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ARTHROSCOPY AND SPORTS MEDICINE

Effectiveness of concurrent procedures during high tibial osteotomy for medial compartment osteoarthritis: a systematic review and meta-analysis

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Abstract

Introduction The purpose of this systematic review and meta-analysis was to evaluate the efficacy of concurrent cartilage procedures during high tibial osteotomy (HTO) for medial compartment osteoarthritis (OA) by comparing the outcomes of studies that directly compared the use of HTO plus concurrent cartilage procedures versus HTO alone.

Materials and methods Results that are possible to be compared in more than two articles were presented as forest plots. A 95% confidence interval was calculated for each effect size, and we calculated the I^2 statistic, which presents the percentage of total variation attributable to the heterogeneity among studies. The random effects model was used to calculate the effect size.

Results Seven articles were included to the final analysis. Case groups were composed of HTO without concurrent procedures and control groups were composed of HTO with concurrent procedures such as marrow stimulation procedure, mesenchymal stem cell transplantation, and injection. The case group showed a higher hospital for special surgery score and mean difference was 4.10 [I^2 80.8%, 95% confidence interval (CI) − 9.02 to 4.82]. Mean difference of the mechanical femorotibial angle in five studies was 0.08° (I^2 0%, 95% CI − 0.26 to 0.43). However, improved arthroscopic, histologic, and MRI results were reported in the control group.

Conclusion Our analysis support that concurrent procedures during HTO for medial compartment OA have little beneficial effect regarding clinical and radiological outcomes. However, they might have some beneficial effects in terms of arthroscopic, histologic, and MRI findings even though the quality of healed cartilage is not good as that of original cartilage. Therefore, until now, concurrent procedures for medial compartment OA have been considered optional. Nevertheless, no conclusions can be drawn for younger patients with focal cartilage defects and concomitant varus deformity. This question needs to be addressed separately.

Keywords Knee · Cartilage · Osteoarthritis · High tibial osteotomy · Arthroscopy

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Introduction

High tibial osteotomy (HTO) is a surgical technique that unloads the affected compartment and aims to relieve pain and improve function in medial compartment osteoarthritis (OA). During the surgery, the degenerative cartilage is frequently observed in the involved compartment and many methods (injection, marrow stimulation techniques, osteochondral autograft and allograft, and autologous chondrocyte implantation) have been tried to promote cartilage regeneration in the hope of delaying the progress of the osteoarthritis [5, 19].

For healing of the degenerative cartilage, both mechanical status and biologic potential are important. However, in the osteoarthritic knee, most cartilage lesions consist of

degenerative articular cartilage and eburnated bone is eventually exposed [17]. Repaired tissue of the eburnated bone has been reported to be healed with fibrocartilage, which has poorer quality than hyaline cartilage [17]. In addition, several articles have reported that regeneration of the articular cartilage with clinical improvement was obtained by unloading the involved part using HTO alone [1, 6, 10, 12]. Therefore, controversy exists regarding the use of HTO in association with concurrent procedures for medial compartment OA [1, 14].

Cartilage regeneration after HTO is also a controversial factor for clinical outcomes [11]. Some studies reported no correlation between clinical outcomes and the extent of cartilage regeneration [1, 12, 17]. Therefore, it is questionable whether we should perform concurrent procedures during HTO for medial compartment OA. Therefore, we intended to search for evidence by performing a thorough analysis of the usefulness of concurrent cartilage procedures during HTO. The purpose of this systematic review and meta-analysis was to evaluate the efficacy of concurrent cartilage procedures during HTO for medial compartment OA by comparing the outcomes of studies that directly compared the use of HTO plus concurrent cartilage procedures versus HTO alone. The hypothesis was that concurrent cartilage procedures would produce little benefit compared with HTO alone, and therefore, concurrent cartilage procedures would not be necessary during HTO for medial compartment OA.

Materials and methods

Search strategy

To test the hypotheses, a rigorous and systematic approach according to the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines was used [13]. In phase 1 of the PRISMA search process, the MEDLINE, EMBASE, and Cochrane database were systematically searched (August 2016). Using a Boolean strategy, all field search terms included the following: search ((((((((((cartilage) OR chondral) OR chondro) OR injection) OR intraarticular injection) OR microfracture) OR drilling) OR chondroplasty) OR abrasion arthroplasty)) AND ((((tibia) OR high) OR proximal) AND osteotomy). The citations in the included studies were screened, and we also checked unpublished articles with hand searches. The bibliographies of the relevant articles were subsequently cross-checked for articles not identified in the search. In phase 2, abstracts and titles were screened for their relevance. In phase 3, the full text of the selected studies was reviewed to assess for the inclusion criteria and methodological appropriateness with a predetermined question. In phase 4, the studies underwent a systematic review process and meta-analysis, if appropriate.

Eligible criteria

The inclusion criteria were as follows: (1) articles written in English, (2) studies reporting clinical and/or radiological results that are comparable to other studies, and (3) case–control studies regarding concurrent procedures (injection, transplantation, marrow stimulation procedure, osteochondral transfer, and chondrocyte implantation) during HTO for medial compartment OA (Fig. 1).

Data extraction

Each of the selected studies was evaluated by two independent authors for methodological quality. Data were extracted according to the following: level of evidence, follow-up, composition of the case and control, method of control selection, enrollment, osteotomy type, site of concurrent procedure, clinical results, radiological results, arthroscopic finding, histologic finding, MRI finding and summary. The extracted data were subsequently cross-checked for accuracy; any disagreements were settled by the third review author.

Quality assessment

The methodological quality of the non-randomized case–control study was assessed using a Newcastle–Ottawa assessment scale. It consisted of three main domains (selection, comparability, and outcome), with four categories in the selection domain, one category in the comparability domain, and three categories in the outcome domain. A study was awarded a maximum of one star for each item within the selection and outcome domains. A maximum of two stars was given for comparability.

The methodological quality of the randomized controlled trials (RCT) was assessed using risk of bias (ROB), based on the Cochrane handbook, with the following nine standard criteria: allocation sequence generation, allocation concealment, baseline outcome measurement, baseline characteristics, incomplete outcome data, knowledge of the allocated interventions, protection against contamination, selective outcome reporting, and other ROB. Each criteria was scored as "Yes (low ROB)", "No (high ROB)", or "Unclear".

Statistical analysis

Statistical analysis regarding clinical and radiological results between case and control group was performed using R version 3.1.1 (The R Foundation for Statistical Computing). Results that are possible to be compared in more than two

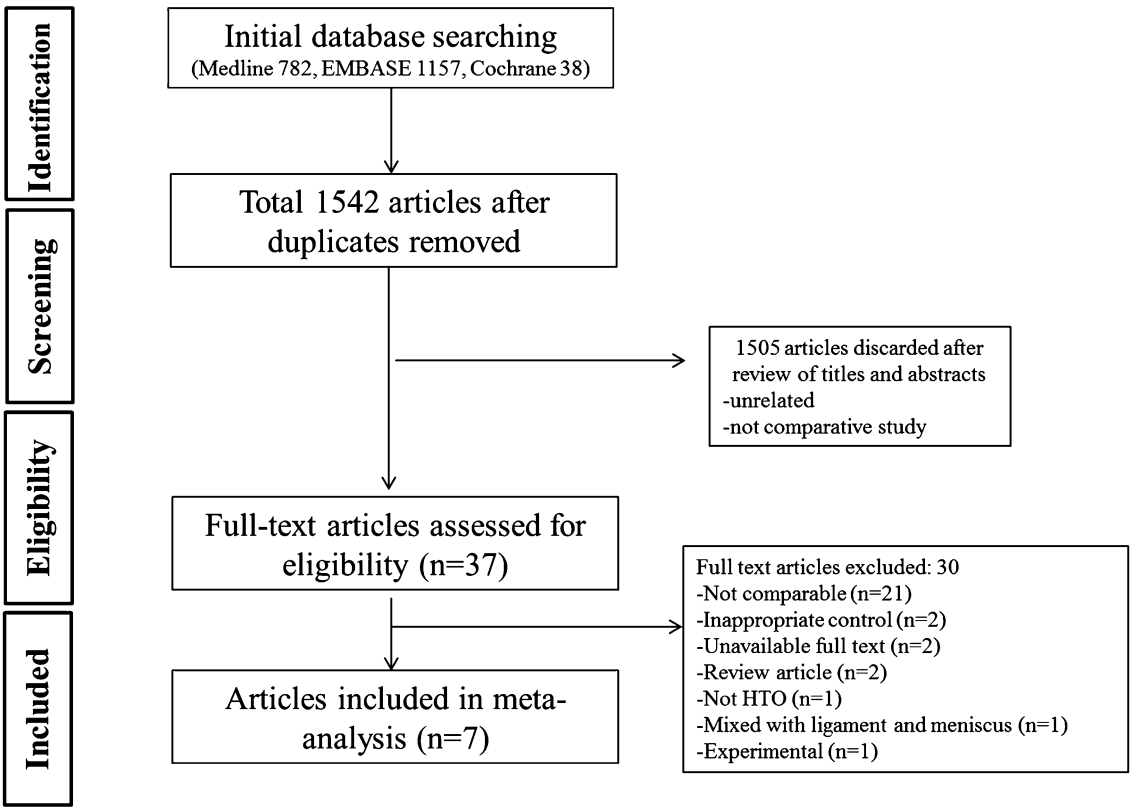

Fig. 1 The PRISMA flow chart

articles were presented as forest plots. A 95% confidence interval (CI) was calculated for each effect size, and we calculated the I^2 statistic, which presents the percentage of total variation attributable to the heterogeneity among studies. The random effects model was used to calculate the effect size rather than the fixed-effect model because studies within each subgroup were not assumed to share a common effect size.

Results

Search

Seven articles were included to the final analysis. There were four RCT [2, 14, 18, 19] studies and three non-randomized case–control [1, 3, 7] studies. There were one level I, three level II, and three level III studies. All case groups were composed of HTO without concurrent procedures for medial compartment OA. All control groups were composed of HTO with concurrent procedures for medial compartment OA and they were concurrent marrow stimulation procedure, mesenchymal stem cell transplantation, and injection. Open-wedge HTO was performed in six studies and dome osteotomy was performed in one study (Table 1).

Quality assessment

Quality assessment details are presented in Table 2. Three non-randomized case–control studies were assessed using a Newcastle–Ottawa assessment scale. In the selection domain, all studies showed a low ROB except for one study that star was not awarded in category of selection of the non-exposed cohort. In the comparability domain, two studies were awarded two stars and one study was awarded one star. In the outcome domain, all studies were awarded one star except for one study that star was not awarded in the category of assessment of outcome and adequacy of follow up. Four RCTs were assessed using ROB, based on the Cochrane handbook. Eight criteria were scored as "Yes" in two studies. However, three categories were scored "No" in one study and one category was scored "No" in another one study.

Clinical results

Clinical results are presented in Table 3. Clinical results were reported in all seven studies. They were reported as hospital for special surgery (HSS) scores, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), knee society knee score (K), knee society function score (F),

Table 1 Demographics of included study

Author	Publication year	Published journal	Level of evidence	Follow up	Case	Control	Control selection	Patients enrolled	Osteotomy type	Cartilage lesion
Ferruzzi et al.	2014	The Knee	III	11 years	HTO only	Control 1: HTO + ACI, control 2: HTO + MFX	Retrospective cohort	Case: 20 (age 54, M; F = 10; 10), control 1: 18 (age 51, M; F = 12; 6), control 2: 18 (age 53, M; F = 13; 5)	OWHTO	MFC
Jung et al.	2015	Arthroscopy	III	2 years	HTO only	HTO + subchondral drilling	Retrospective cohort	Case: 31 (age 58.6, M; F = 3; 28), control: 30 (age 61.5, M; F = 3; 27)	OWHTO	MFC
Pascale et al.	2011	Orthopedics	II	5 years	HTO only	HTO + MFX	Random allocation	Case: 20 (age 49.7, M; F = 15; 5), control: 20 (age 50, M; F = 13; 7)	OWHTO	MFC + MTP
Akizuki et al.	1997	Arthroscopy	III	2–9 years	HTO only	HTO + abrasion arthroplasty	Retrospective cohort	Case: 37 knees in 34 pts (age 64, M; F = 2; 32), control: 51 knees in 45 pts (age 64.6, M; F = 7; 38)	OWHTO	MFC + MTP
Wakitani et al.	2002	Osteoarthritis and Cartilage	II	17.5 and 14.3 months	HTO only	HTO + human autologous culture expanded bone marrow mesenchymal cell transplantation	Randomly stratified	No differences in age and severity of the disease between these two groups	Dome osteotomy fixed with two Steinmann's pins with Charnley clamps and two staples	MFC
Chareancholvanich et al.	2014	Knee Surgery Sports Traumatology Arthroscopy	I	12 months	HTO only	HTO + hyaluronic acid injection (total 10 injections)	Block randomization	Case: 20 (age 58.8, M; F = 2; 18), control: 20 (age 57.7, M; F = 2; 18)	OWHTO	

Table 1 (continued)

Author	Publication year	Published journal	Level of evidence	Follow up	Case	Control	Control selection	Patients enrolled	Osteotomy type	Cartilage lesion
Wong et al.	2013	Arthroscopy	II	2 years	HTO + hyaluronic acid	HTO + hyaluronic acid + bone marrow derived mesenchymal stem cell injection	Envelop randomization	Case: 28 (age 49, M; F = 14; 14), control: 28 (age 53, M; F = 15; 13)	OWHTO	MFC

ACI autologous chondrocyte implantation, *MFX* microfracture, *MFC* medial femoral condyle, *MTP* medial tibial plateau

Japanese orthopedic association (JOA), Tegner, and international knee documentation committee (IKDC) scores. In six studies, clinical results showed no statistically significant differences between groups. One study that performed mesenchymal stem cell injection as a concurrent procedure reported some additional effect of treatment in IKDC, Lysholm, and Tegner score [19]. Pooled analysis was possible only for HSS scores (Fig. 2). The case group showed a higher HSS score and mean difference was 4.10 [I^2 80.8%, 95% confidence interval (CI) − 9.02 to 4.82]. Therefore, it cannot be definitely stated that the score of the case group was better than that of the control group. Interestingly, HTO with microfracture showed a worse HSS score than that of the control group [3].

Radiological results

Radiological results are presented in Table 3. Radiologic results were reported in five studies and they were reported as the mechanical femorotibial (mFTA) or hip–knee–ankle (HKA) angle, and Kellgren–Lawrence (K–L) grade. All five studies reported no significant statistical differences in terms of the mFTA between groups. Mean difference of the mFTA was 0.08° (I^2 0%, 95% CI − 0.26 to 0.43) in the pooled analysis (Fig. 3). One study that evaluated K–L grade reported that a higher progression of arthritis was observed in the HTO with microfracture group [3].

Arthroscopic, histologic, and MRI findings

Arthroscopic, histologic, and MRI findings are presented in Table 4. In three studies, arthroscopic findings were reported. One study compared the arthroscopic findings of the cartilage healing between HTO only and HTO plus arthroscopic drilling. They reported that no significant differences were observed in the formation of fibrocartilage between groups ($p = 0.425$) [7]. In two studies (concurrent abrasion arthroplasty and human autologous culture expanded bone marrow mesenchymal cell transplantation), control groups showed more favorable healing than case groups [1, 18]. Control group showed a higher incidence of grade II healing and a lower incidence of grade IV healing in one study, and higher arthroscopic grading in another study. In two studies (concurrent abrasion arthroplasty and human autologous culture expanded bone marrow mesenchymal cell transplantation) that included histologic findings, contradictory results were reported, with no significant difference in the histologic finding and grade of repair reported in one study (concurrent abrasion arthroplasty) and histologic grading of the control group reported as higher in another study (concurrent human autologous culture expanded bone marrow mesenchymal cell transplantation) [1, 18]. In two other studies (concurrent hyaluronic acid and mesenchymal

Table 2 Quality assessment of the included study

Year	Author	Journal	Selection			Comparability		Outcome		
			1) (**)	2) (*)	3) (**)	4) (*)	1) (**)	1) (**)	2) (*)	3) (**)
Newcastle–Ottawa assessment										
2014	Ferruzzi et al.	The knee	*	*	*	*	**	*	*	*
2015	Jung et al.	Arthroscopy	*	*	*	*	**	*	*	*
1997	Akizuki et al.	Arthroscopy	*		*	*	*		*	

Year	Author	Journal	1	2	3	4	5	6	7	8	9
Risk of bias for RCTs											
2011	Pascale et al.	Orthopedics	Y	Y	Y	Y	Y	Y	Y	Y	Y
2002	Wakitani et al.	Osteoarthritis and Cartilage	N	N	Y	Y	Y	Y	Y	N	N
2014	Chareancholvanich et al.	Knee Surgery Sports Traumatology Arthroscopy	Y	Y	Y	Y	Y	Y	Y	Y	Y
2013	Wong et al.	Arthroscopy	N	Y	Y	Y	Y	Y	Y	Y	Y

Y yes, *N* no, *U* unclear

stem cell injection), MRI findings were reported, and both found a more favorable result in the control group in terms of cartilage volume and magnetic resonance observation of cartilage repair tissue score [2, 19].

Discussion

This systematic review and meta-analysis hypothesized that concurrent cartilage procedures would produce little benefit compared with HTO alone, and thus, a concurrent cartilage procedure would not be necessary during HTO. The principal finding of this systematic review and meta-analysis was that concurrent cartilage procedures, in the majority of the studies, produced little effect in terms of the clinical and radiological results following the HTO procedure. However, improved arthroscopic, histologic, and MRI results were reported. Therefore, our hypothesis was partially accepted and partially denied; indicating that further detailed study according to the different concurrent procedures and different outcomes should be performed. However, until now, concurrent procedures have not been considered necessary of the limited benefits in the clinical and radiological results. If we consider the characteristics of patients undergoing HTO, the clinical and radiological outcomes would be considered more important than the arthroscopic, histologic, and MRI findings because most of these patients have osteoarthritis.

Long-term series of HTO have shown a clinical and radiological deterioration over time, although good results at mid-term follow-up have been reported. Therefore, several authors have suggested using cartilage repair procedures such as marrow stimulation procedures, osteochondral graft, and autologous chondrocyte implantation with the aim of improving the long-term outcomes [3, 15, 16]. Kahlenberg et al. [8] reported that HTO with cartilage restoration procedures provides reliable improvement in functional status at least 2-year follow-up in their systematic review. However, they also addressed that analysis of second look outcome was limited by viability in methodology of each study. In the clinical trials, the data of combined procedures are contradictory and there have also been debates on the correlation between cartilage regeneration and clinical results [1, 4, 10, 12]. In our review, concurrent procedures for medial compartment OA showed little benefits in terms of clinical and radiological results. Most articles reported no significant difference regardless of concurrent procedures. In one article, interesting result was reported and concurrent microfracture contrarily showed worse clinical result than HTO alone [3]. In terms of arthroscopic, histological, and MRI findings, concurrent procedures produced a similar or superior result compared with HTO alone, even though there were some controversies.

Injection with hyaluronic acid, platelet rich plasm (PRP), or mesenchymal stem cell are also performed in the hope of relieving pain, improving function, modification cartilage structure, or exerting a chondroprotective effect [2, 9, 19]. Such injections are also used to augment the effect of arthroscopic microfracture, and arthroscopic and immunohistologic improvement have been found [19]. However, until now, their effects are still controversial. In our review, two studies reporting results of injection procedures were included. They showed improved clinical and radiological outcomes but, no differences compared with HTO alone, although there were benefits in terms of MRI findings. Their results were also similar to other arthroscopic or open cartilage procedures. One interesting paper analyzed factors affecting cartilage repair after open-wedge HTO [11]. They reported that cartilage regeneration is affected by body mass

Table 3 Clinical and radiological results of the included study

Author	Publication year	Clinical results	Radiological results
Ferruzzi et al.	2014	HSS: HTO only 71 (53–82), HTO + ACI: 69 (45–78), HTO + MFX 59 (35–68), scores were significantly higher only for patients treated with HTO and HTO +ACI ($p = 0.01$ and 0.01, respectively), WOMAC: HTO only 73 (57–84), HTO + ACI: 70 (55–81), HTO + MFX 62 (48–75), scores were significantly higher only for patients treated with HTO and HTO +ACI ($p = 0.01$ and 0.01, respectively)	mFTA (o): HTO only 4 (2–7), HTO + ACI: 4 (2–5), HTO + MFX 4 (1–5), K–L grade (final follow up): HTO only [grade III (13), grade IV (9)], HTO + ACI [grade III (11), grade IV (7)], HTO + MFX [grade III (6), grade IV (12)], higher progression of arthritis was observed in the HTO + MFX
Jung et al.	2015	K: case 92.5 (80–100), control 91.2 (83–100), F: case 92.2 (80–100), control 92.8 (76–100)	mFTA(o): case 3.2 (0–7.2), control 3.5 (0.3–6.8), $p = 0.471$
Pascale et al.	2011	Lysholm: case 78.3 ± 7.7, control 80.3 ± 9, $p = 0.425$, IKDC: no. A (case 17, control 16), no. B (case 3, control 4), $p = 0.524$, satisfaction score: case 6.9 ± 0.9, control 7.9 ± 1.1, $p = 0.0036$	mFTA(o): case 4.6 ± 0.9, control 4.5 ± 0.9, no statistical difference between groups
Akizuki et al.	1997	JOA: case 86.5 ± 6.8, control 86 ± 7.2, $p > 0.05$	mFTA(o): case 7 ± 3.3, control 6 ± 2.9, no statistical difference between groups
Wakitani et al.	2002	HSS: case 79.2 ± 8.7, control 81.3 ± 8.6, no significant difference between groups	
Chareancholvanich et al.	2014	No significant difference in the WOMAC score between groups ($p < 0.001$)	mFTA(o): case 2.2 ± 2.5, control 1.8 ± 1.9, no statistical difference between groups
Wong et al.	2013	The effect of treatment showed an added improvement of 7.65 [95% (CI), 3.04–12.26; $p = 0.001$] for IKDC scores, 7.61 (95% CI 1.44–13.79; $p = 0.016$) for Lysholm scores, and 0.64 (95% CI 0.10–1.19; $p = 0.021$) for Tegner scores	

HSS Hospital for Special Surgery, *WOMAC* Western Ontario and McMaster Universities Osteoarthritis Index, *ACI* autologous chondrocyte implantation, *MFX* microfracture, *mFTA* mechanical femorotibial angle, *K–L* Kellgren–Lawrence, *K* knee society knee score, *F* knee society function score, *JOA* Japanese orthopedic association, *IKDC* international knee documentation committee

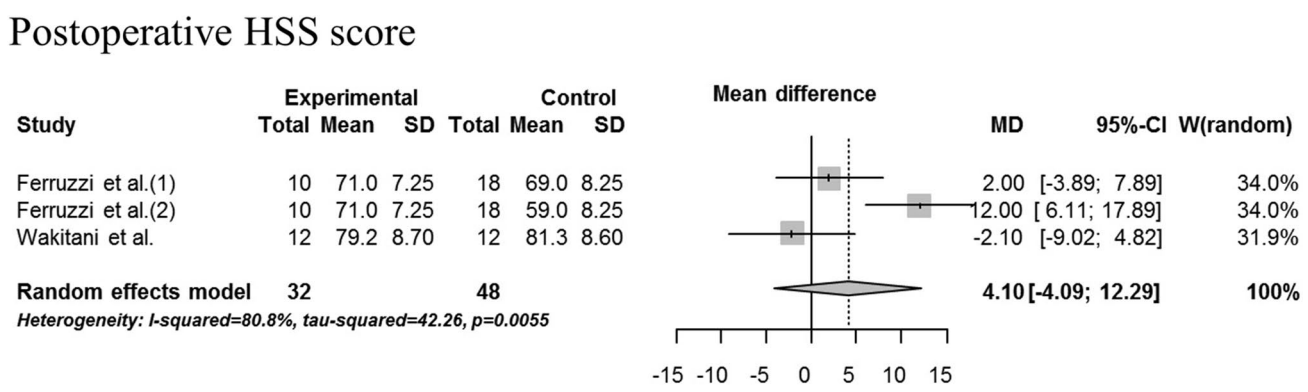

Fig. 2 Forest plots showing postoperative HSS scores between groups

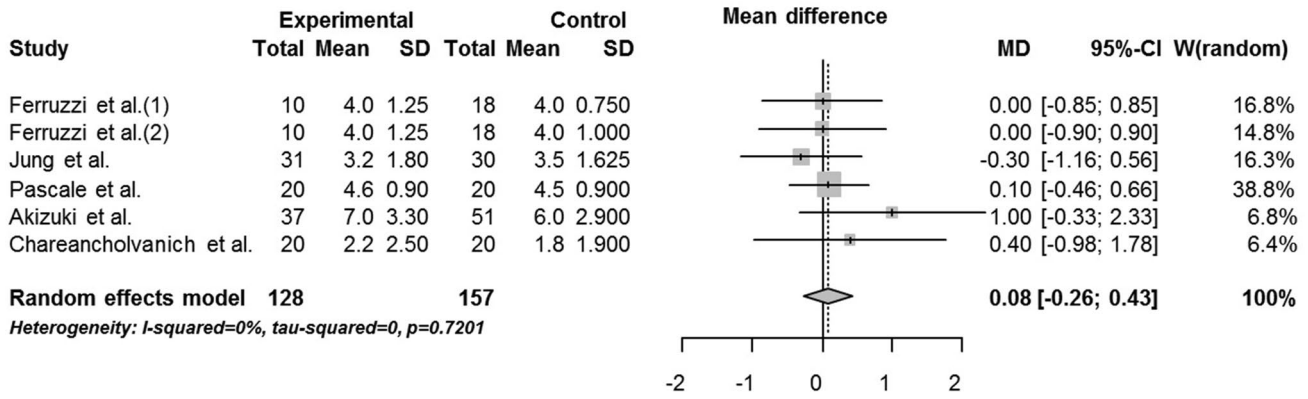

Fig. 3 Forest plots showing mFTA (HKA angle) between groups

index, the difference between the medial femoral condyle and medial tibial condyle, preoperative cartilage degeneration grade, and postoperative limb alignment. This could imply that concurrent procedures for medial compartment OA cannot guarantee successful treatment and superior outcomes.

One remained issue is how to interpret the mismatch between clinical outcome and histologic or MRI outcome. The major feature of osteoarthritis is cartilage erosion, which may lead to eburnation of the underlying subchondral bone. Therefore, main goal of early osteoarthritis treatment is to promote cartilage regeneration [18]. In this respect, improved histologic or MRI findings would indicate success, and therefore, the value of the procedures. However, a problem is that healed cartilage is different from, and the quality is not good as, the original cartilage. Furthermore, success may not lead to a successful clinical or radiological outcome, although this is controversial. Therefore, it is still questionable whether to the improvement in some findings indicate a successful procedure and whether to recommend this kind of procedure. In the future, more technical development in this field may lead to healing with highly qualified cartilage, and then these issues should be reevaluated and the necessity of concurrent procedures revisited.

This study has both strengths and limitations. Our analysis was, to our best knowledge, the first meta-analysis to verify whether concurrent procedures during HTO for medial compartment OA are necessary compared to HTO alone. Regarding the included studies, only comparative studies on concurrent procedures for medial compartment OA were chosen. Therefore, it was possible to come to a qualified conclusion. Limitations of this review should also be noted. First, most studies compared their results using different methods such as clinical, radiological, arthroscopic, histologic, and MRI findings. In addition, different scoring systems were used in the assessment of clinical outcomes. Therefore, it was difficult to perform a pooled analysis. Second, the evaluation periods varied, which could result in bias. Third, it was impossible to analyze efficacy according to the individual procedure because the allocated numbers were too small. Fourth, results of concurrent procedures for medial compartment OA during HTO were only analyzed

Table 4 Arthroscopic, histologic, and MRI findings of the included study

Author	Publication year	Arthroscopic finding	Histologic finding	MRI imaging
Ferruzzi et al.	2014			
Jung et al.	2015	Grade I with no regeneration (case 1), grade II with white scattering (case 11, control 10), grade II with partial coverage (case 17, control 17), grade II with even coverage (case 1, control 3), no significant differences were observed in the formation of fibrocartilage between groups ($p = 0.425$)		
Pascale et al.	2011			
Akizuki et al.	1997	Incidence of Outerbridge's grade II repair was significantly higher and the incidence of grade IV repair was significantly lower in control than in case on both femoral ($p = 0.0003$) and tibial (0.003) joint surfaces	No significant difference of the histologic finding and the grade of repair was observed between groups, There was no significant difference in the incidence of type II collagen between each groups and grade	
Wakitani et al.	2002	Arthroscopic grading (0–12 points): case 7.7 ± 4 and 8.3 ± 0.6, control 10.4 ± 1.2, significant difference between case and control	Histologic grading (0–8 points): case 2.3 ± 2.1 and 3 ± 2.7, control 5 ± 1.2, significant difference between case and control	
Chareancholvanich et al.	2014			Comparison of the change in cartilage volume between the case and control groups revealed a significant increase in the total cartilage volume ($p = 0.033$), lateral femoral condyle volume ($p = 0.044$), tibial plateau volume ($p = 0.035$) and lateral tibial volume ($p = 0.027$) in the control group compared to the case group
Wong et al.	2013			MOCART score: case 43.21 ± 13.55, control 62.32 ± 17.56, $p < 0.001$, the MOCART scores were significantly better in the MSC group

MOCART magnetic resonance observation of cartilage repair tissue, *MSC* mesenchymal stem cell

in this study. Therefore, no results could be obtained for the younger patients with focal cartilage lesions and concomitant varus deformity. Finally, our results do not allow us to draw a definite conclusion regarding which factor is most important for evaluating the effects of concurrent procedures among clinical, radiological, arthroscopic, histologic, and MRI findings.

Conclusion

Our analysis support that concurrent procedures during HTO for medial compartment OA have little beneficial effect regarding clinical and radiological outcomes. However, they might have some beneficial effects in terms of arthroscopic, histologic, and MRI findings even though the quality of healed cartilage is not good as that of original cartilage. Therefore, until now, concurrent procedures for medial compartment OA have been considered optional. Nevertheless, no conclusions can be drawn for younger patients with focal cartilage defects and concomitant varus deformity. This question needs to be addressed separately.

Compliance with ethical standards

Conflict of interest The authors declare that we have no conflict of interest.

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Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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