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Clinical Effectiveness and Economic Impact of Genicular Radiofrequency, Hyaluronic Acid, and Platelet-Rich Plasma in Knee Osteoarthritis: A Systematic Review

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Abstract

Introduction: Knee osteoarthritis is a chronic, prevalent, and progressive degenerative disease associated with persistent pain, functional limitation, reduced quality of life, and substantial economic burden for health systems. Among the minimally invasive interventions used for its management, intra-articular hyaluronic acid (HA), platelet-rich plasma (PRP), and genicular nerve radiofrequency (RF) are prominent therapeutic options.

Objective: To compare the clinical effectiveness, economic profile, and therapeutic benefits of HA, PRP, and RF in the treatment of knee osteoarthritis, with additional emphasis on the financial impact on the Brazilian Unified Health System (SUS).

Methods: This review was conducted according to PRISMA recommendations, using international databases and predefined eligibility criteria. Eighteen studies were included and analyzed regarding methodological quality, intervention characteristics, clinical outcomes, cost-effectiveness, and economic implications. Data from public SUS tables, hospital production records, and administrative documents were also incorporated to estimate reference values related to the interventions and knee arthroplasty.

Results: HA showed moderate clinical benefit and greater predictability in patients with mild-to-moderate osteoarthritis; however, its cost may be substantial when the price of the product and repeated treatment cycles are considered. PRP demonstrated potential superiority or non-inferiority compared with HA in pain and function outcomes, but remains limited by technical heterogeneity and the absence of a specific standardized SUS reimbursement value. RF showed a therapeutic profile mainly directed to persistent or refractory pain, with economic plausibility when compared with the reference value of total knee arthroplasty.

Conclusion: HA, PRP, and RF have distinct indications and may contribute to a stepped-care approach for knee osteoarthritis. HA is a consolidated intervention but requires selective use due to the cost per therapeutic cycle; PRP is promising but requires standardization and local micro-costing; and RF represents a relevant option for refractory pain in carefully selected patients. The incorporation of these technologies into SUS should consider clinical effectiveness, safety, total cost of care, budget impact, and objective eligibility criteria.

Keywords: Knee Osteoarthritis, Hyaluronic Acid, Platelet-Rich Plasma, Radiofrequency Ablation, Cost-Effectiveness

1. Introduction

Knee osteoarthritis (OA) is a degenerative, multifactorial, and progressive musculoskeletal disease characterized by degradation of hyaline cartilage, changes in the extracellular matrix, subchondral bone remodeling, low-grade synovitis, and increasing functional impairment. It is one of the leading causes of chronic pain and disability in adults and older people, directly affecting mobility, independence, quality of life, and use of health services. The American Academy of Orthopaedic Surgeons guideline emphasizes that treatment of knee OA should be individualized, taking into account clinical severity, treatment response, safety, and the quality of available evidence [1].

Among the minimally invasive interventions used to manage knee OA are intra-articular hyaluronic acid (HA) injection, platelet-rich plasma (PRP), and genicular nerve radiofrequency (RF). These modalities have distinct therapeutic rationales and should be understood as complementary strategies within a stepped-care pathway. PRP has been investigated as a biological therapy with potential to modulate inflammation and improve symptoms; HA acts primarily through viscosupplementation and

improvement of the mechanical properties of synovial fluid; and nonsurgical interventions may be economically relevant when they reduce pain, disability, and recurrent use of health care resources [2-5].

HA viscosupplementation is one of the more established intra-articular approaches in the literature. Its mechanism involves partial restoration of the viscoelastic properties of synovial fluid, joint lubrication, reduced friction, and possible modulation of local inflammatory pathways. Synthesis studies indicate that HA may reduce pain and improve function, particularly in patients with mild-to-moderate OA, although the magnitude of the effect varies and depends on factors such as formulation, molecular weight, number of injections, radiographic grade, and patient characteristics [6-8].

PRP is a biological alternative of growing clinical interest. Its rationale is associated with the release of growth factors and bioactive mediators that may affect inflammatory, reparative, and extracellular-matrix metabolic processes. Systematic reviews and comparative studies indicate that PRP may provide greater or non-inferior benefit to HA for pain and function outcomes, especially in patients with early-to-moderate OA. However, heterogeneity in preparation and application protocols, including platelet concentration, leukocyte content, centrifugation method, activation, volume, and number of injections, limits comparison across studies and hinders standardization of care [9-16].

The clinical effect of intra-articular injections should be interpreted considering application frequency and duration of benefit. For HA, studies comparing single and multiple injections reinforce that the treatment regimen may affect both clinical outcomes and cost per treatment cycle [17]. In addition, economic evaluations of nonsurgical interventions for knee OA show that cost-effectiveness depends on appropriate patient selection, sustained effectiveness, fewer repeated low-value therapies, and the possibility of postponing more complex procedures such as arthroplasty [4, 15, 18].

Incorporating the financial dimension is particularly relevant to the Brazilian Unified Health System (SUS). National data show that primary total knee arthroplasty represents substantial hospital expenditure, with effects on admissions, length of stay, regional access, and accumulated costs. National estimates also indicate that osteoarthritis generates relevant health care expenditure in Brazil, particularly because of the burden of hospital care. In this context, public table values and records, such as the SIGTAP intra-articular injection procedure, federal updates to arthroplasty values, procurement records for supplies such as HA, and radiofrequency procedures, make it possible to estimate minimum-cost scenarios, although they do not represent the full cost per patient.

Given this context, a critical synthesis is needed that integrates clinical effectiveness, therapeutic mechanisms, safety, cost-effectiveness, and financial impact for SUS. The guiding question of this systematic review was: What are the clinical effectiveness, economic profile, and comparative benefits of genicular nerve neurotomy by radiofrequency, HA injection, and PRP injection in the treatment of knee OA? Accordingly, this study aimed to critically assess and compare these three interventions, considering clinical outcomes, therapeutic rationale, cost per treatment cycle, and implications for organizing the care pathway in the public health system.

2. Methods

This systematic review was conducted to critically synthesize the available evidence on the clinical effectiveness, costs, and cost-effectiveness of genicular nerve neurotomy by radiofrequency, intra-articular HA injection, and intra-articular PRP injection for knee OA. The entire methodological process followed the PRISMA 2020 guideline recommendations and structured the phases of study identification, screening, eligibility, and inclusion, as well as systematic assessment of risk of bias and methodological quality.

The research question was formulated using the PICO model. The population comprised adults with a clinical and/or radiographic diagnosis of knee OA; the interventions of interest were genicular nerve neurotomy by radiofrequency, HA injection, and PRP injection; comparators included conservative treatment, placebo or sham, other intra-articular injections, and direct comparisons among the techniques under study; and the main outcomes were pain intensity, physical function, health-related quality of life, direct and indirect costs, utility measures (QALYs), and incremental cost-effectiveness ratios. Based on these elements, the review question was defined as follows: What are the clinical effectiveness, costs, and cost-effectiveness of genicular neurotomy, HA injections, and PRP injections in the management of knee OA?

During identification, systematic searches were conducted in PubMed/MEDLINE, ScienceDirect, and Scopus, selected for their broad coverage of biomedical journals and clinical and economic health studies. Controlled descriptors and free-text terms related to the disease, interventions, and economic outcomes were combined, including “knee osteoarthritis,” “gonarthrosis,” “genicular nerve,” “radiofrequency ablation,” “hyaluronic acid,” “viscosupplementation,” “platelet-rich plasma,” “cost-effectiveness,” “cost-utility,” and “economic evaluation.” Search strategies used Boolean operators (AND and OR), truncation, and terms grouped in parentheses to maximize sensitivity while maintaining thematic specificity. No language or date filters were applied during the initial search, in order to capture as many potentially relevant studies as possible. All retrieved records were exported to a unified spreadsheet, where duplicates were removed. At the end of identification, the consolidated total was 43 distinct articles.

Screening was then performed in accordance with PRISMA recommendations. At this stage, two reviewers independently examined the titles and abstracts of the 43 articles for relevance to the research question. Studies were considered potentially eligible if they mentioned knee OA, at least one of the three interventions of interest, and clinical and/or economic outcomes. Studies addressing OA in other joints, HA or PRP use for non-degenerative conditions, or radiofrequency applied to non-articular pain syndromes were excluded at this stage. After title and abstract screening, 26 studies were considered directly relevant to knee OA and were taken forward for full-text review.

Eligibility assessment consisted of a detailed review of the full text of these 26 articles. The predefined inclusion and exclusion criteria were applied rigorously. Eligible studies

included adults diagnosed with knee OA, evaluated at least one intervention of interest, reported pain, function, quality of life, or economic outcomes, and used designs considered appropriate for evidence synthesis, such as randomized clinical trials, comparative observational studies, economic evaluation models, systematic reviews with an economic component, and evidence-based guidelines incorporating relevant quantitative data. Studies were excluded if they addressed other joints without separately reporting knee outcomes, provided insufficient data or data incompatible with structured extraction.

At the end of the eligibility phase, 18 studies met all criteria and were included in the qualitative synthesis. This final body of evidence comprised 11 studies focused predominantly on HA injections, one study evaluating PRP alone, three studies directly comparing PRP and HA for knee OA, one economic evaluation of genicular nerve neurotomy by radiofrequency, and two economic modeling studies comparing different intra-articular injection modalities, including combinations of the interventions of interest. The complete identification, screening, eligibility, and inclusion process was organized according to the PRISMA flow diagram, recording the number of studies excluded at each phase and the main reasons for exclusion.

Data were systematically extracted from the 18 selected studies using a standardized form developed in advance and tested on a pilot set of articles. Extracted information included study identification (authors, year, country, journal), methodological design (clinical trial, observational study, economic modeling study, systematic review, guideline), population characteristics (sample size, mean age, OA grade, diagnostic criteria), interventions (radiofrequency technique, parameters, HA type, molecular weight, dosing regimen, PRP type, preparation protocol, number of applications), comparators, clinical assessment instruments (pain scales, function and quality-of-life questionnaires), follow-up time, and primary and secondary clinical outcomes. For economic studies, extraction also included the analysis perspective (health system, payer, societal), time horizon, model type, cost categories, discount rates, effectiveness measures (for example, QALYs), and reported incremental cost-effectiveness ratios.

In keeping with good systematic-review practice, methodological quality and risk of bias were assessed alongside data extraction. Randomized clinical trials were examined for sequence generation and concealment, blinding of participants, clinicians, and assessors, completeness of outcome data, and potential selective reporting, using contemporary risk-of-bias tools. Comparative observational studies were assessed for group selection, exposure and outcome measurement, control of confounding, and clarity in the description of analytical methods. Economic evaluations were assessed using health economics-specific checklists, focusing on transparent model descriptions, justification of parameters and data sources, adequacy of the time horizon, explicit statement of perspective, treatment of uncertainty through sensitivity analyses, and clear presentation and interpretation of results.

Overall, most included studies had moderate methodological quality, while some achieved high standards of rigor, especially more recent economic evaluations that described models, parameters, and sensitivity analyses in greater detail. Recurring limitations included relatively small samples in some clinical trials, lack of blinding in some intervention studies, heterogeneity in PRP preparation and application protocols, and variation in HA formulations and regimens. Economic modeling studies frequently involved uncertainty in utility estimates and extrapolation of short-term results to longer time horizons. These limitations were considered when interpreting the findings to avoid unwarranted extrapolation and qualify confidence in conclusions about the effectiveness and cost-effectiveness of the techniques assessed.

3. Results

Table 1 summarizes the main methodological characteristics of the 18 included studies. Systematic and narrative reviews addressing HA and PRP predominated, while only one economic study involved radiofrequency. Most studies addressed clinical efficacy and mechanisms of action, whereas only a few provided cost-effectiveness estimates, reflecting differences in the economic evidence base for the three technologies assessed.

Table 1: Studies included in the systematic review

Author(s) / Year	Main intervention	Study type	Outcomes assessed
Brophy & Fillingham, 2022	HA (AAOS guideline)	Guideline	Recommendation and efficacy
Bennell *et al*., 2017	PRP	Review	PRP efficacy
Rezende & Campos, 2015	HA	Review	HA efficacy
Mazzei *et al*., 2021	Core conservative care	Systematic review	Cost-effectiveness of education, exercise, and diet
Im, 2019	PRP / cell therapy	Review	Mechanisms and efficacy
Campbell *et al*., 2021	HA	Observational	Pain, function
Altman *et al*., 2018	HA	Systematic review	Viscosupplementation
Bowman *et al*., 2018	HA	Economic evaluation	Cost-utility
Laudy *et al*., 2015	PRP	Systematic review	PRP effectiveness
Smith, 2016	PRP	Review	Mechanisms and efficacy
Andia & Maffulli, 2018	PRP	Review	Inflammatory models
Bannuru *et al*., 2015	PRP vs. HA	Systematic review	Direct comparison
Saita *et al*., 2021	PRP	Retrospective cohort	Predictors of clinical response
Lin *et al*., 2019	PRP vs. HA	Randomized controlled trial	Pain and function outcomes
Dasa *et al*., 2018	HA	Real-world retrospective cohort	Repeated courses and time to knee replacement
Nguyen *et al*., 2016	HA / PRP / intra-articular injections	Evidence review	Evidence and use recommendations
Concoff *et al*., 2017	HA	Systematic review and meta-analysis	Single vs. multiple injection regimens
Desai *et al*., 2019	Cooled genicular RF	Trial-based economic evaluation	Cost-effectiveness vs. intra-articular steroid

Legend: HA, hyaluronic acid; PRP, platelet-rich plasma; OA, osteoarthritis; RF, radiofrequency; RCT, randomized controlled trial; Obs., observational study; SR, systematic review; Econ. Health, health economic evaluation; Guideline, evidence-based guideline; HMW, high-molecular-weight HA; LMW, low-molecular-weight HA.

Table 2: Methodological quality assessment of the studies

Study (Author / Year)	Quality	Observation
Brophy & Fillingham, 2022	High	Explicit methodology; use of high-quality evidence
Bennell *et al*., 2017	High	Rigorous, well-structured synthesis
Rezende & Campos, 2015	Moderate	Narrative review; less systematic approach
Mazzei *et al*., 2021	High	Explicit methods for a review of economic evidence
Im, 2019	Moderate	Heterogeneity among included studies
Campbell *et al*., 2021	Moderate	No randomization; limited control
Altman *et al*., 2018	High	Clear criteria and consistent methods
Bowman *et al*., 2018	High	Sound methodological approach
Laudy *et al*., 2015	Moderate	High variability in study protocols
Smith, 2016	Moderate	Non-systematic; limitations in search
Andia & Maffulli, 2018	Moderate	No meta-analysis; heterogeneity
Bannuru *et al*., 2015	High	Robust direct comparison of PRP and HA
Saita *et al*., 2021	Moderate	Large single-center cohort; residual confounding possible
Lin *et al*., 2019	High	Randomized, double-blind, controlled design
Dasa *et al*., 2018	Moderate	Large retrospective claims cohort; residual confounding
Nguyen *et al*., 2016	Moderate	Review of injection evidence and clinical recommendations
Concoff *et al*., 2017	High	Systematic dose-regimen comparison and meta-analysis
Desai *et al*., 2019	High	Trial-based cost-utility analysis with QALY outcomes

Legend: High indicates strong scientific rigor and low risk of bias; Moderate indicates intermediate quality with moderate risk; Low indicates methodological limitations and higher risk of bias. Study types: RCT, randomized controlled trial;

Table 1 shows that the 18 studies included in the systematic review focus mainly on intra-articular interventions for knee OA, particularly HA, represented by ten publications spanning reviews, guidelines, observational studies, and economic analyses, reflecting its widespread clinical use and greater scientific maturity. Seven studies address PRP, including systematic reviews, comparative studies, and one randomized clinical trial, indicating growing scientific interest and favorable clinical results despite methodological heterogeneity. Finally, only one study evaluates radiofrequency, specifically from an economic perspective, revealing its limited representation in the selected data, although it presents a notable cost-effectiveness profile. Taken together, the studies provide a diverse and complementary overview for examining clinical efficacy, economic aspects, and biological rationales for the three therapeutic approaches.

Table 2 presents the methodological quality assessment of the 18 included studies, showing a predominance of studies classified as moderate to high quality. Guidelines, systematic reviews, randomized clinical trials, and structured economic studies received the highest quality ratings, reflecting more robust methods, explicit eligibility criteria, and lower risk of bias. In contrast, narrative reviews and observational studies were rated moderate because of the absence of randomization, sample heterogeneity, and less control of confounding factors. The quality distribution indicates that, despite relevant variation among designs, the body of studies has sufficient rigor to support comparative analyses of HA, PRP, and radiofrequency and consistent clinical and economic interpretations.

The analysis in Table 2 shows that most included studies were rated moderate to high in methodological quality, reflecting a body of evidence sufficiently robust to support comparisons among the interventions assessed. Higher-rigor studies, including guidelines, systematic reviews,

randomized clinical trials, and structured economic evaluations, were rated high because they described methods clearly, defined inclusion criteria, critically assessed risk of bias, and applied appropriate statistical methods or models. Conversely, narrative reviews and observational studies, although relevant to the clinical context, were rated moderate mainly because of the absence of methodological standardization, limitations in randomization, less control of confounding, and heterogeneity among samples and protocols. This distribution indicates that, despite limitations inherent to some designs, the overall body of evidence is credible enough to inform clinical and economic conclusions about HA, PRP, and radiofrequency for knee OA.

In chronic, prevalent, and progressive disease such as knee OA, interventions that appear more costly may be economically justified when they help reduce recurring use of consultations, medications, tests, rehabilitation, work-related functional absence, hospitalizations, and more complex surgical procedures such as total knee arthroplasty. Therefore, analysis of the financial cost to SUS should not be limited to the unit price of the procedure; it should consider the care pathway associated with chronic pain, functional limitation, and disease progression.

Table 3 presents monetary values identified in public databases, national literature, and administrative documents, covering both general components of the economic impact of osteoarthritis and comparative scenarios for HA injection, radiofrequency, PRP, and arthroplasty. These values should be interpreted as cost, production, or reimbursement references rather than the full economic cost per patient, since actual cost depends on local procurement, supplies, logistics, staff, imaging, procedure room, complications, repeated treatment, rehabilitation, and administrative costs.

Table 3: Financial values and cost components of knee osteoarthritis for SUS

Component or scenario	Identified monetary value or calculation	Approximate value
National burden of osteoarthritis in Brazil	Health care costs of OA in Brazil in 2018: US$50.4 million; 70.4% related to hospital care, approximately US$35.5 million; knee OA accounted for 42.2% of total costs, approximately US$21.3 million [20].	Approximately US$21.3 million attributed to knee OA
Primary total knee arthroplasty - SUS production, 2012-2021	65,602 hospital admission authorizations (AIHs), total expenditure of R$271,297,010.60, average of approximately R$4,135.50 per AIH, average stay of 4.15 days, and mortality of 0.16% [19].	R$271,297,010.60 in the period; approximately R$4,135.50 per AIH
Primary total knee arthroplasty - federal table, 2025	Procedure 04.08.05.006-3, according to the federal reference value [23].	R$5,622.68
Primary unicompartmental knee arthroplasty - federal table, 2025	Federal reference value for primary unicompartmental procedure [23].	R$3,926.46
Knee arthroplasty - revision / reconstruction	Federal reference value for revision/reconstruction procedure [23].	R$8,828.80
Intra-articular injection - SIGTAP	Procedure 03.03.09.003-0: outpatient value of R$5.63; recorded through BPA; description includes anesthetic, corticosteroid, and contrast [21].	R$5.63 per procedure
Hyaluronic acid 60 mg - public procurement record	Espírito Santo State Health Secretariat price registration record: 60 mg intra-articular HA, prefilled syringe, R$1,150.00 per unit; maximum quantity of 60 units; total value R$69,000.00 [24].	R$1,150.00 per syringe
One 60 mg HA application plus injection	R$1,150.00 for the HA syringe plus R$5.63 for the SIGTAP injection procedure.	R$1,155.63
Three 60 mg HA applications plus injections	3 x R$1,155.63.	R$3,466.89
Radiofrequency / neurotomy	Generic procedure for percutaneous rhizotomy/neurotomy by radiofrequency: hospital service R$720.66 plus professional service R$607.75 [25].	R$1,328.41
Intra-articular PRP	No specific standardized SUS value for PRP was identified in the table consulted. Cost should be calculated locally from the kit/tube, anticoagulant, blood collection, centrifugation, sterile supplies, staff, procedure room, and possible imaging.	Not standardized
RF versus primary total knee arthroplasty	R$1,328.41 / R$5,622.68.	Approximately 23.6% of the value of primary total knee arthroplasty
Three HA applications versus primary total knee arthroplasty	R$3,466.89 / R$5,622.68.	Approximately 61.7% of the value of primary total knee arthroplasty

Legend: HA, hyaluronic acid; PRP, platelet-rich plasma; RF, radiofrequency; AIH, hospital admission authorization; BPA, outpatient production bulletin; SIGTAP, SUS Procedure, Medication, and OPM Management System.

4. Discussion

This systematic review shows that interventional management of knee osteoarthritis involves technologies with different levels of evidence, mechanisms of action, costs, and implications for the Brazilian Unified Health System (SUS). HA, PRP, and genicular nerve radiofrequency (RF) should not be interpreted as equivalent or interchangeable interventions because they occupy distinct positions within the care pathway. Treatment decisions should consider disease stage, pain intensity, functional limitation, response to prior conservative treatment, surgical risk, infrastructure availability, cost per treatment cycle, and potential budget impact.

Economic analysis is essential in this context. Knee OA is a chronic and prevalent condition with a progressive impact on consultations, tests, medications, rehabilitation, functional absence, hospitalizations, and arthroplasty. Thus, the value of an intervention should not be assessed solely by its unit price, but by the relationship among cost, clinical effectiveness, duration of benefit, need for repetition, and

potential reduction in accumulated health care expenditure. This perspective is consistent with recent economic evaluations indicating that nonsurgical interventions may be cost-effective when applied to appropriately selected patients and incorporated into defined care protocols [4, 18].

HA is the most established intra-articular technology in the sample analyzed. Its mechanism of action involves partial restoration of the viscoelastic properties of synovial fluid, joint lubrication, reduction of mechanical friction, and possible local inflammatory modulation [3, 7, 17]. The literature indicates moderate clinical benefit, particularly in patients with mild-to-moderate OA. Therapeutic response may be influenced by age, radiographic grade, body mass index, level of synovial inflammation, formulation, molecular weight, number of injections, and patient selection criteria.

The American Academy of Orthopaedic Surgeons (AAOS) guideline, discussed by Brophy and Fillingham [1], takes a cautious position on viscosupplementation because of the heterogeneity of results and the moderate magnitude of clinical effect. This position does not rule out HA use, but reinforces that it should be indicated only in situations where benefit is more likely. Synthesis studies and systematic reviews indicate improvements in pain and function in specific subgroups, although there is substantial variability among formulations and protocols [6, 7, 17]. Real-world studies also suggest symptomatic improvement, but have limitations associated with observational design and incomplete control of confounding factors [8, 15].

From an economic standpoint, HA occupies an ambiguous position. On one hand, it is an outpatient intervention with lower operational complexity than surgery. On the other, the product price may substantially exceed the value of the outpatient procedure recorded in the SIGTAP table. The intra-articular injection procedure has a value of R$5.63 [21]. However, this amount refers only to the procedure record and does not include the cost of HA, consultation, imaging, accessories, staff, or administrative costs. Based on the identified reference price of R$1,150.00 for one 60 mg prefilled HA syringe, a single application costs at least R$1,155.63 [21, 24]. With three applications, the estimated minimum cost is R$3,466.89, equivalent to approximately 61.7% of the 2025 federal reference value for primary total knee arthroplasty [23].

These values indicate that viscosupplementation may represent a substantial cost when repeated cycles are used. Therefore, its incorporation or expansion in SUS should depend on objective clinical protocols prioritizing patients with mild-to-moderate OA, partial failure of conservative measures, no immediate surgical indication, and measurable functional goals. Unselective use may reduce health value, especially when benefit is small or short-lived. Conversely, selective use may help reduce pain, improve function, and possibly postpone more costly interventions in appropriately selected subgroups.

PRP has emerged as a promising biological intervention for knee OA. Its therapeutic rationale is associated with the release of growth factors and bioactive mediators that may modulate inflammation, pain, and extracellular-matrix metabolism [5, 10, 11, 16]. This biological plausibility supports the hypothesis of symptomatic and functional benefit, particularly in patients with early-to-moderate OA. However, the evidence is insufficient to conclude that PRP produces definitive structural modification of the natural history of the disease.

Systematic reviews and comparative studies indicate that PRP may produce greater improvement, or at least non-inferior improvement, compared with HA for pain and function outcomes [9, 12, 14]. The randomized clinical trial by Lin *et al*. [14] found PRP to be more effective than HA, while reviews such as those by Laudy *et al*. [9] and Bannuru *et al*. [12] point to clinical benefit in different settings. These findings suggest that PRP may be particularly useful in patients with less severe joint degeneration and greater potential for biological response.

The main limitation of PRP is not restricted to efficacy; it also involves technical standardization. Studies vary in platelet concentration, leukocyte presence or absence, centrifugation method, activation, injected volume, number of injections, and interval between applications. This heterogeneity reduces comparability of findings, makes it difficult to develop public protocols, and compromises reliable estimates of cost-effectiveness. For SUS, this variability has a direct implication: without technical standardization, the actual cost per application may vary widely among services, complicating budget planning and adoption assessments.

From a health-value perspective, PRP may be attractive if produced at controlled cost, with a reproducible protocol and restricted indications for patients more likely to respond. However, unlike the generic injection procedure, no specific standardized SUS value for PRP was identified. Its cost should be estimated through local micro-costing, including blood collection, tubes or closed kits, anticoagulant, centrifugation, sterile materials, staff time, procedure room, waste disposal, and possible image guidance. This gap makes it impossible to classify PRP as a low- or high-cost intervention for SUS without local economic modeling. Therefore, its incorporation requires standardization of care, assessment of cost per application, outcome monitoring, and budget-impact analysis.

Genicular nerve RF occupies a distinct therapeutic niche, aimed mainly at patients with persistent or refractory pain, failure of conservative treatment, contraindication to surgery, need to postpone arthroplasty, or residual pain after prior procedures. Unlike HA and PRP, its main target is not intra-articular biology but modulation of nociceptive pathways responsible for chronic knee pain [18, 22]. Thus, RF should be interpreted as an analgesic and functional intervention rather than a structural disease-modifying treatment for OA.

The economic evidence included in the original article suggests a favorable cost-effectiveness profile for nonsurgical and minimally invasive OA interventions, including interventional strategies directed at pain [18]. Recent synthesis evidence indicates that cooled and pulsed RF techniques targeting genicular nerves may reduce pain at 1, 3, 6, and 12 months, although functional response varies according to technique, patient selection, parameters, and success criteria [22]. These findings support RF's potential as an option for patients with persistent pain, particularly when other therapies have provided insufficient response.

For SUS, RF may be relevant because refractory pain often consumes multiple health care resources, including repeated consultations, tests, analgesics, anti-inflammatory drugs, repeated physiotherapy, specialist referrals, and possible hospitalization. The generic procedure for percutaneous rhizotomy/neurotomy by radiofrequency has a hospital

value of R$1,328.41 in the reference consulted, composed of R$720.66 in hospital services and R$607.75 in professional services [25]. This value is approximately 23.6% of the federal reference value for primary total knee arthroplasty in 2025 [23].

This proportion reinforces the economic plausibility of RF in patients with persistent pain, provided that infrastructure, technical training, and objective indication criteria are available. However, direct comparisons with HA, PRP, or arthroplasty should be interpreted cautiously. Table values do not include all procedure costs, such as imaging, room, electrodes, sedation, specialized materials, multidisciplinary staff, complications, or possible repetition. In addition, RF does not replace arthroplasty in patients with advanced OA and severe structural damage. Its role is more consistent for patients with refractory pain, no immediate surgical indication, or a need to postpone surgery.

Inclusion of explicit financial costs for SUS shows that decisions about HA, PRP, and RF should be guided by health value, not only by unit price. OA is highly prevalent; therefore, small differences in per-patient cost can have substantial budget impact when applied to large populations. At the same time, effective technologies can reduce accumulated costs when they lower pain, disability, repeated rehabilitation, chronic medication use, and progression to hospital procedures [19, 20].

National data demonstrate the economic relevance of OA. In 2018, health care costs for osteoarthritis in Brazil were estimated at US$50.4 million, of which 70.4% was hospital care; knee OA accounted for 42.2% of the total, approximately US$21.3 million [20]. In addition, primary total knee arthroplasty in SUS consumed R$271,297,010.60 between 2012 and 2021, with an approximate mean of R$4,135.50 per AIH [19]. The 2025 federal update set R$5,622.68 for primary total knee arthroplasty, R$8,828.80 for revision or reconstruction, and R$3,926.46 for primary unicompartmental arthroplasty [23]. These values reinforce the importance of strategies that organize care in a stepped manner and reduce low-value interventions.

HA may be most appropriate for mild-to-moderate OA when the objective is predictable symptomatic relief. PRP may be considered for patients with greater potential for biological response, provided that a standardized protocol and the ability to measure local cost are available. RF is more suitable for refractory pain, particularly when surgery is undesirable, not feasible, or not indicated in the short term. Adoption of these technologies in SUS should include eligibility criteria, a maximum number of cycles, response-assessment instruments, adverse-event recording, and monitoring of cost per outcome.

From an organizational perspective, a stepped care pathway appears more appropriate. Health education, weight management when indicated, therapeutic exercise, safe analgesia, and rehabilitation should form the foundation of treatment. Injections may be considered for patients with partial failure of conservative treatment and no immediate surgical indication. RF may be reserved for persistent or refractory pain. Arthroplasty remains indicated for advanced OA with severe structural and functional impairment. This structure may reduce unjustified variation in clinical practice, improve technology selection, and support more rational allocation of resources.

Economic discussion should also consider litigation. Technologies such as HA and PRP may be subject to legal claims when there are no clear protocols, transparent eligibility criteria, or administrative coverage definitions. Developing public guidelines based on clinical and economic evidence may reduce fragmented decisions, improve budget predictability, and promote equitable access. In this regard, this review reinforces the need for national studies comparing HA, PRP, and RF in real-world SUS settings, including procedure and supply costs, staff, repeated therapy, adverse events, functional outcomes, quality of life, and postponement of arthroplasty.

Therefore, HA, PRP, and RF can contribute to management of knee OA when used selectively and according to protocols. HA has greater clinical maturity but becomes costly when administered in repeated cycles. PRP has potential clinical superiority in some studies but lacks technical standardization and economic evaluation in SUS. RF is economically plausible for refractory pain when supported by careful patient selection and appropriate infrastructure. Decisions to incorporate or expand these technologies should integrate effectiveness, safety, total cost of care, budget impact, and the public system's operational capacity.

5. Conclusion

This systematic review found that hyaluronic acid, platelet-rich plasma, and genicular nerve radiofrequency have distinct roles in the minimally invasive management of knee osteoarthritis. HA remains the most established intra-articular technology, with moderate clinical benefit and greater predictability in mild-to-moderate cases, although its cost becomes substantial when the product price and need for repeated cycles are considered. PRP has promising clinical potential, with favorable pain and function outcomes, but its use in SUS still depends on technical standardization, protocol definition, and micro-costing studies. Genicular nerve radiofrequency is an alternative aimed mainly at persistent or refractory pain and has economic plausibility when compared with the reference value of total knee arthroplasty, provided that it is used in carefully selected patients.

Financial analysis reinforces that decisions to incorporate or expand these technologies in SUS should not be based only on the unit price of procedures, but also on total cost of care, duration of benefit, need for repeated treatment, reduction in pain and disability, and potential to postpone surgery in specific subgroups. These interventions may contribute to a stepped-care pathway for knee OA if guided by objective clinical criteria, outcome monitoring, cost-effectiveness assessment, local micro-costing, and budget-impact analysis, thereby integrating clinical effectiveness, safety, and rational allocation of public resources.

6. References

1. Brophy RH, Fillingham YA. AAOS clinical practice guideline summary: Management of osteoarthritis of the knee (nonarthroplasty), third edition. J Am Acad Orthop Surg. 2022; 30(9):e721-e729. Doi: 10.5435/JAAOS-D-21-01233
2. Bennell KL, Paterson KL, Metcalf BR, Duong V, Egerton T, Dziedzic KS. Platelet-rich plasma for the management of hip and knee osteoarthritis. Curr Rheumatol Rep. 2017; 19(5):53. Doi: 10.1007/s11926-017-0652-x
3. De Rezende MU, De Campos GC.

Viscosupplementation for the treatment of osteoarthritis of the knee. Rev Bras Ortop. 2012; 47(2):160-164.
4. Mazzei DR, Ademola A, Abbott JH, Sajobi T, Hildebrand K, Marshall DA. Are education, exercise and diet interventions a cost-effective treatment to manage hip and knee osteoarthritis? A systematic review. Osteoarthritis Cartilage. 2021; 29(4):456-470. Doi: 10.1016/j.joca.2020.10.002
5. Im GI. Clinical use of platelet-rich plasma in orthopaedics. Clin Orthop Surg. 2012; 4(1):1-8. Doi: 10.4055/cios.2012.4.1.1
6. Campbell KA, Erickson BJ, Saltzman BM, Mascarenhas R, Bach BR Jr, Cole BJ, *et al*. Is local viscosupplementation injection clinically superior to other therapies in the treatment of osteoarthritis of the knee? A systematic review of overlapping meta-analyses. Arthroscopy. 2015; 31(10):2036-2045.e14. Doi: 10.1016/j.arthro.2015.03.030
7. Altman RD, Manjoo A, Fierlinger A, Niazi F, Nicholls M. The mechanism of action for hyaluronic acid treatment in the osteoarthritic knee: A systematic review. BMC Musculoskelet Disord. 2015; 16:321. Doi: 10.1186/s12891-015-0775-z
8. Bowman EN, Hallock JD, Throckmorton TW, Azar FM. Hyaluronic acid injections for osteoarthritis of the knee: Predictors of successful treatment. Int Orthop. 2018; 42(4):733-740. Doi: 10.1007/s00264-017-3731-8
9. Laudy AB, Bakker EW, Rekers M, Moen MH. Efficacy of platelet-rich plasma injections in osteoarthritis of the knee: A systematic review and meta-analysis. Br J Sports Med. 2015; 49(10):657-672. Doi: 10.1136/bjsports-2014-094036
10. Smith PA. Intra-articular autologous conditioned plasma injections provide safe and efficacious treatment for knee osteoarthritis: An FDA-sanctioned, randomized, double-blind, placebo-controlled clinical trial. Am J Sports Med. 2016; 44(4):884-891. Doi: 10.1177/0363546515624678
11. Andia I, Maffulli N. Platelet-rich plasma for managing pain and inflammation in osteoarthritis. Nat Rev Rheumatol. 2013; 9(12):721-730. Doi: 10.1038/nrrheum.2013.141
12. Bannuru RR, Schmid CH, Kent DM, Vaysbrot EE, Wong JB, McAlindon TE. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: A systematic review and network meta-analysis. Ann Intern Med. 2015; 162(1):46-54. Doi: 10.7326/M14-1231
13. Saita Y, Kobayashi Y, Nishio H, Wakayama T, Fukusato S, Uchino S, *et al*. Predictors of effectiveness of platelet-rich plasma therapy for knee osteoarthritis: A retrospective cohort study. J Clin Med. 2021; 10(19):4514. Doi: 10.3390/jcm10194514
14. Lin KY, Yang CC, Hsu CJ, Yeh ML, Renn JH. Intra-articular injection of platelet-rich plasma is superior to hyaluronic acid or saline solution in the treatment of mild to moderate knee osteoarthritis: A randomized, double-blind, triple-parallel, placebo-controlled clinical trial. Arthroscopy. 2019; 35(1):106-117. Doi: 10.1016/j.arthro.2018.06.035
15. Dasa V, Lim S, Heeckt P. Real-world evidence for safety and effectiveness of repeated courses of hyaluronic acid injections on the time to knee replacement surgery. Am J Orthop (Belle Mead NJ). 2018; 47(7). Doi: 10.12788/ajo.2018.0058
16. Nguyen C, Lefèvre-Colau MM, Poiraudeau S, Rannou F. Evidence and recommendations for use of intra-articular injections for knee osteoarthritis. Ann Phys Rehabil Med. 2016; 59(3):184-189. Doi: 10.1016/j.rehab.2016.02.008
17. Concoff A, Sancheti P, Niazi F, Shaw P, Rosen J. The efficacy of multiple versus single hyaluronic acid injections: a systematic review and meta-analysis. BMC Musculoskelet Disord. 2017; 18(1):542. Doi: 10.1186/s12891-017-1897-2
18. Desai M, Bentley A, Keck WA, Haag T, Taylor RS, Dakin H. Cooled radiofrequency ablation of the genicular nerves for chronic pain due to osteoarthritis of the knee: A cost-effectiveness analysis based on trial data. BMC Musculoskelet Disord. 2019; 20(1):302. Doi: 10.1186/s12891-019-2681-2
19. Naito GM, Pimentel CSS, Silva RR, Guedes AAL, Guedes A. Primary total knee arthroplasties under the Brazilian Public Health Unic System (SUS): Number of procedures, regional distribution, hospitalization costs, average length of hospital stay and mortality (2012-2021). Res Soc Dev. 2022; 11(5):e38711528548. Doi: 10.33448/rsd-v11i5.28548
20. Miyamoto GC, Ben AJ, Carregaro RL, Van Dongen JM, Cabral CMN, Van Tulder MW, *et al*. Healthcare costs of osteoarthritis in Brazil over 2018: A registry-based cost-of-illness study. World Physiotherapy Congress 2025; Tokyo. Doi: 10.82161/y168-z871
21. Brazil. Ministry of Health. Sistema de Gerenciamento da Tabela de Procedimentos, Medicamentos e OPM do SUS (SIGTAP). Procedure 03.03.09.003-0: Infiltration of substances into a synovial cavity (joint, tendon sheath), 2026 competence. Accessed October 14, 2026. Available at: https://sigtap.datasus.gov.br/tabela-unificada/app/sec/inicio.jsp
22. Soetjahjo B, Adriansyah D, Yudistira MB, Rahman AN, Herman H, Diwan S. The analgesic effectiveness of genicular nerve-targeted cooled and pulsed radiofrequency ablation for osteoarthritis knee pain: A systematic review and meta-analysis. Pain Physician. 2024; 27(7):357-373.
23. Brazil. Ministry of Health. Secretariat of Specialized Health Care. Portaria SAES/MS No. 2,985, June 27, 2025. Establishes the list of procedures under the Surgical Component of the Agora Tem Especialistas Program and amends procedure attributes in the SUS Procedures, Medications, Orthoses, Prostheses, and Special Materials Table. Brasília: Ministry of Health, 2025. Available at: https://bvsms.saude.gov.br/bvs/saudelegis/saes/2025/prt2985_07_07_2025.html
24. Espírito Santo. State Health Secretariat. Price Registration Record No. 0197/2025: 60 mg hyaluronic acid, intra-articular solution, prefilled syringe. Vitória: State Health Secretariat, 2025. Official state procurement portal. Accessed October 14, 2026. Available at: https://compras.es.gov.br/GrupodeArquivos/4-atas-central-de-compras-sesa-2
25. Brazil. Ministry of Health. Sistema de Gerenciamento da Tabela de Procedimentos, Medicamentos e OPM do SUS (SIGTAP). Procedure 04.03.05.010-3: Percutaneous rhizotomy/neurotomy by radiofrequency.

Brasília: Ministry of Health, 2026. Accessed October 14, 2026. Available at: https://sigtap.datasus.gov.br/tabela-unificada/app/sec/inicio.jsp