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Review Article

Cartilage regeneration techniques with concomitant high tibial osteotomy (HTO), An innovative biomechanical therapy for osteoarthritis (OA) knee – Systematic review

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ABSTRACT

In orthopedic surgery, a high tibial osteotomy (HTO) is a common treatment. Indications, patient selection, pre-operative planning, surgical procedure, fixation methods, and complications are all covered in detail. This research concentrated on the factors that should be examined in order to produce positive long-term results. To examine the stated hypothesis "medium- to long-term outcomes of high tibial osteotomy and therapies for cartilage healing". A thorough search of the database like MEDLINE was done. A clinical outcome investigation employing HTO as the main technique, the usage of a sort of cartilage repair, & a minimum follow-up period of 2 years were all necessary. Everything from the research layout to the patient demographics to the sorts of procedures conducted, the clinical consequences to eventual overall knee arthroplasty progression and consequences was investigated in depth. As a result of a combination of HTO and cartilage regeneration procedures, patients may avoid or delay knee arthroplasty surgery in the medium to long term.

1. Introduction

Treatment of unicompartmental (UC) knee osteoarthritis among young, active patients represents a substantial challenge for orthopaedic doctors.[1–3] Total and UC knee replacements deliver excellent relief in discomfort like pain and results for elderly persons, but the risks of executing arthroplasty procedures on younger, more active patients are greater because they have a greater chances of prosthesis wear and may therefore require one or more revised processes with greater morbidity. For younger, more active persons with isolated medial compartment osteoarthritis, a long-term alternative to joint replacement is High Tibial Osteotomy (HTO).[4–6] The aim of HTO is to shift the mechanical axis of the knee from medial to slightly lateral to the midline, lowering the load and delaying the onset of osteoarthritis (OA).[7–9] According to several studies, the healing process began after realignment. Jackson described an isolated medial compartment OA in various knees in 1958, and HTO was evaluated as a treatment option.[10] Until Coventry reported positive outcomes in 1973, this operation was not widely used. HTO became more common among active young patients with advancements in surgical method, fixation devices, and patient selection.[11]

Patients having ankle discomfort and instability due to a Value of Actual Micromotion (VAM) may exhibit a wider range of symptoms and indicators. Secondary degenerative arthritis and medial joint line pain in a varus knee, as well as ligamentous instability with varus thrust, in which correction of the VD unloads the recreated ligament while it heals, are all other indications for meniscal transplantation following total medial meniscectomy.[11,12] Osteoarthritis of

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the medial compartment in individuals younger than 65 should be treated with HTO.[13] In some cases, HTO may assist patients avoid or delay surgery.[5] HTO has even been referred to as an alternative method in respect to cost as compared to knee replacement surgery for younger, more active individuals.[14]

A new surgical option for the mentioned population with problems & abnormalities has been introduced to orthopaedic surgeons' repertoire. HTO and knee realignment appear to have a synergistic relationship, with greater alignment enabling improved cartilage condition and enhanced pain reduction after HTO.[6,14] For the objective of assessing the reported long-term effects of HTO and other cartilage regeneration treatments, a systematic review was conducted. The primary aim of this review was to evaluate reported "medium- to long-term outcomes after high tibial osteotomy (HTO) with associated cartilage restoration procedures". The secondary aim was to make recommendations for performing future studies.

2. Materials and Methods

The search protocol is planned according to "PRISMA" (Preferred reporting Items for systematic Reviews and meta-analysis) guidelines 2009.

2.1. Search strategy

The databases MEDLINE, Embase, Cochrane, Google Scholar, Scopus, and PubMed were searched electronically. In addition, all relevant publications and textbooks' bibliographies were personally searched. Based on the criteria of including and excluding, two reviewers independently chose relevant papers. Discussions between the two reviewers resolved any discrepancies. The PICO-format inquiry was used to create methodological MeSH terms that were more subtle in the identification of research. ("High Tibial Osteotomy" [MeSH] AND (HTO" [MeSH]) AND ("Cartilage Regeneration Technique" [MeSH]) were among the terms used. Critical analysis was performed on studies that met these inclusion criteria. The listed studies' attributes were assessed using a proposed specialized quality assessment scale.

2.2. Inclusion criteria

The below mentioned studies were considered:

1. Research work published in peer-reviewed scientific journals in the English language till 2022.
2. Randomized controlled trial.
3. Case Control studies.
4. Cohort researches.
5. Quasi Trials.
6. Single Arm Intervention.
7. All the articles published till June 2022 were included.
8. Full articles in English.

2.3. Exclusion criteria

Excluded type of studies are following:

1. Retrospective Studies
2. Case reports & case series,
3. Cross-sectional researches,
4. Or animal researches,
5. Reviews
6. Abstracts,
7. Technical reports
8. Expert opinions

Articles with incomplete data and patients with presence of any lesions were excluded. The references of selected articles were also analyzed for additional studies and any other studies that were included in exclusion criteria

2.4. Formulating the review question

The research question was set in accordance with (Population, Intervention, Comparison, and Outcome) the "PICO" format

Population – Patient with osteoarthritis

Intervention – Cartilage regeneration

Comparison – NAOutcome – High tibial osteotomy (HTO) with associated cartilage restoration procedures

2.5. Selection of studies

Selection of study was done in a three-step process. All the titles were reviewed and based on the mentioned criteria of inclusion and exclusion, appropriate studies had been selected as mentioned in Table 1. For all the selected titles, abstracts were obtained and reviewed, from which appropriate abstracts were selected based on the criteria. For all the selected abstracts, full text articles were obtained and analyzed, and the final set of articles were obtained keeping in mind the selection criteria.

Table 1: Selection of studies

Study selection	No. of articles
Initial search	220
Duplicates and non-relevant	90
Case reports and series	52
Reviews	45
Abstract	26

2.6. Data extraction

Data from all trials was extracted into an Excel data sheet when the final study sample was selected. The 1^{st} author, the year of publication, the study design, the no. of subjects, cartilage regeneration techniques, complications, and aesthetic outcomes were all included.

2.7. Quality assessment

Studies in situations when randomization is not always possible. However, conducting a thorough evaluation of the available literature and answering queries in that subject was still beneficial. In light of the foregoing, we determined that the MINORS index was the best quality assessment index for evaluating the papers in this systematic review. The publications were categorized into comparative and non-comparative research using this measure, with different grading for each group. "Each scale item was allotted a score of

1. 0 = not reported,
2. 1 = reported but inadequate,
3. 2 = reported but adequate & reported and adequate".

Non-comparative studies must score 8 items, resulting in a universal ideal score of 16, but comparative research must score 4 additional items, resulting in a global ideal score of 24.

3. Results

Overall, 220 items were found during the original search. After eliminating duplicates and eliminating publications based on eligibility criteria, an aggregate of 7 studies were carefully chosen for analysis from a total of 220 studies found in the database search. The PRISMA flowchart is depicted in Figure 1.

3.1. Synthesis of results

Narrative synthesis has been provided for the findings obtained from the studies. The data extracted has been presented in Table 2.

3.2. Risk of bias assessment

Risk of bias was assessed using the "Cochrane Risk of Bias Assessment tool". To determine bias, a score is assigned to each factor in five different categories (high, low, or uncertain) (reporting, attrition, performance, selection and other). Bias in various areas are all taken into consideration when completing the "Quality Assessment Form Part I". Bias like attrition, performance and detection can all be evaluated using the "Quality Assessment Form Part II". There were three options to choose from when deciding if a judgment had a high, medium, or low risk of bias as shown in Table 3.

4. Discussion

Hypothesis that HTO with cartilage regeneration provided consistent relief in pain and functional scores for osteoarthritis patients was supported by the results of a comprehensive analysis. Increased function and reduced pain have been shown to be achieved by using HTO in conjunction with cartilage regeneration procedures. Osteoarthritis of the knee has previously been thought to have no role for HTO, but new research has revealed that HTO can have a major impact, especially when paired with cartilage regeneration procedures.[22,23] Total complications in this study may be higher than those in similar knee operations. Most people who took part in this research experienced mild soft tissue infections as a side effect. As previously stated, surgeons must be wary of post-HTO complications including compartment syndrome, however there were no cases of it in the trials. There were no fatal pulmonary embolisms in our examination, despite the fact that pulmonary embolism had been described in a previous study of HTO for osteoarthritis.[24] If HTO and concurrent cartilage surgeries can be shown to be safe in the medium term, this could delay the need for a full knee arthroplasty, according to our findings. In most of the trials, long-term survival was not thoroughly recorded, and more study is required.[25] Whether HTO used in conjunction with cartilage repair treatments increases fibrocartilage development is yet unproven. An investigation into the effects of individual cartilage restoration procedures on fibrocartilage growth is needed. The amount of fibrocartilage coating on joint surfaces and clinical improvement need more investigation. These problems hindered an accurate meta-analysis in this review. Inconsistencies in result assessments and the vast range of HTO and cartilage regeneration techniques employed in the study slowed progress on the project from the start. Before integrating the data, researchers can create impact size metrics like risk ratios or odds ratios to account for this, however most studies used small case sequences with badly defined or non-existent groups as their comparison. An important meta-analysis could not be done at the time of this evaluation since it is impossible to assess the extent of the effect without a solid counterfactual. To learn more about the possible risks and benefits of cannabis, researchers will need to conduct large-scale studies using standardized approaches, results with validation, and control groups.

5. Conclusion

As a result of a combination of HTO and cartilage regeneration procedures, patients may avoid or delay knee arthroplasty surgery in the medium to long term. The development of this sector appears to be driven by demand of patients, curiosity of surgeons, and a structural regulation i.e. improving at the equivalent speed as new advancements. For the interest of patients, funding bodies should commission research that has a clear translational purpose in mind.

Table 2: Synthesis of results

Author	Study	Population	Intervention	Regeneration Technique	Conclusion
Kim MK et al, 2019 [15]	Retrospective	HTO with cartilage operations on 66 knees that had follow-up period of 2 years.	Concomitant cartilage procedures	Mesenchymal stem cells (MSC) generated from allogeneic human umbilical cord blood	It may be possible to lower the postoperative mechanical axis to a neutral or valgus axis of less than 3° by utilizing concurrent cartilage treatments in conjunction with HTO.
Jing et al, in 2019 [16]	study of case series	27 HTO all-inside repair With MMPRT	Concomitant cartilage procedures were performed	MOWHTO	• HSS: 45.3 to 84.2 • Lysholm score: 51.3 to 85.9
Kim YS et al, 2020 [17]	Prospective randomized trial	HTO and cartilage repair procedures were performed on a total of 80 patients.	It was determined at each follow-up visit that the Lysholm KOOS scores were used to evaluate clinical outcomes.	MSC implantation with allogenic cartilage	MSC implantation with allogenic cartilage is superior to MSC implantation alone and in terms of cartilage regeneration and clinical outcomes.
Faber S et al, 2020 [18]	Longitudinal	A total of 4986 participants with knee cartilage abnormalities were included in the study. A total of 736 patients met the eligibility criteria.	Concomitant HTO	NA	Further HTO is often performed in conjunction with medial femoral condyle cartilage repair therapies, even in moderate varus deformities less than 5°. Several other aspects appear to play a role in the HTO's decision making process.
Song JS et al, 2020 [19]	Retrospective	125 patients were over the age of 40 and had a varus deformity of greater than 5 degrees.	after undergoing simultaneous HTO and HUCBMSCs implantation for the treatment of MCOA, patients who had had second-look arthroscopy during hardware removal	Implantation of mesenchymal stem cells from human umbilical cord blood	Patients with medial compartment osteoarthritis and varus deformity can benefit from the use of hUCB-MSCs combined with HTO.
Faber S et al, 2021 [20]	Longitudinal	Focused cartilage defects in 788 patients	High tibial osteotomy (HTO)	NA	HTO should be seriously considered and offered to patients with medial femoral condyle cartilage anomalies and varus deformity.
Kim YS et al, 2021 [21]	Retrospective	Seventy-one patients' knees were examined.	Concomitant HTO	Implantation of MSC and HTO at the same time	Patients with varus knee OA who had MSC implantation and HTO showed viable cartilage repair and good clinical outcomes.

[HTO - High tibial osteotomy, MSC - Mesenchymal stem cells, MMPRT - Medial Meniscus Posterior Root Tear, MOWHTO - Medial Open Wedge High tibial Osteotomy, OA – Osteoarthritis]

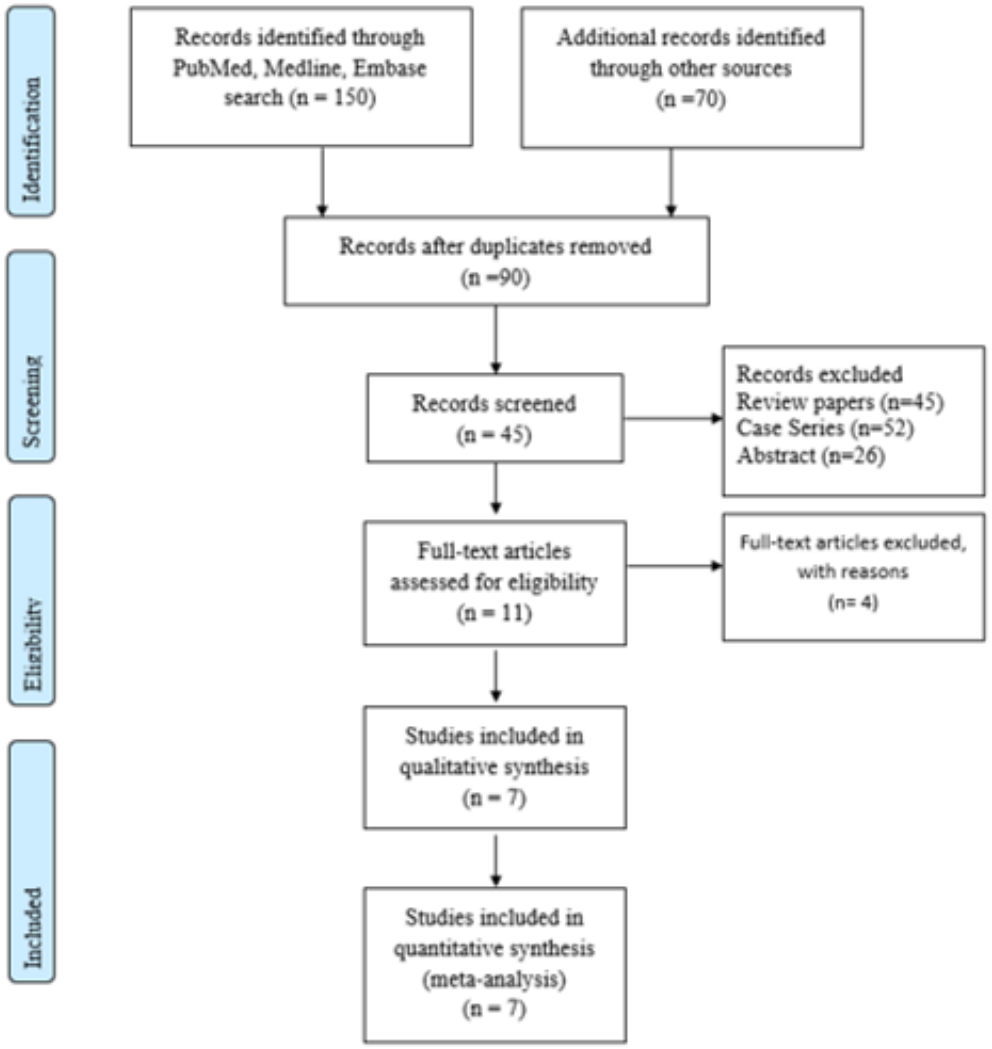

Fig. 1: PRISMA flowchart of included studies

Table 3: Risk ofbias assessment

Authors name	Random sequence generation with selection bias	Allocation concealment	Reporting bias	Others	Performance bias	Blinding outcome	Attrition bias
Kim MK et al, 2019 [15]	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	High risk
Jing et al, 2019 [16]	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kim YS et al, 2020 [17]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Faber S et al, 2020 [18]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Song JS et al, 2020 [19]	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk
Faber S et al, 2021 [20]	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk
Kim YS et al, 2021 [21]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

6. Conflicts of Interests

None.

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