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Review Article

Differences between open-wedge versus closed-wedge high tibial osteotomy on clinical and radiological outcomes and adverse events

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Abstract: High tibial osteotomy (HTO) is a widely accepted procedure to treat medial knee osteoarthritis, which is performed either with open-wedge (OWO) or closed-wedge osteotomy (CWO). This meta-analysis was designed to evaluate whether OWO had an advantage over CWO regarding the clinical and radiographic results, and complications. Multiple comprehensive databases, including PubMed, Embase, Web of Science and Cochrane Library, were searched from their inception to October 2017. A total of 28 publications reporting 24 clinical trials were finally eligible. The OWO showed significantly greater posterior tibial slope compared to CWO, and the result remained unchanged over time. Moreover, patellar height decreased after OWO, but increased after CWO. No significant difference was detected for complications, such as infection, re-operation, nonunion, and revision to joint arthroplasty. No difference was found between them regarding the improvement of pain and knee function. Although both techniques led to the good and comparable clinical results, we recommended OWO as an alternatively effective treatment option for selected younger patients, which is easier to perform and to convert to TKA, avoids tibiofibular joint disruption and common peroneal nerve palsy, and permits multiplanar correction, as compared to CWO. However, additional well-designed studies are required to identify fixation type and augment selection in OWO.

Keywords: Total knee arthroplasty, high tibial osteotomy, clinical outcome, meta-analysis

Introduction

Varus deformity of knee joint increases the risk of progression of medial compartment osteoarthritis (OA) [1, 2]. High tibial osteotomy (HTO) is a well-established surgical technique for individuals with medial OA and varus deformity. It can shift the mechanical axis towards the lateral compartment to change the load distribution across the knee and weaken the stress concentration in the medial compartment of knee [3, 4]. Two techniques, such as closed-wedge osteotomy (CWO) and open-wedge osteotomy (OWO), are commonly available [5-7]. Many studies showed good clinical and radiological results for both OWO and CWO techniques [8-10]. The CWO has several disadvantages, such as more demanding subsequent TKA, the need for fibular osteotomy, more neurovascular complications, and bone stock loss [5, 6, 11]. Compared to CWO, OWO is described later in order to avoid fibular osteotomy and thereby reduce the rate of co-morbidity related to it. In addition, with the introduction of specific locked implants and bone-substituting biomaterials, OWO has gained popularity in recent years, because it has several advantages over CWO, including rapid rehabilitation, easier subsequent TKA, and easier adjustment of alignment correction [12-15]. Nevertheless, OWO can result in some complications, such as relatively high nonunion rates at the osteotomy site, patella baja and increased posterior tibial slope [5, 6, 16]. In addition, many of these studies contained relatively small cohorts and demonstrated inconsistent outcomes [2, 17-20]. Thus, no superiority of any technique over the other has been proven, and the choice remains basically on the surgeon's preference.

Several meta-analyses were published on this topic without conclusive results [21-24]. Smith *et al*. reported that no difference was identified for any clinical outcome or complication between OWO and CWO [24]. However, Sun *et al.* demonstrated that CWO led to a higher incidence of opposite cortical fracture, and OWO provided higher accuracy of correction [21]. Unfortunately, these studies contained some methodological shortcomings, errors in inclusion criteria and data extraction, and high heterogeneity. Not only did these studies have these limitations, but also their conclusions were inconsistent (**Table 1**). Two meta-analyses only investigated the radiographic results between OWO and CWO [22, 25]. But we think that the "safety" and "clinical outcomes" of the two techniques should also be the key words. Considering all these issues, whether OWO has advantages over CWO for the patients with medial compartment OA remains controversial, and it is impossible to give clear advice on which method to adopt. Recently, numerous studies on this topic have been published with inconclusive results [2, 11, 17, 19, 26-33]. Moreover, two investigations with longer follow-up time have been published recently, so we can conduct subgroup analysis to evaluate whether the clinical and radiological effect of HTO changes with time [2, 17].

Thus, we conducted this meta-analysis to determine whether OWO was superior to CWO with respect to: 1) clinical outcomes; 2) radiological outcomes; and 3) complications. Furthermore, to perform a reliable and comprehensive evaluation of the advantages and disadvantages of these two procedures, we added many new statistical indicators that have not been reported before.

Materials and methods

This meta-analysis design was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) prospectively.

Literature search

We systematically searched multiple electronic databases including PubMed, Embase, Web of Science, and Cochrane Library from their inception to 29th October 2017. The search strategies adopted included the following terms: ("High tibial osteotomy" OR "Tibial osteotomy" OR "Osteotomy") AND ("Open" OR "Close" OR "Closed" OR "Closing").

After the initial electronic search, Google Scholar and the citation lists of the studies included were checked for relevant articles. Searches of relevant journals, medical association and society web sites were also conducted. Each eligible study's corresponding author was contacted via e-mail to obtain any further information. There were no restrictions in terms of the date, research site, or status of publication.

Study selection

All randomized controlled trials (RCTs) and non-RCTs (n-RCTs) were eligible for inclusion if they satisfied the search strategy and compared OWO to CWO regarding the following outcomes: Clinical outcomes (length of hospital stay, operation time, patient satisfaction, Hospital for Special Surgery (HSS) knee score, Lysholm knee score, knee range of motion (ROM), knee pain visual analog score (VAS); Radiographic outcomes (patellar height measured by three different methods, posterior tibial slope angle, hip-knee-ankle (HTA) angle, and mean angle of correction); Complications (infection, revision surgery, non-union, common peroneal nerve palsy, tibial plateau fracture, and revision to TKA). Any cadaver and animal study, comment, letter, editorial, protocol, guideline, and review papers were excluded.

Study identification was performed based on the predefined eligibility criteria. After eliminating duplications, two reviewers independently screened the titles and abstracts of all studies that were identified with the search strategy and discarded those that were obviously ineligible. If suitability could not be determined, the full article was assessed. Any disagreement was resolved through discussion.

Data extraction

The data were collated independently by two reviewers onto a predefined data extraction form. Variables recorded included: patient demographics, surgical technique, implant used, follow-up period, methodology, complica-

Table 1. Details of meta-analyses and systematic review published on this subject

Author	Year	Studies included	Patients (knees)	Indicators	Conclusions	Main Shortcoming
Smith et al.	2011	12 pubications (9 clinical trials)	621 (642)	Clinical and radiological results	1. No significant difference was found for any clinical outcome; 2. Significantly greater posterior tibial slope and reduced patellar height and hip-knee-ankle angle following opening-wedge HTO	1. Numerous studies on this subject have been published with inconclusive results; 2. Two investigations with longer follow-up time have been published
Brouwer et al.	2014	21 pubications (14 clinical trials)	1065	Clinical and radiological results	1. No evidence suggests differences between different osteotomy techniques; 2. No evidence shows whether an osteotomy is more effective than alternative surgical treatment such as unicompartmental knee replacement or non-operative treatment	1. CWO was compared with other types of HTO such as OWO, combined high tibial osteotomy, etc.; 2. All the osteotomy techniques except CWO were considered as identical method
Bin et al.	2016	23 studies	1150	Patellar height	1. The patellar height decreased after OWO, except when assessed by ISI; 2. Patellar height was unchanged after closing wedge HTO, regardless of the measurement method	1. They did not use sensitivity analysis to investigate the origin of high heterogeneity, thereby resulting in an unstable result; 2. The meta-analysis included OCS, PCS and RCS, but subgroup analysis based on article type was not conducted to evaluate the stability of the meta-analysis; 3. These included studies with different follow-up times was pooled for analysis. They should conduct subgroup analysis to evaluate whether the clinical and radiological effect of HTO changes with time; 4. They only focused on the patellar height, we think that "safety" of the two techniques should be the key words
Sun et al.	2016	23 publications (17 clinical trials)	1444 (1483)	Clinical and radiological results	1. OWO increased the posterior slope angle and decreased the patellar height, and provided higher accuracy of correction; 2. CWO led to a higher incidence of opposite cortical fracture.	1. They stated that they excluded the duplicated publications and chose one of them, but two duplicated publications were included in this study; 2. The significant difference between the groups regarding complications was conducted based on two publications. They concluded that CWO led to a higher incidence of opposite cortical fracture, which was not credit; 3. They used "Cochrane tool" to assessing risk of bias for RCTs and n-RCTs; 4. A sensitivity analysis was conducted to compare the outcomes between OWO and CWO for RCTs only. With a small number of studies, authors have suggested that random effects models may not be reliable irrespective of the homogeneity test; 5. The random-effects model should be compared with the fixed-effects model
Nha et al.	2016	27 studies	1260	Posterior tibial slope	1. Posterior tibial slope increased after OWO and decreased after CWO; 2. Both osteotomy techniques may have little effect on the biomechanics of the cruciate ligaments	1. They did not use sensitivity analysis to investigate the origin of high heterogeneity, thereby resulting in an unstable result; 2. The meta-analysis included OCS, PCS and RCS, but subgroup analysis based on article type was not conducted to evaluate the stability of the meta-analysis; 3. These included studies with different follow-up times was pooled for analysis. They should conduct subgroup analysis to evaluate whether the clinical and radiological effect of HTO changes with time; 4. They only focused on the patellar height, we think that "safety" of the two techniques should be the key words

CWO, closed wedge high tibial osteotomy; OWO, open wedge high tibial osteotomy; HTO, high tibial osteotomy; PCS, prospective comparison study; RCS, retrospective comparison study; OCS, observational case series.

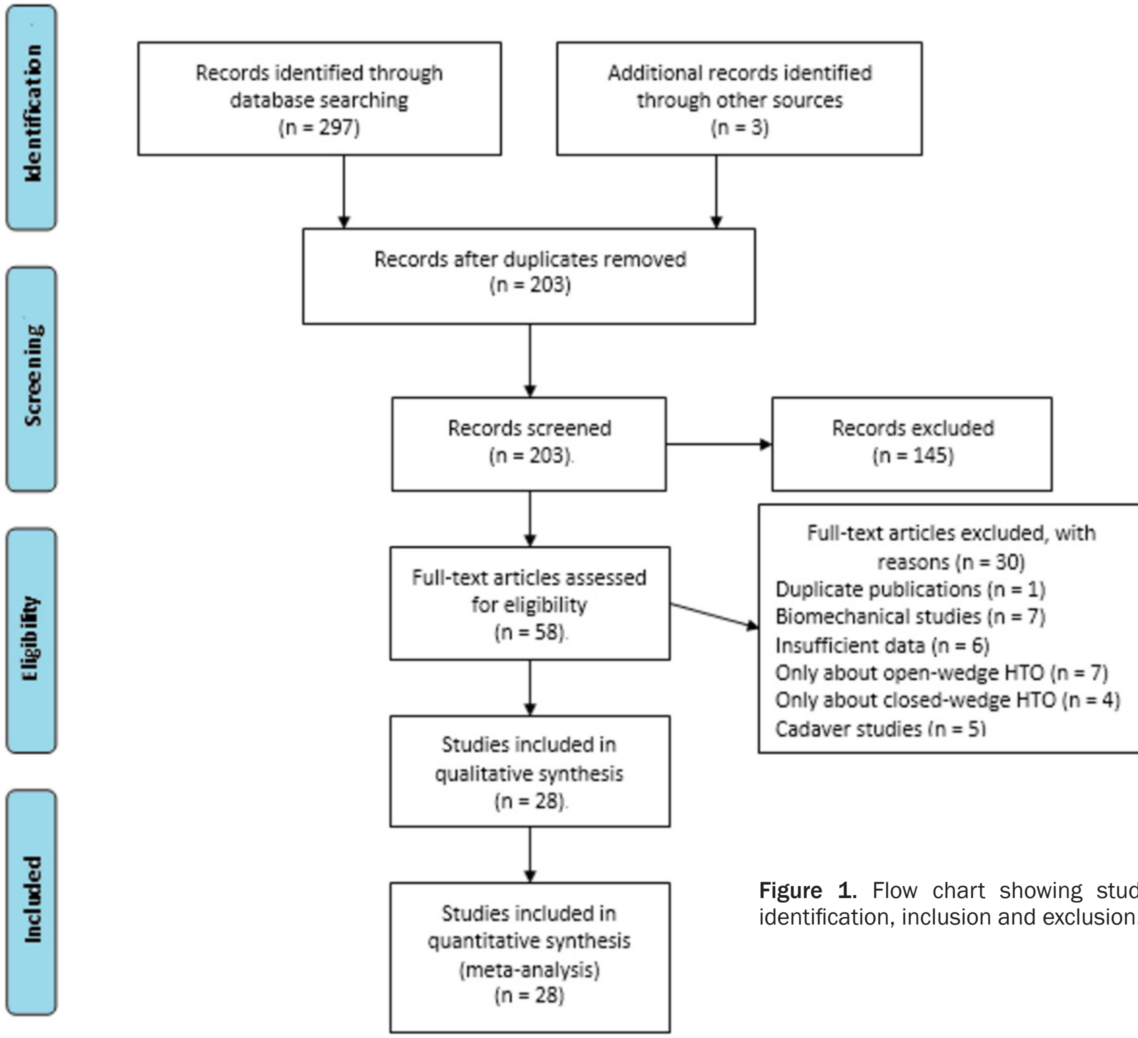

Figure 1. Flow chart showing study identification, inclusion and exclusion.

tions, and clinical and radiographic outcomes. Any disagreement unresolved after discussion was decided by a third reviewer. In addition, the study authors were contacted by email to request these variables that were not provided in the publications. Missing standard deviations were calculated through the confidence intervals (CI) or range of values available in the studies.

Special focus was paid on knee function outcomes between OWO and CWO. Therefore, the primary outcomes were severity of pain, the improvement in HSS and ROM. While, other clinical outcomes, radiographic assessment, and complications were regarded as secondary outcomes.

Assessment of study quality

Two independent reviewers evaluated the methodological quality of eligible studies using the modified Jadad scale for RCTs and the Newcastle-Ottawa Scale for n-RCTs. The modified Jadad scale contains four questions evaluating random sequence generation (2 points), allocation concealment (2 points), blinding appropriateness (2 points), and dropouts or withdrawn description (1 point). The total score is 7 points, and a study with 4-7 points is considered as a high-quality study. The Newcastle-Ottawa Scale awards stars depending on the level of bias, which includes low (1 star), high, and unclear bias. We assessed each study on 3 criteria: the selection of the study groups (0-4 stars), the comparability of the groups (0-2 stars), and the ascertainment of the exposure or outcome of interest (0-3 stars). Total scores range from 0 to 9 points. A study with scores of 7-9 points is regarded as a high-quality study. Any discrepancies were settled by consensus or by consultation with a third reviewer.

Statistical analysis

The statistical analysis was performed using Review Manager 5.3 software (The Nordic Cochrane Center, The Cochrane Collaboration) and a *P*-value <0.05 was considered to be significant. For each eligible study, the results of dichotomous variables were presented as odds ratios (OR) with corresponding 95% CI. If continuous variables were measured in the same way between studies, the mean differences (MD) were used. Otherwise, standardized mean differences (Std MD) with 95% CI values were adopted.

The assessment of heterogeneity was conducted with use of the chi-squared test and I^2 statistic to determine appropriateness for meta-analysis. If statistical heterogeneity was moderate ($P<0.1$ or $I^2>50\%$), a random-effects model was chosen to estimate the overall effect sizes. When these conditions were not satisfied, fixed-effects model was used. Moreover, publication bias was assessed with funnel plots and the Egger test of the primary outcomes. Subgroup analysis was performed for different time points (<1 year or >1 year). Moreover, sensitivity analysis was carried out to investigate the potential sources of heterogeneity and to determine the effect of study quality on the results.

Results

Literature search and population characteristics

The process of study selection was showed in **Figure 1**. We totally identified two hundred and ninety-seven records via our search strategy. Another three studies were identified through manual searching. After screening the search results, eleven investigations had been published by the four independent research teams. To eliminate the effect of duplicate data, we attempted to contact each author in order to confirm whether the data in their studies were reported from the same patient cohorts. One study [8] was a duplicate of a previous study presenting the same parameters [34]. However, eight publications reported the results of different parameters from three separate studies [2, 11, 12, 34-38]. In addition, two investigations were conducted as an update of two previous reports after longer follow-up time [2, 17, 20, 34]. Therefore, these studies were included in this meta-analysis, but we only analyzed the population characteristics of these four individual patient cohorts once. After removing duplications and reading the full-text, a total of 10 RCTs and 18 n-RCTs met our inclusion criteria (**Figure 1**).

Table 2 displayed the detailed characteristics of the studies. A total of 2701 evaluable knees were available for analysis in this study. These 24 eligible studies included 1368 knees that underwent closed-wedge HTO and 1335 knees that underwent open-wedge HTO. All publications were published in English from 1999 to 2016. The mean age of the patients ranged from 34 to 60 years. And, 44.7% of the patients were males. Although the osteotomies were fixated using plates or staples in the majority of the studies, we included all different fixation methods to compare the two approaches. The evidence-based methodological assessment was varied. **Table 2** presented the results of modified Jadad and the Newcastle-Ottawa clinical critical appraisal. Nineteen of the twenty-four studies achieved a high-quality score (modified Jadad ≥4 or Newcastle-Ottawa ≥7) (**Table 2**). We used data reporting a change from baseline as our effect index in primary outcomes (VAS, HSS and ROM).

Primary outcomes

VAS pain score

Data on 336 knees (including 166 knees that underwent open-wedge HTO and 170 knees that underwent closed-wedge HTO) were pooled from seven trials in eight publications [2, 17, 18, 20, 27, 34, 35, 39] analyzing the VAS pain scores. Pooled results illustrated no significant difference in the improvement of knee pain in the OWO group, when compared to the CWO group (MD=-0.15, 95% CI=-0.22 to 0.52; *P*=0.24; I^2=40%). Considering that the origin of heterogeneity may be attributed to the duration of follow-up, subgroup analysis was conducted based on different follow-up time (Group A: less than 1 year follow-up; Group B: more than 1 year follow-up). No statistically significant difference was identified either in Group A (*P*=0.45; I^2=34%) or in Group B (*P*=0.68; I^2=35%) with low heterogeneity (**Figure 2** and **Table 3**).

Table 2. Characteristics of the included studies

Author	Year	Study	Cases (n)		Age (mean)		Gender (M/F)		Fixation		Quality score
			CW	OW	CW	OW	CW	OW	CW	OW	
Kim et al.	2016	RCT	30	30	54	54	10/20	9/21	Stepped plate	TomoFix plate	6
Van Egmond et al.	2016	RCT	19	19	NA	NA	NA	NA	Locked plate	Locked plate	4
Nerhus et al.	2015	RCT	35	35	30-60	30-60	NA	NA	Puddu titanium plate	Staples	6
Duivenvoorden 1 et al.	2014	RCT	45	36	50	50	27/18	21/33	Staples	Puddu plate	4
Gaasbeek et al.	2010	RCT	25	25	50	47	16/9	14/11	Locked plate	Locked plate	4
Luites et al.	2009	RCT	19	23	53	53	NA	NA	TF plates and screws	TF plates and screws	5
Brouwer 1 et al.	2006	RCT	47	45	51	50	24/20	27/20	Staples	Puddu plate	4
Brouwer 2 et al.	2005	RCT	24	26	53	48	12/12	20/6	Staples	Puddu plate	4
Magyar 1 et al.	1999	RCT	15	18	53	55	12/3	10/8	Bone staple	Orthofix OF-Garche Fixtior	5
Magyar 2 et al.	1999	RCT	25	25	55	55	NA	NA	Bone staple	External fixation	5
Agarwala et al.	2016	PCS	25	23	55	56	13/10	13/12	Locked plate and screws	Locked plate and screws	6
Duivenvoorden 2 et al.	2015	RCS	354	112	49	48	NA	NA	Three different staples	Puddu plate/Tomofix plate	7
Portner et al.	2014	RCS	18	26	46	44	15/3	20/6	Staple gun	Plate and screws	7
Deie et al.	2014	RCS	12	9	58	58	3/9	3/6	Plate and screws	Plate and screws	6
Tabrizi et al.	2013	PCS	21	21	37	35	12/4	13/3	Plates	L or T plates	8
Bae et al.	2013	RCS	78	30	58	56	4/70	2/25	Miniplate staple	Puddu plate	6
Amzallag et al.	2013	PCS	97	224	50	53	NA	NA	NA	NA	8
Songet I.H. al	2012	RCS	50	50	60	58	12/38	10/40	Stepped staples	Wedge plates	7
Ducat et al.	2012	PCS	92	210	50	52	NA	NA	NA	NA	7
Magnussen et al.	2011	RCS	32	32	59	54	21/9	22/10	Blade and screws	Tomofix plate	8
Song E.K. et al.	2010	RCS	104	90	57	51	16/88	21/69	Two staples	Aescula plates	6
Hankemeier et al.	2010	RCS	26	35	53	44	NA	NA	Screw-plate fixation	Fixed-angle plates	6
El-Azab 1 et al.	2010	RCS	50	50	NA	NA	NA	NA	L-plate	Self-locking plate	7
Schiedel et al.	2009	RCS	30	31	34	45	18/7	19/10	T-Clamp and half pins	Wedge staple	6
Van den Bekerom et al.	2008	PCS	20	20	52	52	9/11	10/10	AO/ASIF L-plate	Modified puddu Plate	8
Schaefer et al.	2008	RCS	66	90	47	46	NA	NA	Wedge Blount's staples	T-Clamp and half pins	7
El-Azab 2 et al.	2008	RCS	60	60	NA	NA	NA	NA	L-plate	Non-locking/locking plate	7
Hoell et al.	2005	RCS	57	51	52	46	40/17	32/19	Coventry	Puddu plate	8

TF, TomoFix; CWO, closed wedge high tibial osteotomy; OWO, open wedge high tibial osteotomy; RCT, randomized controlled trial; RCS, retrospective cohort study; PCS, prospective cohort study; NA, not available.

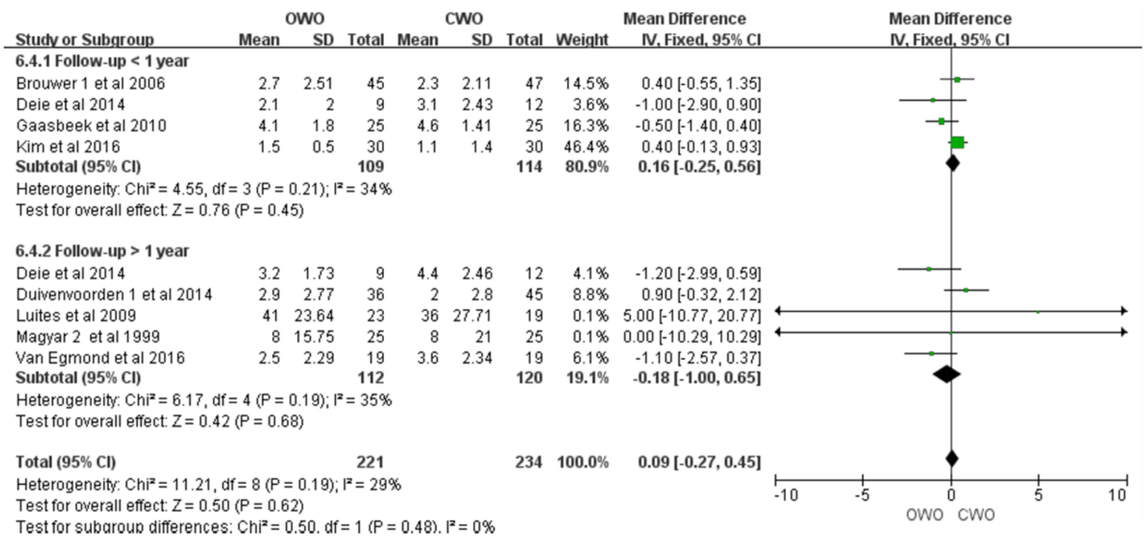

Figure 2. Forest plot of the improvement of VAS knee pain score between OWO and CWO (OWO open-wedge osteotomy, CWO closed-wedge osteotomy, CI confidence interval, df degrees of freedom).

ROM

Data on 571 knees in six trials [18, 31, 40-43] (including 277 knees in OWO Group and 294 knees in CWO Group) were analyzed with use of ROM for knee function assessment. There was no significant difference between the two groups in terms of the improvement of ROM (MD=-0.75, 95% CI=-1.92 to 0.41; *P*=0.2), and no significant heterogeneity between studies was seen (*P*=0.79, I^2=0%) (**Figure 3** and **Table 3**).

HSS

Data on 594 knees (including 290 knees that underwent OWO and 304 knees that underwent CWO) in seven trials [2, 17, 20, 31, 34, 35, 42, 43] were analyzed with regard to the HSS for overall clinical assessment. The findings demonstrated no significant difference between the two groups with respect to the improvement of HSS score (MD=-0.12, 95% CI=-1.01 to 0.76; *P*=0.78) with low heterogeneity (*P*=0.33, I^2=13%) (**Figure 3** and **Table 3**). Furthermore, in the subgroup analysis of follow-up time, there was no significant difference in Group A (MD=1.04, 95% CI=-2.39 to 0.32; *P*=0.13; I^2=0%) and Group B (MD=0.71, 95% CI=-0.61 to 1.71; *P*=0.2; I^2=7%).

Secondary outcomes

Clinical outcomes

There was no statistically significant difference in Wallgren-Tegner score [28, 35] (MD=0.87, 95% CI=-0.02 to 1.77; *P*=0.06), Lysholm score [28, 35, 39, 40] (MD=1.83, 95% CI=-0.99 to 4.65; *P*=0.20), or leg length (MD=-0.38, 95% CI=-10.18 to 9.43; *P*=0.94) between open-wedge and closed-wedge HTO with no heterogeneity (**Table 3**). In addition, no statistically significant difference between the two groups was identified with regard to complete weight bearing time [28, 40] (*P*=0.08), hospital stay [11, 20, 35] (*P*=0.25), and surgery time [11, 20, 28, 40] (*P*=0.83) with moderate heterogeneity (**Table 3**). Furthermore, the CWO group was associated with statistically higher patient satisfaction score compared with OWO group (*P*=0.0001), while no significant difference between the two groups was found in terms of the number of satisfied patients (*P*=0.33) with low heterogeneity (**Table 3**).

Radiological outcomes

Posterior tibial slope angle: Data on 1304 knees were pooled from twelve trials in fourteen publications [17-20, 26, 28, 29, 32, 36-38, 40, 42, 44] analyzing posterior tibial slope angle. There was a significantly greater posterior tibial slope angle in open-wedge HTO group compared to closed-wedge HTO group at any follow-up time point (Group A: MD=3.64, *P*<0.0001, I^2=86%; Group B: MD=5.64, *P*=0.009, I^2=70%) with moderate heterogeneity (**Figure 4** and **Table 4**).

HKA angle and Mean angle of correction: Data on 1226 knees in fifteen studies [2, 16-20,

Table 3. Results of meta-analyses in included studies

Variables	Studies (n)	Sample size	Overall Effect		Heterogeneity *P* Value (I^2)	Model
			P value	MD/OR (95% CI)		
Clinical outcomes						
HSS						
<1 year	4	250	0.13	1.04 (-2.39, 0.32)	0.70 (0%)	F
>1 year	6	511	0.2	0.71 (-0.38, 1.81)	0.37 (7%)	F
VAS knee pain						
<1 year	4	223	0.45	0.16 (-0.25, 0.56)	0.21 (34%)	F
>1 year	5	232	0.68	-0.18 (-1.00, 0.65)	0.19 (35%)	F
ROM	6	571	0.2	-0.75 (-1.92, 0.41)	0.79 (0%)	F
Wallgren-Tegner score	2	92	0.06	0.87 (-0.02, 1.77)	0.71 (0%)	F
Lysholm score	4	242	0.2	1.83 (-0.99, 4.65)	0.58 (0%)	F
Complete weight bearing	3	198	0.08	-15.19 (-32.4, 2.09)	<0.0001 (97%)	R
Hospital stay	3	566	0.25	-1.19 (-3.22, 0.85)	<0.0001 (95%)	R
Surgery time	4	666	0.83	-2.14 (-21.5, 17.2)	<0.0001 (97%)	R
Patients satisfaction score	2	90	0.0001	-1.32 (-1.99, -0.65)	0.21 (37%)	F
Leg length	4	302	0.94	-0.38 (-10.18, 9.43)	0.6 (0%)	F
Patients satisfaction (n)	2	198	0.33	0.74 (0.40, 1.36)	0.21 (38%)	F
Radiological outcomes						
Hip-Knee-Ankle angle						
<1 year	11	821	0.28	-0.20 (-0.57, 0.17)	0.19 (27%)	F
>1 year	8	622	0.3	0.59 (-0.51, 1.69)	<0.0001 (85%)	R
Mean angle of correction						
<1 year	10	887	0.97	-0.01 (-0.39, 0.37)	0.003 (64%)	R
>1 year	7	574	0.46	0.64 (-1.05, 2.33)	<0.0001 (92%)	R
Posterior tibial slope angle						
<1 year	9	894	<0.0001	3.64 (2.36, 4.92)	<0.0001 (86%)	R
>1 year	5	548	0.0001	5.64 (4.48, 6.81)	0.009 (70%)	R
PH: Caton index (cm)	4	532	0.0004	-0.80 (-1.10, -0.50)	0.007 (82%)	R
PH: Insall salvati index (cm)	6	367	0.04	-0.07 (-0.13, -0.00)	0.06 (52%)	R
PH: Blackburn peel ratio	4	311	0.0006	-0.09 (-0.14, -0.04)	0.04 (65%)	R
Complications						
Convert to joint arthroplasty	6	419	0.35	0.57 (0.17, 1.88)	0.17 (41%)	R
Infection	11	1347	0.92	0.97 (0.49, 1.91)	0.52 (0%)	F
Re-operation	7	1030	0.6	1.18 (0.64, 2.18)	0.76 (0%)	F
Deep vein thrombosis	4	780	0.73	0.76 (0.16, 3.54)	0.75 (0%)	F
Removal of OSM	2	142	0.06	2.09 (0.97, 4.47)	0.74 (0%)	F
Nonunion	6	874	0.93	0.96 (0.39, 2.35)	0.16 (42%)	F
Fracture of tibial plateau	4	860	0.01	4.88 (1.47, 16.20)	0.73 (0%)	F
Peroneal nerve neuropathy	9	1121	0.02	-0.03 (-0.06, -0.00)	0.72 (0%)	F
Anterior pain	3	234	0.71	1.14 (0.56, 2.30)	0.75 (0%)	F
Opposite cortical fracture	4	620	0.71	1.22 (0.42, 3.35)	0.46 (22%)	F
Removal of OSM	2	142	0.06	2.09 (0.97, 4.47)	0.74 (0%)	F
Iliac crest morbidity	2	558	0.0002	44.6 (5.93, 336.4)	0.57 (0%)	F

ROM, range of motion; VAS, Visual Analogue Scale; HSS, Hospital for Special Surgery; F, fixed-effects model; R, random-effects model; OSM, osteosynthesis material; OR, odds ratios; MD, mean differences.

26-30, 33, 35, 36, 39, 42, 43] were analyzed with use of HKA angle for radiological assessment. There was no significant difference between the groups regarding the HKA angle in either Group A (P=0.28, I^2=27%) or Group B (P=0.3, I^2=85%). Data on 1292 knees were pooled from fourteen studies in seventeen papers [2, 16-20, 26, 27, 29, 30, 33-35, 39, 42, 44] analyzing mean angle of correction. No significant difference was identified in respect

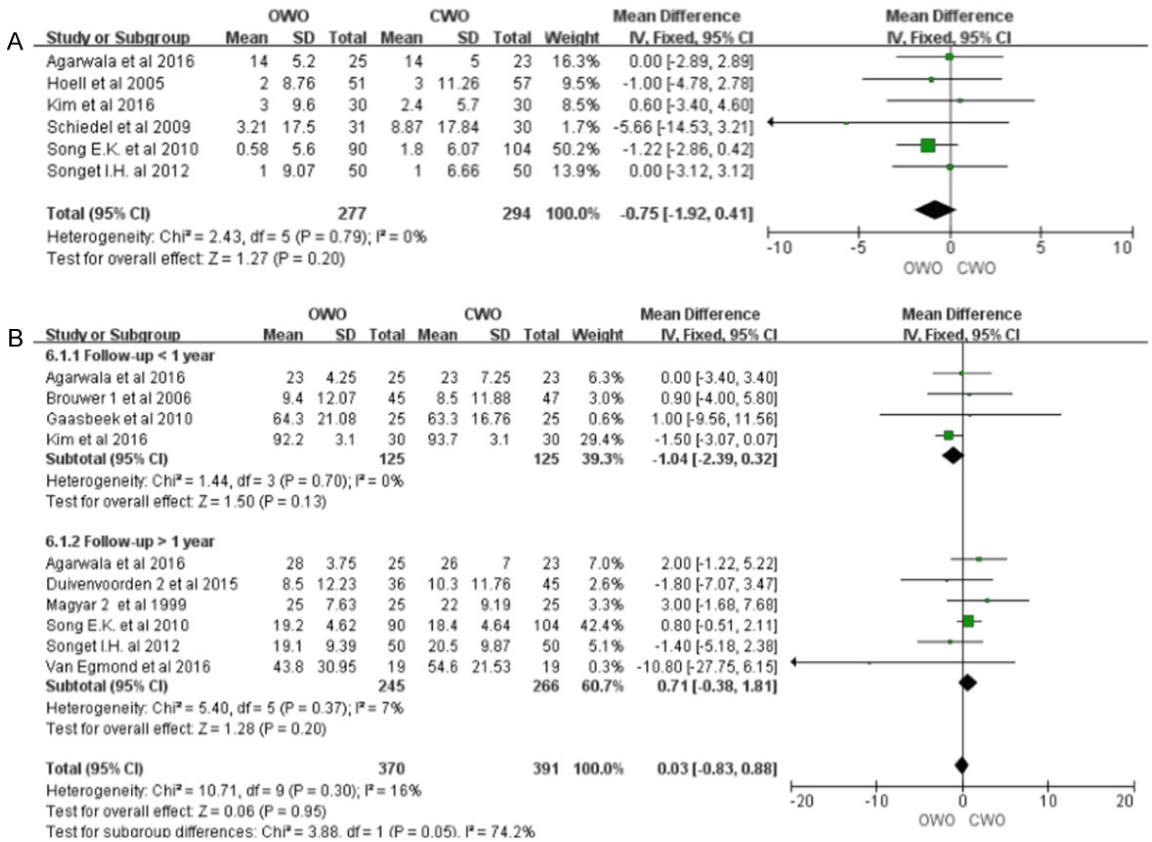

Figure 3. Forest plot of clinical knee function between OWO and CWO. A) for the improvement of ROM; B) for the improvement of HSS (OWO open-wedge osteotomy, CWO closed-wedge osteotomy, CI confidence interval, df degrees of freedom).

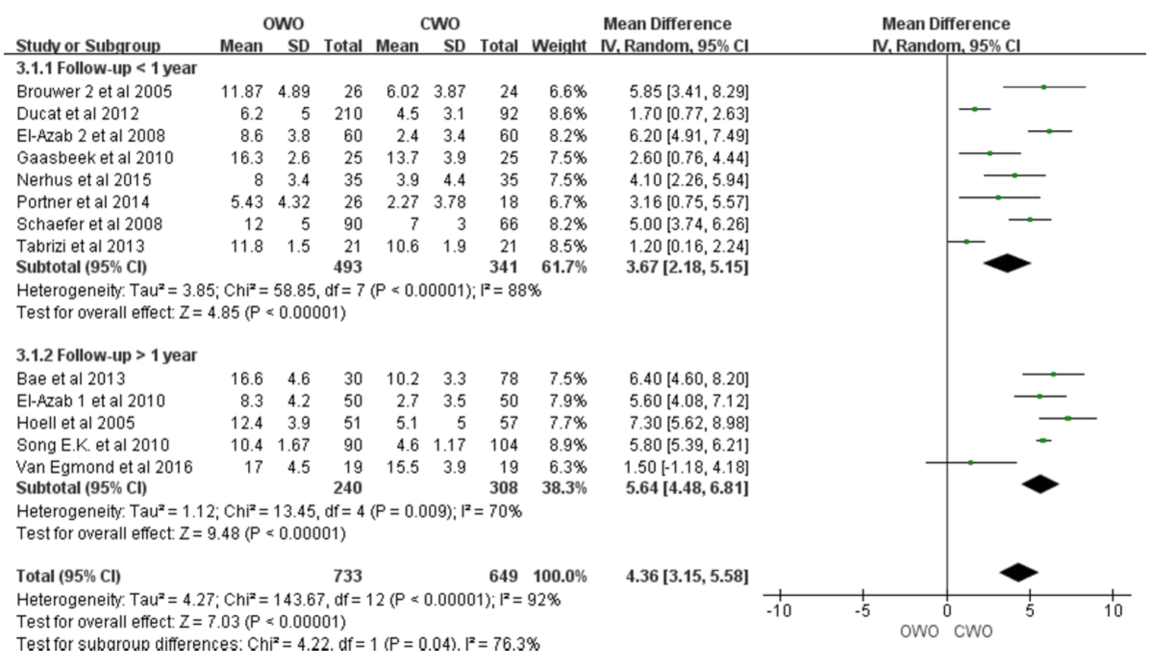

Figure 4. Forest plot of posterior tibial angle value between OWO and CWO (OWO open-wedge osteotomy, CWO closed-wedge osteotomy, CI confidence interval, df degrees of freedom).

Table 4. Results of the sensitivity analysis meta-analysis in included randomized controlled trials

Variables	Studies (n)	Sample size	Overall Effect		Heterogeneity *P* Value (I^2)	Model
			P value	MD/OR (95% CI)		
Radiological outcomes						
Hip-Knee-Ankle angle						
<1 year	5	322	0.51	-0.30 (-1.20, 0.60)	0.07 (55%)	R
>1 year	4	211	0.71	0.50 (-2.17, 3.18)	0.0001 (89%)	R
Mean angle of correction						
<1 year	5	322	0.18	-0.45 (-1.10, 0.20)	0.66 (0%)	F
>1 year	4	211	0.81	-0.25 (-2.35, 1.84)	0.0008 (82%)	R
Posterior tibial slope angle						
<1 year	5	350	<0.0001	4.42 (3.01, 5.83)	0.005 (73%)	R
>1 year	2	138	<0.0001	4.61 (3.29, 5.92)	0.34 (10%)	F
PH: Caton index (cm)	2	150	<0.0001	-0.15 (-0.19, -0.10)	0.34 (0%)	F
PH: Insall salvati index (cm)	3	220	0.03	-0.05 (-0.09, -0.00)	0.37 (0%)	F
PH: Blackburn peel ratio	2	150	0.0002	-0.09 (-0.14, -0.04)	0.55 (0%)	F
Migration						
Tx	2	75	0.38	0.50 (-0.62, 1.62)	0.09 (66%)	R
Ty	2	75	0.41	-0.86 (-2.89, 1.17)	0.003 (89%)	R
Tz	2	75	0.93	0.01 (-0.23, 0.25)	0.31 (2%)	R
Rx	2	72	0.39	1.01 (-1.30, 3.32)	0.03 (78%)	R
Ry	2	72	0.3	0.73 (-0.66, 2.11)	0.02 (82%)	R
Rz	2	72	0.48	1.21 (-2.14, 4.56)	0.0001 (93%)	R
Clinical outcomes						
HSS						
<1 year	3	202	0.1	-1.23 (-2.71, 0.25)	0.60 (0%)	F
>1 year	3	169	0.82	0.40 (-3.02, 3.83)	0.17 (43%)	F
VAS knee pain						
<1 year	3	202	0.32	0.21 (-0.20, 0.62)	0.22 (35%)	F
>1 year	4	221	0.83	0.10 (-0.83, 1.04)	0.21 (34%)	F
Lysholm score	2	92	0.07	5.34 (-0.44, 11.12)	0.87 (0%)	F
Complications						
Convert to joint arthroplasty	3	202	0.31	0.48 (0.12, 2.00)	0.14 (54%)	R
Infection	4	272	0.71	0.73 (0.14, 3.76)	0.53 (0%)	F
Peroneal nerve neuropathy	3	202	0.21	-0.03 (-0.08, 0.02)	0.94 (0%)	F
Re-operation	3	222	0.56	1.36 (0.49, 3.77)	0.31 (14%)	F

to mean angle of correction at any follow-up time point (Group A: $P=0.97$; Group B: $P=0.46$) with moderate heterogeneity (**Table 3**).

Patellar height: There was a significantly greater patellar height measured by the Caton index [20, 30, 38, 41] (MD=-0.13, $P<0.0001$), Blackburn Peel ratio [31, 36, 38, 41] (MD=-0.09, $P<0.0001$), and Insall Salvati index [19, 26, 28, 36, 38, 41] (MD=-0.05, $P=0.007$) in the CWO group, compared to the OWO group (**Figure 5** and **Table 4**).

Migration: Translation along the x-, y-, and z-axis (Tx, Ty, and Tz) and rotations about the x-, y-, and z-axes (Rx, Ry, and Rz) was record in two trials [12, 39] (73 knees). The diagram of the six directions, in which migration of the center of gravity of the proximal aspect of the tibia, was calculated. There were no significant differences with respect to the six directions in either less than or more than 6 months follow-up time (**Table 4**).

Complications

There was no statistically significant difference identified between open-wedge and closed-wedge HTO with regard to the incidence of deep or superficial infection, reoperation, DVT, non-union, removal of osteosynthesis, anterior pain or revision to joint arthroplasty. However,

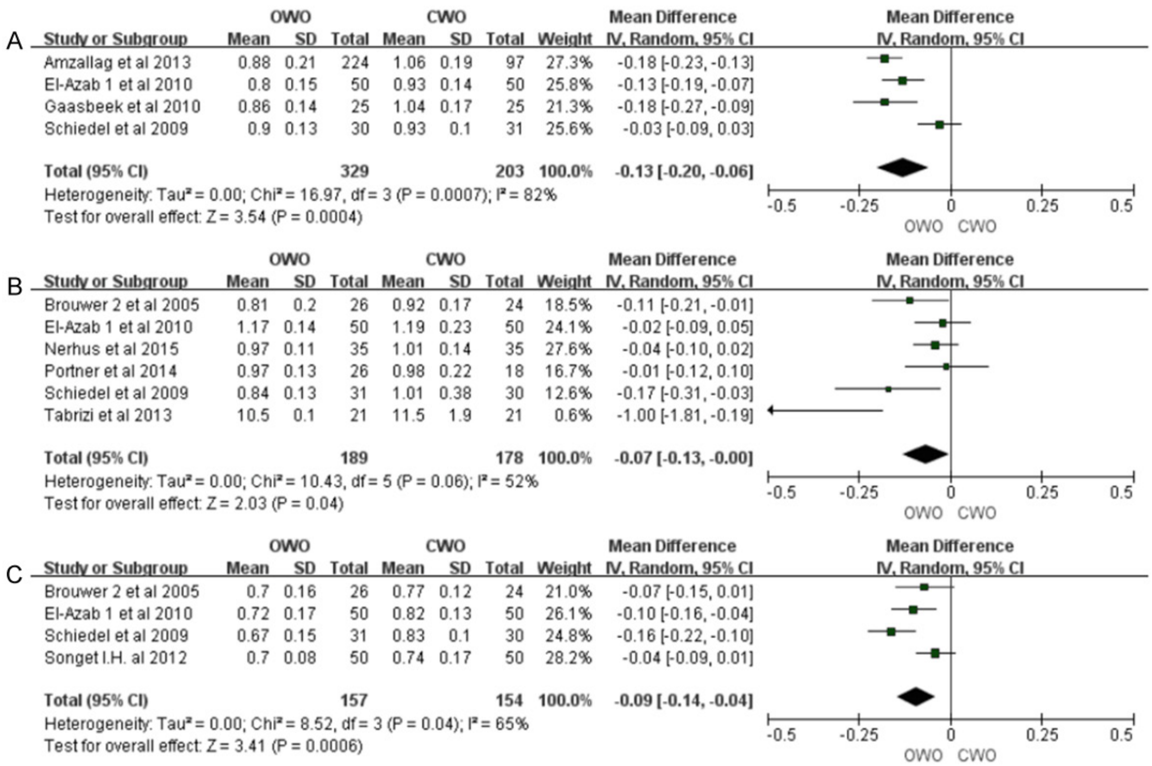

Figure 5. Forest plot of patellar height value between OWO and CWO. A) for patellar height measured by Caton-Deschamps index; B) for patellar height measured by Insall-Salvati; C) for patellar height measured by Blackburne-Peel index (OWO open-wedge osteotomy, CWO closed-wedge osteotomy, CI confidence interval, df degrees of freedom).

closed-wedge HTO was associated with lower incidence of intra-operative fracture of the tibial plateau (MD=4.88, *P*=0.01) and iliac crest morbidity (MD=44.6, *P*=0.0002) with no heterogeneity (**Table 3**). In addition, CWO showed higher incidence of common peroneal nerve palsy compared with OWO (MD=-0.03, *P*=0.02).

Sensitivity analysis

To validate our results, we conducted sensitivity analyses to determine the effect of study quality on the results. Firstly, the random-effects model was compared with the fixed-effects model, and the statistically similar results were obtained in respect to any outcome (data not shown). Secondly, a sensitivity analysis was performed to compare the outcomes between OWO group and CWO group for RCTs only. Compared to RCTs outcomes alone using the sensitivity analysis, no statistically significant difference was detected from this secondary sensitivity analysis to the main analysis in respect to clinical and radiological outcomes, suggesting the stability of our meta-analysis (**Table 4**). However, the sensitivity analysis did indicate that there was no significantly higher incidence of the common peroneal nerve palsy following CWO.

Publication bias

Publication bias was assessed through the Funnel plot. The shape of the funnel plots analyses on the improvement of VAS, HSS and ROM did not reveal basically asymmetric distribution, indicating that bias was minimal (**Figure 6**).

Discussion

The most important findings of this study were that significantly lower posterior tibial slope, greater patellar height measurements, and decreased incidence of patellar baja were observed following CWO, when compared to OWO. However, there were no significant differences regarding HKA angle, mean angle of correction and leg length between the two groups. Moreover, no significant differences were identified with respect to clinical outcomes.

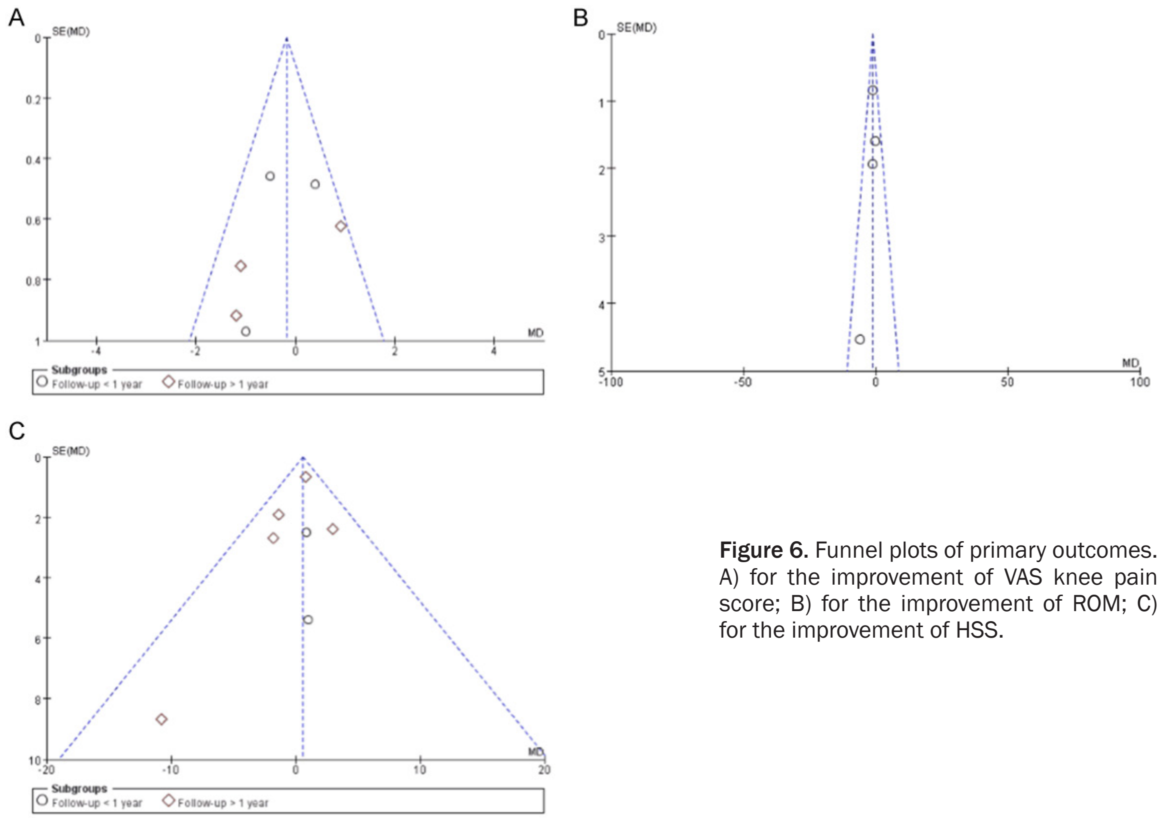

Figure 6. Funnel plots of primary outcomes. A) for the improvement of VAS knee pain score; B) for the improvement of ROM; C) for the improvement of HSS.

The results showed that posterior slope increases after open-wedge HTO and decreases after closed-wedge HTO. The unique anatomic geometry of the proximal tibia may cause the change of posterior tibial slope following HTO [36, 45, 46]. Increased tibial slope following OWO can produce an anterior translation in tibial resting position and increase the strain in the anterior cruciate ligament (ACL) [47, 48], while decreased slope following CWO can increase the strain in the posterior cruciate ligament (PCL) [49]. Thus, some studies reported that CWO was a therapeutic option for those with concomitant ACL injuries or insufficiency, while OWO was an appropriate method for those with PCL deficiency [46, 47, 50]. However, the study Nha *et al.* found that the change in posterior tibial slope was less than 5° (approximately 2°), indicating that both open- and closed-wedge HTO may have little effect on the in situ forces in the cruciate ligaments [22].

Three reference methods (Caton-Deschamps, Insall-Salvati or Blackburne-Peel index) were used to evaluate patellar height in these eligible studies. The findings demonstrated that patellar height decreased after OWO and increased after CWO using any measure. A possible interpretation is the shift of tibial tubercle at the distal section of the osteotomy. The CWO could elevate the tibial tuberosity due to a proximalisation of the proximal tibia and result in an increase in patellar height. Conversely, the OWO could lower the tibial tuberosity and resulted in a decrease in patella height [36]. Decreasing patellar height would result in patella baja, thereby generating technical difficulties during TKA, such as patella eversion and lateral compartment exposure. However, there was no difference regarding the improvement of pain and knee function outcomes (VAS pain score, ROM, and HSS) between OWO and CWO, suggesting that the difference in the patellar height has little influence on the clinical outcomes.

The HKA angle was calculated on standing whole leg radiographs, which was defined as the angle between the mechanical axis of the femur and tibia. A RCT by Brouwer *et al.* showed more accurate correction after CWO, compared to OWO [34]. Nevertheless, Magyar *et al.* reported that OWO with external fixator could lead to higher accuracy of the correction since it provides continuous radiographic evaluation [12]. Hankemeier *et al.* reported that it was difficult to correct such subtle difference in CWO [16]. Moreover, Gaasbeek *et al.* reported that no loss of correction was identified after one-year follow-up, suggesting that both OWO and CWO resulted in an accurate correction [20]. In this study, there was no statistically significant difference regarding the HKA angle and mean angle of correction at any follow-up time. Interestingly, our result was not consistent with the findings of the previous meta-analysis by Smith *et al.* suggesting that open-wedge HTO provided superior anatomical correction and might be interpreted by the following reasons: Firstly, two publications were conducted as an update of two previous studies, which had a longer follow-up time than previous studies did. The results of these studies suggested that the radiographic and clinical outcomes might change over time. Therefore, it is necessary to conduct subgroup analysis based on follow-up duration. Secondly, the small sample was included in the previous meta-analysis on this topic. Therefore, the results may reduce the power to reveal a reliable relationship. Thirdly, the sensitivity analysis including only two trials changed the results regarding HKA angle and mean angle of correction in previous meta-analysis. However, the sensitivity analysis was conducted through two different methods in this meta-analysis, and the results were consistent with the previous results regarding clinical and radiographic results, suggesting the results of this study were stable. In addition, the accuracy of the correction was highly important in the long-term results of HTO, such as fixation stability.

As for complications, closed-wedge HTO implied lateral muscle detachment, higher risk of peroneal nerve injury, more demanding subsequent TKA, bone stock loss and fibular osteotomy or proximal tibiofibular joint disruption. For the above-mentioned disadvantages of CWO, OWO was regarded as a safe and reproducible procedure and gained the popularity for being a widely accepted alternative option [51]. However, OWO was not free from some complications, such as nonunion, the necessity of bone graft, disease transmission and possible loss of correction [52]. In this meta-analysis, OWO showed higher incidence of intra-operative fracture of tibial plateau. Interpretation of the outcomes must be made with caution because the sample size was relatively small and the data were combined from one RCT and three n-RCTs, which may produce confounding factors and affect the validity. In addition, the only eligible RCT by Duivenvoorden *et al.* demonstrated that there was no difference between the two groups regarding intra-operative fracture of tibial plateau [2]. Therefore, we may not draw the conclusion that OWO increased the risk of intra-operative fracture of tibial plateau, compared with CWO. During open-wedge HTO, we may release the soft-tissues medially, leave appropriately lateral cortex intact and create an osteotomy parallel to the posterior tibial slope in the sagittal plane to decrease the risk of this complication [42].

No significant difference was identified for the incidence of opposite cortical fracture between the two groups. Interestingly, these findings were inconsistent with the previous meta-analyses, and we believe our meta-analysis was more accurate and comprehensive [21]. This might be interpreted by the following reasons: Firstly, the previous meta-analysis by Sun *et al.* only included two n-RCTs, But the present study included four studies and had a larger sample size than the study by Sun *et al*. which made a more robust conclusion. Secondly, they did not use sensitivity analysis to investigate the origin of high heterogeneity, thereby resulting in an unstable result. In our study, sensitivity analysis was utilized to further investigate the significant heterogeneity in our study, and the results were in line with the previous analysis. Thirdly, the aforementioned meta-analysis included two duplicated publications [8, 10], which may have substantial effect on the results. In this meta-analysis, the overall result showed significantly lower rate of common peroneal nerve palsy in OWO group. Nevertheless, the sensitivity analysis showed no significant difference between the two groups. In the three RCTs, the rate of injury to the peroneal nerve during CWO was 4% (5/125), but with OWO this complication was avoided. Several factors may have contributed to this complication during CWO, including the improper position of or excessive pressure utilized with a retractor or the improper detachment of muscle from the lateral side of the proximal tibia in proximal tibiofibular disruption [42]. CWO was technically harder than OWO, thereby orthopedic surgeons may need more time to master the surgical technique of CWO and minimize the risk of common peroneal nerve palsy [52]. In addition, Han *et al*. in a systematic review demonstrated that more surgical technical concerns were identified in TKA conversion from CWO than from OWO group [23]. Robertsson *et al.* compared the results of primary TKR and HTO revision to TKR regarding clinical outcomes and demonstrated that the risk of revision was significantly higher after the previous CWO than primary TKR, whereas OWO had no effect on the outcome [53].

Another major adverse event was iliac crest morbidity, which was caused by harvesting bone to fill the osseous gap in opening wedge osteotomy. Autograft was regarded as the most successful bone filling material due to its osteoinductive, osteoconductive and osteogenic properties, as compared to allograft. The overall result showed significantly higher rate of iliac crest morbidity in OWO group. However, we must treat the result with caution due to the small sample size. If bone grafting at the iliac crest could be avoided, the rate of such complication could be decreased. Some surgeons recommended that the cancellous autograft was only applied for opening wedges <12.5 mm, and allograft or synthetic bone substitute (hydroxyapatite, β-tricalcium phosphate, and bone cement etc.) was utilized for all cases or only for larger opening wedges, which could decrease the incidence of complications related to autograft donor site morbidity [54]. Some studies demonstrated that platelet-rich plasma (PRP), bone marrow stromal cells and growth factor combined with bone graft or substitute showed encouraging results regarding maintaining the desired correction and long-term stability and allowing early weight bearing [6, 52]. However, no clear evidence was found that whether PRP and augmentation showed superiority of decreasing union rates compared with autologous iliac crest graft.

Reliable fixation was fundamental in achieving good results in open-wedge HTO, but the most stable fixation system was still controversial. External fixators and plates (conventional, locking, long or short plates) are the most commonly used fixation devices. Numerous biomechanical studies have compared different implants. Agneskirchner *et al*. in their investigation on four different plates concluded that rigid long plate fixator with angle-stable locking bolts yields the best results [55]. In addition, Spahn *et al*. compared the four different fixation devices and reported that implants with a spacer had superior biomechanical properties and seem to be more reliable in predictable maintenance of correction [56]. Some studies showed better biomechanical properties and early weight bearing in long-locking plate, but it was bulky, expensive and frequently require hardware removal in many cases [52]. Spacer plates show more reliable fixation and lower risk of hardware removal and correction loss [6]. Although The results are still inconclusive, the gold standards may be locked plates and autologous graft based on the current evidence. Similar results were described by Amendola *et al.* [57] and Bonasia *et al*. [52].

According to literature, the carefully preoperative planning and selection of ideal candidate for HTO is essential. In general, a slight valgus correction (5°-6° degree) is associated with better results. However, the achievement of a neutral alignment is recommended in young patients and athletes [48]. Surgeons should be aware of several risk factors related to poor outcomes, such as bad range of motion, old inactive patients (>65) [58], severely medial isolated osteoarthritis (more than grade III according to Ahlbäck classification) [59], joint instability [60], patellofemoral arthrosis [5, 6] and lateral tibial thrust [15, 46].

This study has several strengths. Firstly, the extensive search strategy and broad inclusion criteria were applied to search all related literature and ensured thoroughness. Secondly, we screened duplicate articles to minimize reviewers' bias. The sample size in this review was quite bigger than that in previous meta-analysis to permit subgroup analysis, which provide a relatively unbiased picture of the results. Thirdly, since different validated scoring systems may lead to unclear functional assessment findings and moderate heterogeneity, we evaluate the knee function with the use of more complete scoring systems than previous meta-analyses, including ROM, HSS, Wallgren-Tegner score, and Lysholm score. In addition, we used the change in knee functional assessments from baseline as our effect index to assess actual improvement in knee function, which eliminated the influence of different baselines. The pooled results found no difference regarding knee function between OWO and CWO. However, no study was available to investigate whether there was a difference regarding time to occupational or sporting pursuits. Therefore, the basis of this suggestion of longevity of rehabilitation remains unclear, and future studies will have to investigate the cost-effectiveness by assessing the rehabilitation time.

We note several potential limitations in this meta-analysis. Firstly, some of the eligible studies were observational comparison studies, leading to some inherent heterogeneity due to uncontrolled bias. In addition, heterogeneity may come from some risk factors, such as age, gender, fixation position, the reliability of radiographs, and especially fixation methods. Some studies comparing the biomechanical properties and stability of the different fixation devices had been published, but the most reliable fixation system still remains controversial [55, 61]. Secondly, sample sizes were not calculated based on power analysis. Therefore, this may possibly result in type II statistical error. Thirdly, it was impossible to blind the observer assessing the radiographs regarding HTO type [19]. As a result, there remains a possibility that assessor bias has a substantial effect on the clinical outcomes recorded.

This meta-analysis confirmed that posterior tibial slope increased and patellar height decreased following OWO. Conversely, posterior tibial slope decreased and patellar height increased following CWO. Although both techniques led to the good and comparable clinical results, we recommend OWO as an alternatively effective treatment option for selected younger patients, which was easier to perform and to convert to TKA, avoids tibiofibular joint disruption and common peroneal nerve palsy, and permits multiplanar correction, as compared to CWO. However, additional well-designed studies and long-term follow-up data are required to identify the ideal candidates, the type of fixation and augment selection in OWO.

Disclosure of conflict of interest

None.

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