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Osteoarthritis Following ACL Injury: A Narrative Review of Homoeopathic Interventions and Clinical Evidence

Dr. Vasim Dadi, MD (Hom)

Department of Practice of Medicine, Valan Homoeopathic Medical College and Hospital, Valan, Gujarat, India.
Corresponding author:

ABSTRACT

Background: Anterior cruciate ligament (ACL) injury is associated with an increased risk of post-traumatic osteoarthritis (PTOA) of the knee. Although ACL reconstruction and rehabilitation can improve stability and function, they do not consistently prevent long-term osteoarthritis. Homoeopathic interventions have been investigated in general knee and hip osteoarthritis; their effectiveness in osteoarthritis specifically following ACL injury remains uncertain.

Objective: To review the relationship between ACL injury and subsequent knee osteoarthritis, examine clinical evidence concerning homoeopathic interventions in osteoarthritis, and identify research priorities for patients with post-ACL injury osteoarthritis.

Methods: A narrative review approach was used to examine publications concerning ACL injury, post-traumatic osteoarthritis, long-term outcomes following ACL reconstruction, and clinical studies of homoeopathic interventions for osteoarthritis. Relevant literature included systematic reviews, meta-analyses, and randomized placebo-controlled trials identified through biomedical literature databases and journal records. This manuscript is not a systematic review; no pooled analysis or formal certainty-of-evidence assessment was performed.

Results: Systematic reviews indicate that ACL injury is associated with increased risk of subsequent knee osteoarthritis.

Meniscal and combined ACL-meniscal injuries are also associated with increased risk. Clinical trials of homoeopathic interventions in general osteoarthritis populations have produced mixed findings. A 2015 feasibility trial involving 60 patients found no statistically significant difference between individualized homoeopathic treatment and placebo for principal symptom outcomes. A 2024 feasibility trial involving 40 patients reported favorable differences across several patient-reported outcomes, but its small sample and feasibility design limit definitive conclusions. A 2023 randomized trial involving 60 patients with knee or hip osteoarthritis also reported favorable outcomes. These studies did not establish effectiveness specifically in post-ACL injury osteoarthritis.

Conclusion: Post-traumatic osteoarthritis following ACL injury is an important long-term clinical problem. Direct evidence supporting homoeopathic interventions in post-ACL injury osteoarthritis remains insufficient. Adequately powered, preregistered, placebo-controlled trials using validated clinical outcome measures are

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required to determine whether individualized homoeopathic treatment provides additional symptomatic benefits alongside appropriate standard care.

Keywords: Anterior cruciate ligament; ACL injury; post-traumatic osteoarthritis; knee osteoarthritis; homoeopathy; individualized homoeopathic medicine; WOMAC; KOOS; quality of life.

1. INTRODUCTION

The knee is a complex weight-bearing joint whose function depends on the coordinated interaction of bones, articular cartilage, menisci, ligaments, muscles, and surrounding soft tissues. Normal joint function requires mechanical stability and appropriate distribution of forces across articular surfaces.

The anterior cruciate ligament (ACL) is a major stabilizing structure that helps control anterior translation of the tibia relative to the femur and contributes to rotational stability. ACL injuries frequently occur during pivoting, sudden deceleration, landing, and changes in direction. They may also result from accidental falls and other traumatic events.

The consequences of ACL injury extend beyond the initial ligament damage. Some patients experience persistent instability, reduced muscle strength, limitations in physical activity, and progressive degenerative changes within the affected knee.

Post-traumatic osteoarthritis is an important long-term consequence. It may develop following direct cartilage injury, meniscal damage, subchondral bone injury, altered joint mechanics, or a combination of these factors.

Poulsen and colleagues conducted a systematic review and meta-analysis examining the risk of knee osteoarthritis following ACL, meniscal, and combined injuries. Their findings indicated that the odds of developing knee osteoarthritis were approximately four times higher following ACL injury and approximately six times higher following combined ACL-meniscal injury compared with relevant non-injured controls. Substantial heterogeneity between studies limits the precision with which these estimates can be generalized [1].

ACL reconstruction is commonly undertaken to restore stability and facilitate functional recovery in appropriately selected patients. Nevertheless, restoration of ligament stability does not necessarily reverse the biological consequences of the original injury or eliminate all factors contributing to osteoarthritis.

An umbrella systematic review and meta-analysis published in 2022 found that osteoarthritis risk remained elevated after ACL injury and that osteoarthritis was common at long-term follow-up after reconstruction. Higher long-term osteoarthritis prevalence in surgically treated than nonsurgically treated populations was reported in included evidence, but such comparisons require caution because treatment selection, injury severity, associated damage, and population differences may influence findings [2].

Homoeopathic interventions have been investigated in clinical studies involving general knee and hip osteoarthritis. However, the existence of studies in general osteoarthritis populations does not establish that the same interventions are effective in osteoarthritis arising specifically after ACL injury.

The central question is whether existing clinical evidence supports homoeopathic interventions in post-ACL injury osteoarthritis and what additional research is required to evaluate their potential clinical role.

2. OBJECTIVES

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2.1 Primary objective: To critically review the relationship between ACL injury and subsequent knee osteoarthritis and examine the clinical evidence concerning homoeopathic interventions in this context.

2.2 Secondary objectives: 1. Describe mechanisms contributing to post-traumatic osteoarthritis after ACL injury.
2. Discuss the influence of associated meniscal injuries, cartilage damage, and altered biomechanics. 3. Summarize clinical trials investigating homoeopathic interventions in general knee and hip osteoarthritis.
4. Evaluate the applicability and limitations of existing research for post-ACL injury osteoarthritis. 5. Identify appropriate clinical outcome measures for future investigations.
6. Propose a framework for a rigorous clinical trial addressing the evidence gap.

3. METHODS

3.1 Review design: This article was developed as a narrative review. Narrative reviews integrate clinical, epidemiological, and mechanistic evidence from different study designs and can identify inconsistencies and research questions. They differ from systematic reviews in their search procedures, study selection methods, and approaches to critical appraisal.

3.2 Literature sources and evidence identification: Relevant literature was identified through searches of PubMed, journal websites, and reference records of relevant review articles. Literature considered included systematic reviews and meta-analyses concerning ACL injury and knee osteoarthritis; studies of long-term outcomes after ACL reconstruction; clinical trials of individualized homoeopathic medicines in knee or hip osteoarthritis; randomized placebo-controlled feasibility studies; and publications reporting pain, stiffness, function, or quality-of-life outcomes. This process does not establish that every eligible study has been identified.

3.3 Eligibility and scope: Publications were considered relevant when they addressed (1) the risk or development of osteoarthritis following ACL injury; (2) long-term osteoarthritis outcomes following ACL reconstruction; (3) clinical investigations of homoeopathic interventions in knee or hip osteoarthritis; or (4) validated outcome measures relevant to pain, function, or quality of life. A key distinction was maintained between studies directly investigating post-ACL injury osteoarthritis and studies investigating osteoarthritis more generally.

3.4 Interpretation of evidence: Findings were interpreted according to study design, sample size, comparator, duration of follow-up, and relevance to the target population. Particular attention was given to distinguishing within-group improvement from between-group differences; statistical significance from clinical importance; symptom improvement from structural disease modification; feasibility findings from definitive efficacy evidence; and general osteoarthritis findings from directly applicable post-traumatic osteoarthritis evidence. No pooled effect estimates were calculated.

4. PATHOPHYSIOLOGY OF OSTEOARTHRITIS FOLLOWING ACL INJURY

4.1 Initial traumatic injury: ACL injury may occur during a traumatic event that simultaneously affects multiple structures within the knee. The original injury may involve articular cartilage, menisci, subchondral bone, and other ligaments. Damage to these structures can alter mechanical force distribution and initiate biological processes contributing to joint degeneration. Risk therefore depends not only on the ACL tear but also on the severity and extent of associated injury.

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4.2 Articular cartilage damage: Articular cartilage provides a smooth, low-friction surface that distributes load across the knee. Traumatic loading can damage cartilage directly or initiate cellular and biochemical changes affecting the extracellular matrix. Progressive changes in cartilage composition and organization may reduce its capacity to tolerate repetitive mechanical stress. However, cartilage injury does not inevitably lead to symptomatic osteoarthritis in every patient.

4.3 Meniscal injury: The menisci contribute to load distribution, shock absorption, joint congruity, and stability. Meniscal tears associated with ACL injury may compromise these functions, and meniscectomy can further reduce tissue available to distribute mechanical forces. A systematic review and meta-analysis found higher odds of osteoarthritis following meniscal injury and combined ACL-meniscal injury than following ACL injury alone [1].

4.4 Inflammatory and biochemical changes: Joint trauma may initiate inflammatory responses involving synovial tissues, chondrocytes, and other intra-articular structures. Inflammatory mediators and enzymes involved in extracellular matrix degradation may contribute to cartilage damage and altered joint homeostasis. These biological changes interact with mechanical abnormalities, but inflammation alone does not explain the entire disease process.

4.5 Altered biomechanics: Following ACL injury, changes in knee kinematics and muscle activation may influence force distribution across the joint. Potential contributors include persistent instability, altered gait, reduced quadriceps strength, impaired neuromuscular control, meniscal dysfunction, and changes in activity or joint loading. The relationship between individual biomechanical abnormalities and osteoarthritis progression remains complex.

4.6 Osteoarthritis after ACL reconstruction: ACL reconstruction can improve mechanical stability and facilitate rehabilitation in appropriately selected patients, but it should not be considered a guaranteed method of preventing osteoarthritis. Rothrauff and colleagues reviewed long-term radiographic outcomes following ACL reconstruction and reported lower osteoarthritis prevalence in included studies of anatomically reconstructed knees than in studies of non-anatomic or unspecified techniques, while emphasizing the need for additional high-quality studies [3]. A 2026 systematic review and meta-analysis reported an association between earlier reconstruction and lower osteoarthritis incidence than delayed reconstruction; because the evidence was observational, this does not establish that surgical timing independently prevents osteoarthritis [4].

5. CLINICAL PRESENTATION AND ASSESSMENT

5.1 Clinical symptoms: Patients may experience pain during walking and other weight-bearing activities, stiffness after inactivity, reduced knee flexion or extension, difficulty climbing stairs, limitations in squatting or kneeling, reduced walking endurance, difficulty returning to sport or work, and reduced confidence in knee function. Symptom severity may not correspond directly to radiographic disease severity.

5.2 Clinical history: Assessment should document the original ACL injury, associated meniscal or cartilage damage, previous surgery, rehabilitation history, and current activity limitations. Relevant symptoms include pain, swelling, stiffness, giving-way episodes, and restrictions in daily activities. Alternative causes of persistent symptoms, including recurrent ligament injury, meniscal pathology, tendinopathy, inflammatory arthritis, and other musculoskeletal disorders, should also be considered.

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5.3 Imaging: Weight-bearing radiographs can help identify joint-space narrowing, osteophytes, subchondral sclerosis, and other features associated with osteoarthritis. The Kellgren–Lawrence grading system is commonly used to classify radiographic severity. MRI may be indicated when additional information about menisci, cartilage, ligaments, or other soft tissues is clinically necessary. Imaging should be interpreted alongside symptoms and function.

5.4 Outcome measures: WOMAC assesses pain, stiffness, and physical function in osteoarthritis. KOOS evaluates pain, other symptoms, activities of daily living, sport and recreation, and knee-related quality of life. EQ-5D-5L assesses health-related quality of life through mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. These measures can complement one another in clinical research. Improvement in patient-reported scores does not establish cartilage regeneration or structural disease modification.

6. HOMOEOPATHIC INTERVENTIONS IN OSTEOARTHRITIS

6.1 Individualized homoeopathic treatment: Individualized homoeopathic treatment involves selecting a medicine according to the practitioner's assessment of the patient's reported symptoms and clinical presentation. In research, this approach can be investigated by comparing individualized treatment with an appropriate placebo while maintaining equivalent specified concomitant care. Randomized, blinded studies can help assess whether differences exceed those associated with placebo effects, clinical attention, natural symptom variation, and shared care.

6.2 Symptomatic improvement and structural disease modification: Pain relief and improved physical function are important outcomes. However, they must be distinguished from evidence that an intervention prevents cartilage loss or slows structural progression. Improvement in pain or quality of life does not, by itself, establish cartilage regeneration, reversal of osteoarthritis, or prevention of long-term joint degeneration. Such claims require direct evidence from appropriately designed studies.

6.3 Earlier systematic review: Long and Ernst published a systematic review of randomized clinical trials investigating homoeopathic remedies for osteoarthritis in 2001. The review identified four trials and concluded that the available evidence was insufficient to establish firm conclusions about effectiveness. The small number of trials and their limitations restricted the strength of the findings [5]. This review is historically important but predates subsequent trials.

7. CLINICAL TRIALS OF HOMOEOPATHIC INTERVENTIONS IN OSTEOARTHRITIS

7.1 Koley and colleagues, 2015: Koley and colleagues conducted a double-blind, randomized, placebo-controlled feasibility study involving 60 patients experiencing acute painful episodes of knee osteoarthritis. Both groups showed improvements in several symptom measures during the two-week study period, but differences between groups were not statistically significant.

The authors concluded that individualized homoeopathic treatment did not appear superior to placebo in that trial and recommended further rigorous investigation using a larger sample [6]. The short follow-up and modest sample size limit conclusions about long-term outcomes. The study did not specifically address osteoarthritis following ACL injury.

7.2 Khadim and colleagues, 2023: Khadim and colleagues conducted a double-blind, randomized, placebo-controlled trial involving 60 participants with knee or hip osteoarthritis. The study evaluated pain, stiffness,

functional limitations, and quality of life over three months. The authors reported statistically significant differences favoring individualized homoeopathic medicines for the measured outcomes. Frequently indicated medicines included Rhus toxicodendron, Medorrhinum, Bryonia alba, and Syphilinum [7]. The small sample and inclusion of both knee and hip osteoarthritis limit subgroup conclusions. The findings cannot be directly generalized to patients with post-ACL injury osteoarthritis.

7.3 Bhattacharyya and colleagues, 2024: Bhattacharyya and colleagues conducted a double-blind, randomized,
placebo-controlled feasibility trial involving 40 patients with knee osteoarthritis. Participants received individualized homoeopathic medicines or identical-looking placebos alongside mutually agreed-upon concomitant care guidelines. The study assessed KOOS, derived WOMAC scores, EQ-5D-5L, and visual analogue scale measures. The authors reported statistically significant group differences favoring individualized homoeopathic medicines across several patient-reported outcomes. They also emphasized recruitment difficulties and the need for larger, more definitive studies and independent replication [8]. The feasibility design, small sample, and limited follow-up restrict conclusions about effectiveness. The trial did not establish effectiveness specifically in post-ACL injury osteoarthritis.

7.4 Comparative summary: The 2015 study involved 60 patients and found no statistically significant between-group differences for principal symptom outcomes over two weeks. The 2023 study involved 60 patients with knee or hip osteoarthritis and reported favorable differences over three months. The 2024 feasibility study involved 40 patients with knee osteoarthritis and reported favorable differences across several KOOS and quality-of-life outcomes. These studies investigated general osteoarthritis rather than a population specifically defined by previous ACL injury. Their findings therefore do not establish effectiveness for post-ACL injury osteoarthritis.

8. APPLICABILITY OF THE EVIDENCE TO POST-ACL INJURY OSTEOARTHRITIS

8.1 Differences in disease mechanisms: Post-traumatic osteoarthritis may involve specific structural and biomechanical abnormalities arising from the original injury. Meniscal damage, cartilage injury, previous reconstruction, and persistent instability may influence presentation and may differ from characteristics of patients with osteoarthritis arising predominantly from other causes.

8.2 Differences in patient characteristics: Patients with previous ACL injury may be younger or more physically active than many patients enrolled in general osteoarthritis trials. Their goals may include returning to work, sports, and physically demanding activities. Applicability of evidence from one population to another must therefore be assessed cautiously.

8.3 Differences in previous treatment: Patients may have received ligament reconstruction, meniscal surgery, rehabilitation, analgesics, or other interventions that influence symptoms and function. Future trials should document previous treatment and standardize or carefully record concomitant care.

8.4 Symptom management versus disease modification: If the aim is symptom management, appropriate outcomes include pain, stiffness, function, and quality of life. If the aim is disease modification, structural outcomes and longer follow-up are also necessary. Improvement in symptoms alone cannot establish prevention or reversal of osteoarthritis.

9. RESEARCH GAPS

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9.1 Lack of direct ACL-specific evidence: The most important gap is the absence of established clinical evidence directly demonstrating the effectiveness of homoeopathic interventions in patients with osteoarthritis following ACL injury. The trials discussed above cannot resolve this question because their study populations were not specifically defined by previous ACL injury.

9.2 Need for adequately powered randomized trials: Feasibility studies help evaluate recruitment, retention, acceptability, and trial procedures. Confirmatory trials require sample sizes based on a prespecified primary outcome and a clinically meaningful treatment difference. Designs should distinguish intervention-associated benefits from natural symptom fluctuation, placebo effects, regression to the mean, and shared concomitant care.

9.3 Need for clearly defined study populations: Future research should document previous ACL injury and mechanism; whether reconstruction was performed; time since injury; associated meniscal or cartilage damage; clinical and radiographic evidence of osteoarthritis; baseline symptoms and function; and previous rehabilitation and other treatments.

9.4 Standardized outcomes: Future trials should select validated measures such as WOMAC, KOOS, and EQ-5D-5L according to the research objective. The primary outcome, secondary outcomes, measurement time points, and statistical analysis plan should be prespecified.

9.5 Longer follow-up: Short-term symptom improvement does not establish long-term benefit. Symptom-management studies should evaluate persistence of improvement. Research investigating disease modification should include appropriate structural outcomes and sufficiently long follow-up.

9.6 Transparent reporting and replication: Future studies should incorporate prospective trial registration, appropriate randomization, allocation concealment, blinding where feasible, transparent reporting of withdrawals, and systematic adverse-event assessment. Independent replication is essential to determine whether reported benefits are reproducible.

10. PROPOSED FRAMEWORK FOR FUTURE RESEARCH

Proposed study title: Effect of Individualized Homoeopathic Treatment as an Adjunct to Standard Care in Patients with Knee Osteoarthritis Following Anterior Cruciate Ligament Injury: A Randomized, Placebo-Controlled Trial.

10.1 Study design: A randomized, double-blind, placebo-controlled trial could be considered following feasibility assessment and approval by an appropriate ethics committee.

10.2 Study population: Participants should have a documented history of ACL injury and clinically established knee osteoarthritis. Previous reconstruction, associated meniscal injuries, time since injury, and baseline disease severity should be documented.

10.3 Intervention and comparator: Participants could be randomized to individualized homoeopathic treatment or a matched placebo, with both groups receiving the same specified standard care. Appropriate rehabilitation and medically indicated treatment should not be withheld.

10.4 Primary outcome: A validated measure of knee pain or physical function should be selected as the primary outcome. The choice should reflect the main research question and support a prespecified sample-size calculation.

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10.5 Secondary outcomes: Possible secondary outcomes include WOMAC pain, stiffness, and function; KOOS domains; EQ-5D-5L; objective physical performance; rescue medication use; patient global assessment; and adverse events.

10.6 Statistical analysis: The primary analysis should compare outcomes between randomized groups using an appropriate prespecified statistical method. Effect estimates and confidence intervals should be reported alongside statistical significance. Missing data, withdrawals, and protocol deviations should be addressed transparently.

10.7 Ethical considerations: The study should receive appropriate ethics committee approval and be prospectively registered in a recognized clinical-trial registry, such as the Clinical Trials Registry–India, where applicable. Participants should provide informed consent and continue to receive appropriate clinical care. The protocol should include adverse-event reporting and confidentiality protections.

11. DISCUSSION

The development of osteoarthritis following ACL injury represents an important long-term clinical concern. Systematic reviews indicate that ACL injury is associated with increased risk of knee osteoarthritis, and associated meniscal injury is an important risk factor [1,2]. Long-term outcomes vary between individuals and depend on structural, biomechanical, and biological factors.

ACL reconstruction can improve stability and facilitate functional recovery, but it does not consistently prevent osteoarthritis. Against this background, the possibility of additional interventions to improve symptoms and function warrants careful scientific investigation.

Homoeopathic interventions have been investigated in clinical trials involving general osteoarthritis populations. The results are not uniform. The 2015 feasibility trial found no statistically significant superiority over placebo for principal symptom outcomes, whereas the 2023 randomized trial and the 2024 feasibility trial reported favorable differences for selected outcomes [6–8]. These findings must be interpreted in the context of sample size, design, follow-up, and the need for independent replication.

A favorable finding in an individual trial does not automatically establish a reproducible treatment effect. Statistical significance does not necessarily demonstrate clinical importance, and symptomatic improvement does not establish structural disease modification.

The applicability of these findings to post-ACL injury osteoarthritis is particularly uncertain because the studies discussed here did not specifically investigate that population. The evidence therefore supports identifying post-ACL injury osteoarthritis as an area for further research rather than claiming that homoeopathic interventions have already been proven effective for this condition.

A rigorous trial should evaluate whether individualized homoeopathic treatment, when added to appropriate standard care, produces clinically meaningful improvements beyond placebo in a clearly defined post-ACL injury population. Such a trial should use validated outcome measures, appropriate randomization and blinding, a prespecified statistical analysis plan, adequate follow-up, and transparent reporting. If structural disease modification is the intended claim, symptom measures alone would be insufficient.

The principal contribution of this review is the identification of a specific evidence gap at the intersection of post-traumatic osteoarthritis and homoeopathic clinical research.

12. LIMITATIONS

This review is a narrative review rather than a systematic review. It does not provide an exhaustive, reproducible search strategy or a complete account of all potentially eligible studies. No formal risk-of-bias assessment, quantitative synthesis, or formal certainty-of-evidence assessment was performed. The clinical trials discussed primarily investigated general knee or hip osteoarthritis rather than osteoarthritis specifically following ACL injury, limiting their direct applicability. The reviewed studies do not establish whether homoeopathic interventions prevent structural progression, regenerate cartilage, or reverse post-traumatic osteoarthritis. Conclusions may change as additional well-designed clinical studies become available.

13. CONCLUSION

Osteoarthritis following ACL injury is a multifactorial condition influenced by the severity of the original trauma, associated meniscal and cartilage damage, altered joint mechanics, and other individual risk factors. Although ACL reconstruction can improve stability and functional recovery, it does not consistently prevent long-term osteoarthritis.

Clinical studies have investigated homoeopathic interventions in general knee and hip osteoarthritis, with variable findings. Some studies have reported favorable differences in selected outcomes, whereas an earlier feasibility trial did not demonstrate statistically significant superiority over placebo for its principal symptom outcomes.

The available evidence does not establish the effectiveness of homoeopathic interventions specifically in osteoarthritis following ACL injury. The most important research priority is the conduct of adequately powered, preregistered, placebo-controlled trials in clearly defined post-ACL injury populations, alongside appropriate standard care. Such research should use validated clinical outcome measures, adequate follow-up, transparent statistical analysis, and systematic safety monitoring.

As a single homoeopathic remedy for consideration, Bryonia alba is described in homoeopathic materia medica for joint pains aggravated by movement and relieved by rest. It may be considered as a possible option for partial symptomatic relief in appropriately selected cases; however, this is not proof of clinical effectiveness. Osteoarthritis trials have included Bryonia alba among individualized prescriptions, but have not established its independent effect, and no direct evidence specific to post-ACL injury osteoarthritis is available [9,10].

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No new datasets were generated or analysed for this narrative review. All information discussed is derived from previously published literature cited in the manuscript

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