee osteoarthritis, its effectiveness decreases with time [19], with a survival rate of 60% at 15 years follow-up (chapter 6). Patients eligible for conversion from HTO to TKA may exhibit persistent pain and functional impairment, and the decision may be influenced by the progression of medial knee osteoarthritis or malalignment issues that were not effectively addressed through HTO. In addition, although uni-compartmental knee arthroplasty (UKA) is a common tool for treating medial knee osteoarthritis, careful thought is necessary. Contraindications may arise for a conversion from HTO to UKA, especially with post-HTO valgus malalignment and technical challenges due to anatomical changes in the proximal tibia [30]. Hence, in clinical practice, the broader applicability lies in converting from HTO to TKA rather than from HTO to UKA [30].

Future research directions

In the subsequent discussion, I outline the identified limitations within this thesis, address existing evidence gaps, and propose future research directions derived from these limitations and gaps.

First, it is important to note that the outcomes presented in our studies described in Chapters 5, 6, and 7 are exclusively derived from cases involving lateral closing-wedge HTO. It is crucial to recognize the biomechanical distinctions between lateral closing-wedge HTO and medial opening-wedge HTO. For instance, lateral closing-wedge HTO may introduce a defect laxity at the lateral side due to a reduction in the lateral tibial plateau. In contrast, medial opening-wedge HTO may potentially elevate medial strain unless a release is performed at the superficial medial collateral ligament [9].

Future research endeavours should delve into the nuances of medial opening-wedge HTO, drawing inspiration from our study design, which incorporates a control of confounding variables, a use of MPTA for assessing KJLO, an involvement of a sufficiently large patient cohort, and an employment of regression models. This approach aims to determine if the observed findings align consistently with our lateral closing-wedge HTO study outcomes.

Second, this thesis evaluated the KJLO with anteroposterior long-standing radiographs, providing a limited 2D assessment in the frontal plane. However, it is crucial to acknowledge that an HTO correction not only influences alignment in the frontal plane but also in the sagittal plane. This necessitates a comprehensive assessment.

Subsequent research endeavours could employ 3D measurement software, such as Mimics, in conjunction with CT imaging, to conduct a thorough evaluation of KJLO and alignment changes in both the frontal and sagittal planes following HTO [31]. It is important to highlight the current absence of a valid, verified, and standardized global coordinate system for the lower limb in clinical practice. Future investigations are necessary to develop a comprehensive 3D coordinate system for evaluating KJLO and other alignment parameters involved in HTO. This system should be characterized by robustness, high repeatability, and accurate representation of anatomical structures.

Third, the conclusions drawn from the comparison between TKA after HTO and primary TKA in Chapter 7 were based on a relatively short-term follow-up period of 1 year. Limited follow-up duration may influence conclusions, and extended follow-up could yield different outcomes. Moreover, prior studies, despite examining extended follow-up duration, frequently faced challenges related to confounding variables and variations in duration owing to their retrospective design [32].

Subsequent research should encompass both mid-term and long-term follow-up periods, adopting a prospective study design with standardized intervals for follow-up, and meticulous control of confounding variables, using registered data. Additionally, a more extended follow-up of the patients highlighted in Chapter 7 has already been planned for future investigations.

Fourth, all our studies to date have concentrated exclusively on the clinical aspects of an increased KJLO following HTO. However, there is a notable lack of understanding regarding how this increased KJLO following HTO affects biomechanics as well as patients' gait patterns.

I already designed a finite element analysis study examining the influence of increased KJLO on biomechanics, utilizing a validated knee model (not published yet). Additionally, a gait analysis will be conducted to compare patients with increased KJLO to those with acceptable KJLO following HTO, emphasizing various parameters such as stride length, step length/width, joint angles/moments, left-right symmetry, and functional performance. Through these investigations, I can have a deeper insight into the biomechanical implications and alterations in gait associated with increased KJLO post-HTO.

Fifth, although this thesis offers a comprehensive, step-by-step approach to KJLO-related issues post-HTO, it is important to note that all the studies conducted were based on data from a single hospital, primarily involving Caucasian patients. As a result, the findings may be influenced by the specific characteristics of this localized patient population. Furthermore, potential variations related to ethnicity, culture and healthcare providers must be considered.

Future research is suggested to adopt a multicentre approach, involving diverse regions and encompassing patient populations of various racial backgrounds, beyond Caucasians. The influence of ethnicity of ethnicity on anatomical structures, including morphological measurements like KJLO, cannot be overlooked [33].

Clinical implications of this thesis

While acknowledging the limitations and evidence gaps mentioned above, it is noteworthy that my thesis holds significant implications for clinical practice.

1. I recommend adopting the medial proximal tibial angle for measuring knee joint line obliquity, to be utilized by knee surgeons, orthopaedic research groups, and established as a consensus within international orthopaedic associations.
2. An increased postoperative knee joint line obliquity (assessed by medial proximal tibial angle) exceeding 95° or a knee joint line obliquity change exceeding 8° after a lateral closing-wedge high tibial osteotomy may not be a matter of concern for knee surgeons.
3. Male patients might be better candidates for a lateral closing-wedge high tibial osteotomy in terms of long-term survival compared to females.
4. An optimal correction range of 2°-6° valgus hip-knee-ankle angle (targeted at 4° valgus) is clinically valid, and achieving this target is pivotal for the success of lateral closing-wedge high tibial osteotomy in terms of long-term survival.
5. The presence of a prior high tibial osteotomy is not a concern when contemplating a total knee arthroplasty, particularly in the context of patient-reported outcomes.

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Chapter 9

Summary
Nederlandse samenvatting

English summary

Knee osteoarthritis induces pain, stiffness and reduced mobility, imposing a burden on individuals and society. A valgus-producing high tibial osteotomy (HTO) is an effective surgery for treating medial knee osteoarthritis with varus malalignment. However, this surgery increases the knee joint line obliquity (KJLO) in the frontal plane. This poses a challenge for knee surgeons in deciding whether to include a predicted KJLO increase in preoperative planning for HTO.

To address this clinical challenge, the first step is to establish a standardized method for measuring KJLO. Subsequently, the clinical consequences of an increased KJLO after lateral closing-wedge HTO can be determined. Sometimes, even after an HTO, osteoarthritis progresses and a total knee arthroplasty (TKA) is indicated. It is of interest, whether a prior HTO influences the outcome of a consequent TKA.

This thesis has three main objectives: (1) To investigate the methodology for measuring knee joint line obliquity, including a description of current techniques used and to recommend the preferred knee joint line obliquity measurement method in high tibial osteotomy; (2) To explore the influence of increased knee joint line obliquity on patient-reported outcomes (PROMs), on radiological results, and on the survivorship of lateral closing-wedge high tibial osteotomy; (3) To assess the disparities between total knee arthroplasty following high tibial osteotomy and total knee arthroplasty without prior high tibial osteotomy, with a focus on contrasting patient-reported outcomes and radiological parameters.

After the general introduction, **Part I** addresses the first objective through **Chapter 2 and 3**, **Part II** focuses on the second objective in **Chapter 4, 5 and 6**, and **Part III** delves into the third objective in **Chapter 7**.

Chapter 2 is a scoping review that highlights the lack of consensus in measuring KJLO. Five different methods are identified, including the use of anteroposterior long single leg standing and double legs standing filming techniques, and varying bipedal distance during double legs standing. This chapter advocates for the establishment of a preferred method for KJLO measurement, which is a crucial foundation for future clinical and biomechanical KJLO studies. Additionally, standardizing measurement methods is important to enable meaningful comparisons of KJLO study outcomes across various hospitals with diverse filming protocols.

As a subsequent study, **Chapter 3** is a cross-sectional study that compares the five KJLO measurement methods regarding their measurement stability and reliability. The

results of this study indicate the medial proximal tibial angle (MPTA) as the preferred KJLO measurement method. This is because MPTA measurement maintains adequate reliability, which is unaffected by differences in patient positioning, for example anteroposterior long single leg standing and double legs standing, as well as the bipedal distance in double legs standing. Additionally, the MPTA is convenient to be measured. Therefore, a wider implementation of MPTA as the standardized method for KJLO measurement among knee surgeons and research groups is desired. Ideally, the MPTA is included as preferred measurement method in the HTO guidelines, endorsed by international orthopaedic associations.

Chapter 4 is a systematic review that delves into the clinical relevance of KJLO after HTO. This review concludes that the existing evidence regarding the clinical consequences of an increased KJLO after HTO is controversial and somewhat limited. These controversies and limitations arise from the use of an inadequate KJLO measurement method, insufficient control over preoperative confounders that influence clinical outcomes, short-term follow-up duration post-HTO, and a limited number of included patients. Additionally, a significant portion of HTO studies (88% of included studies) employed a medial opening-wedge approach, leaving a notable gap in evidence concerning lateral closing-wedge HTO.

As a subsequent study, **Chapter 5** is a cohort study investigating the influence of increased KJLO (postoperative MPTA≥95°) and KJLO change (MPTA change≥8°) on patient-reported outcomes and radiological progression of osteoarthritis after lateral closing-wedge HTO. Propensity score matching method was employed to control for preoperative confounders. Analysis of the data show that an increased KJLO or KJLO change after lateral closing-wedge HTO does not adversely influence the patient-reported outcomes and radiological progression of osteoarthritis at a follow-up length of 5 years.

Chapter 6 is a cohort study investigating the influence of increased KJLO (postoperative MPTA≥95°) on the survival of lateral closing-wedge HTO. An increased KJLO does not seem to influence the long-term survival of lateral closing-wedge HTO (mean follow-up 13 years). Additionally, female gender and an untargeted valgus alignment (hip-knee-ankle angle <2° or >6° valgus) are risk factors for conversion to TKA after lateral closing-wedge HTO.

Chapter 7 investigates situations where HTO is no longer effective, leading to TKA as an alternative treatment. The study compares patient-reported outcomes and radiological parameters between patients after TKA with and without a prior HTO, showing no significant differences in patient-reported outcomes and radiological parameters between the two groups.

The final chapter, **Chapter 8**, presents a general discussion and outlines future perspectives based on the findings in **Part I**, **Part II**, and **Part III**. The current long leg filming techniques used are discussed, as well as the rationale for advocating MPTA as the preferred KJLO measurement method. Other major discussions include the HTO indication criteria, the choice between Fujisawa point and lateral tibial spine as the correction points, and technical challenges in TKA with a prior HTO. Future research is suggested to focus on long-term outcome of medial opening-wedge HTO in order to compare this with the findings of this thesis focusing on lateral closing wedge HTO. Additionally, adopting 3D techniques for KJLO measurement and exploring the influence of increased KJLO on gait pattern is recommended.

In conclusion, the adoption of the medial proximal tibial angle (MPTA) for knee joint line obliquity measurement is recommended in orthopaedic practices. Postoperative knee joint line obliquity exceeding 95° or changes over 8° after lateral closing-wedge high tibial osteotomy may not be of concern. Successful outcomes in lateral closing-wedge high tibial osteotomy rely on a correction range of 2°-6°, with a target of 4° valgus, and males exhibit better long-term survival than females. The presence of a prior high tibial osteotomy is not a concern when performing total knee arthroplasty in terms of patient-reported outcomes.

Nederlandse Samenvatting

Artrose van de knie veroorzaakt pijn, stijfheid en een verminderde mobiliteit, wat een zware last betekent voor patiënten en de samenleving. Een valgiserende proximale of hoge tibia osteotomie (HTO) is een effectieve operatie voor de behandeling van mediale knieartrose bij een varusbeenas. Deze operatie vergroot echter de scheefstand van het kniegewricht (KJLO) in het frontale vlak. Het is voor kniechirurgen de vraag in hoeverre rekening moet worden gehouden met deze KJLO in de preoperatieve planning van een HTO.

Om deze klinische vraag te kunnen beantwoorden, is de eerste stap het vaststellen van een gestandaardiseerde methode voor het meten van KJLO. Vervolgens kunnen de klinische consequenties van een toegenomen KJLO na een laterale gesloten wig HTO worden bepaald. Soms neemt ook na een HTO artrose dusdanig toe dat alsnog een totale knieprothese (TKP) nodig is. De vraag daarbij is, of een eerdere HTO een negatieve invloed heeft op de uitkomst van een totale knie prothese.

Dit proefschrift heeft drie doelstellingen: (1) Het onderzoeken van de meetmethoden voor het meten van de scheefstand van de joint line (KJLO), inclusief een beschrijving van de huidige gebruikte methoden en het aanbevelen van een voorkeursmethode voor het meten van KJLO bij HTO; (2) Het onderzoeken van de invloed van een toegenomen KJLO op door de patiënt gerapporteerde uitkomsten (PROMs), op de radiologische resultaten en op de overleving van een laterale gesloten wig HTO; (3) Het beoordelen van de verschillen tussen de uitkomsten van het plaatsen van een totale knieprothese na een HTO en die van een totale knieprothese zonder voorafgaande HTO, met de focus op PROMs en radiologische parameters.

Na de algemene inleiding behandelt deel I de eerste doelstelling in hoofdstuk 2 en 3, deel II richt zich op de tweede doelstelling in hoofdstuk 4, 5 en 6, en deel III gaat dieper in op de derde doelstelling in hoofdstuk 7.

Hoofdstuk 2 is een scoping review waarin het gebrek aan consensus bij het meten van KJLO wordt belicht. Er zijn vijf verschillende meetmethoden geïdentificeerd, waarbij gebruik werd gemaakt van anteroposterieure beenas opnames met patiënten zowel staande op één als op twee benen, en waarbij de afstand tussen de voeten bij de twee-benige opnames varieerde. Dit hoofdstuk pleit voor het vaststellen van een voorkeursmethode voor de KJLO-meting, die vervolgens een cruciale basis moet vormen voor toekomstige klinische en biomechanische KJLO-studies. Bovendien is het standaardiseren van de meetmethode van belang om zinvolle vergelijkingen van KJLO-onderzoeksresultaten in verschillende klinieken met verschillende protocollen ten aanzien van de beenas opnames mogelijk te maken.

Vervolgens wordt in Hoofdstuk 3 een cross-sectioneel onderzoek beschreven waarin de vijf KJLO-meetmethoden worden vergeleken met betrekking tot hun meetstabiliteit en betrouwbaarheid. De resultaten van dit onderzoek geven aan dat de mediale proximale tibia hoek (MPTA) de voorkeursmethode is om KJLO te bepalen. Dit komt omdat de MPTA-meting voldoende betrouwbaarheid toont, die niet wordt beïnvloed door verschillen in de positionering van de patiënt, bijvoorbeeld door het staan op één of twee benen of door verandering van de afstand tussen beide voeten. Bovendien is de MPTA eenvoudig te meten. Daarom is een bredere implementatie van MPTA als de gestandaardiseerde methode voor KJLO-meting onder kniechirurgen en onderzoeksgroepen gewenst. Idealiter wordt de MPTA als voorkeursmeetmethode opgenomen in de HTO-richtlijnen, onderschreven door internationale orthopedische verenigingen.

Hoofdstuk 4 is een systematische review waarbij ingegaan wordt op de klinische relevantie van KJLO na HTO. Er wordt geconcludeerd dat het bestaande bewijs met betrekking tot de klinische gevolgen van een toegenomen KJLO na HTO controversieel en enigszins beperkt is. Deze controverses en beperkingen komen voort uit het gebruik van een inadequate KJLO-meetmethode, onvoldoende controle over preoperatieve confounders die de klinische uitkomsten beïnvloeden, de korte follow-upduur na HTO, en een beperkt aantal geïncludeerde patiënten. Bovendien maakte een aanzienlijk deel van de HTO-onderzoeken (88% van de geïncludeerde onderzoeken) gebruik van een mediale open wig benadering, waardoor er een opmerkelijke leemte achterbleef in het bewijsmateriaal met betrekking tot laterale gesloten wig HTO.

Als vervolgstudie wordt in Hoofdstuk 5 een cohortstudie beschreven die de invloed onderzoekt van een toegenomen KJLO (postoperatieve MPTA≥95°) en KJLO-verandering (MPTA-verandering≥8°) op door de patiënt gerapporteerde uitkomsten en radiologische progressie van artrose na een laterale gesloten wig HTO. De Propensity Score Matching-methode werd gebruikt om te controleren op preoperatieve confounders. Analyse van de gegevens toont aan dat een toegenomen KJLO of KJLO-verandering na laterale gesloten wig HTO geen nadelige invloed heeft op de door de patiënt gerapporteerde uitkomsten en radiologische progressie van artrose bij een follow-upduur van 5 jaar.

Hoofdstuk 6 beschrijft een cohortstudie die de invloed van toegenomen KJLO (postoperatieve MPTA≥95°) op de overleving van laterale gesloten wig HTO onderzoekt. Een toegenomen KJLO lijkt de overleving op lange termijn van een laterale gesloten wig HTO niet te beïnvloeden (gemiddelde follow-up 13 jaar). De resultaten laten bovendien zien dat het vrouwelijk geslacht en een onnauwkeurige valgusuitlijning (heup-knie-enkelhoek <2° of >6° valgus) risicofactoren zijn voor conversie naar een TKP na een laterale gesloten wig HTO.

In Hoofdstuk 7 worden patiënten onderzocht die een TKP hebben gekregen na een laterale gesloten wig HTO. De studie vergelijkt PROMs en radiologische parameters van patiënten na TKP met en zonder eerdere HTO, waarbij geen significante verschillen in PROMs en radiologische bevindingen tussen de twee groepen zijn aangetoond.

Het laatste hoofdstuk, Hoofdstuk 8, beschrijft een algemene discussie en schetst toekomstperspectieven op basis van de bevindingen in Deel I, II en III. De huidige gebruikte beenas-opnametechnieken worden besproken, evenals de redenen voor het bepleiten van MPTA als de voorkeursmeetmethode om de KJLO te bepalen. Andere belangrijke discussies zijn onder meer de HTO-indicatie criteria, de keuze tussen het Fujisawa-punt en de laterale tibiale eminentia als correctiepunten, en technische uitdagingen bij het plaatsen van een TKP na een eerdere HTO.

Er wordt gesuggereerd dat toekomstig onderzoek zich zou kunnen richten op de langetermijnresultaten van de mediale open wig HTO, om zodoende te vergelijken met bevindingen uit dit proefschrift wat draaide om lateraal gesloten wig HTO. Daarnaast wordt aanbevolen om 3D-technieken toe te passen voor KJLO-meting en om de invloed van een toegenomen KJLO op het looppatroon te onderzoeken.

Concluderend wordt het gebruik van de mediale proximale tibia hoek (MPTA) aanbevolen voor het meten van KJLO. Een postoperatieve MPTA groter dan 95° of veranderingen van meer dan 8° na een laterale gesloten wig HTO hoeven geen klinische consequentie te hebben. Succesvolle resultaten zijn afhankelijk van een correctiebereik van 2°-6°, met een streefwaarde van 4° valgus, en mannen vertonen een betere overleving op de lange termijn dan vrouwen. Een eerder uitgevoerde HTO hoeft bij het plaatsen van een totale knieprothese geen reden tot zorg te zijn als het gaat om patiënt gerapporteerde uitkomsten.

Chapter 10

Appendices
Acknowledgement
About the author

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About the author

Tianshun Xie is from Shenzhen, China. After graduating from high school in 2009, he enrolled in university to study electronic information engineering. In his second year of undergraduate studies, he found his interest in medicine and subsequently changed his major to clinical medicine. After obtaining his Bachelor of Medicine degree, he pursued further studies abroad, completing the master program in Ireland in 2017.

He has already obtained the medical license and registration in China. After finishing his master degree, he returned to China to undergo the national residency training in surgery, successfully obtaining the certificate. Then, he served as a resident doctor in orthopaedics and traumatology at a teaching hospital. During this period, he successfully passed the examination for the attending doctor certificate in orthopaedics in China. In addition, he has completed the Part I and II of LMCHK examination.

In August 2021, he came to the Netherlands to conduct clinical and biomechanical research on knee joint preserving surgery, which resulted in this PhD thesis. After completing the PhD, he will work as a surgeon in a teaching hospital in China, specializing in orthopaedics and sports medicine.

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