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EVIDENCE-BASED REVIEW

Update of Evidence-Based Interventional Pain Medicine According to Clinical Diagnoses

9. Chronic knee pain

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Abstract

Introduction: Chronic knee pain is defined as pain that persists or recurs over 3 months. The most common is degenerative osteoarthritis (OA). This review represents a comprehensive description of the pathology, diagnosis, and treatment of OA of the knee.

Methods: The literature on the diagnosis and treatment of chronic knee pain was retrieved and summarized. A modified Delphi approach was used to formulate recommendations on interventional treatments.

Results: Patients with knee OA commonly present with insidious, chronic knee pain that gradually worsens. Pain caused by knee OA is predominantly nociceptive pain, with occasional nociplastic and infrequent neuropathic characteristics occurring in a diseased knee. A standard musculoskeletal and neurological examination is required for the diagnosis of knee OA. Although typical clinical OA findings are sufficient for diagnosis, medical imaging may be performed to improve specificity. The differential diagnosis should exclude other causes of knee pain including bone and joint disorders such as rheumatoid arthritis, spondylo- and other

arthropathies, and infections. When conservative treatment fails, intra-articular injections of corticosteroids and radiofrequency (conventional and cooled) of the genicular nerves have been shown to be effective. Hyaluronic acid infiltrations are conditionally recommended. Platelet-rich plasma infiltrations, chemical ablation of genicular nerves, and neurostimulation have, at the moment, not enough evidence and can be considered in a study setting. The decision to perform joint-preserving and joint-replacement options should be made multidisciplinary.
Conclusions: When conservative measures fail to provide satisfactory pain relief, a multidisciplinary approach is recommended including psychological therapy, integrative treatments, and procedural options such as intra-articular injections, radiofrequency ablation, and surgery.

KEYWORDS
chronic knee pain, corticosteroids, genicular nerves, hyaluronic acid, osteoarthritis, radiofrequency treatment, spinal cord stimulation

INTRODUCTION

> This narrative review on chronic knee pain is part of a series "Update of evidence-based interventional pain medicine according to clinical diagnoses."

Chronic knee pain is defined as knee pain that persists or recurs for more than 3 months.[1] The most common cause of chronic knee pain is degenerative osteoarthritis (OA).[2–4] Other etiologies of knee pain include rheumatoid arthritis, crystal and spondylo-arthropathies, post-traumatic pain, and persistent postsurgical pain (PPSP). Discussion of all these conditions is beyond the scope of this narrative review, and we will focus on a comprehensive description of the pathology, diagnosis, and treatment of OA of the knee. Special attention will be given to minimally invasive interventional treatments of knee pain due to OA, how they are performed, and their complications. Based on the discussed literature, recommendations are formulated for these treatment techniques.

OA is a degenerative condition that causes progressive loss of articular cartilage and remodeling of the underlying bone, fibrocartilage, and synovium.[3] OA can affect any joint, with the knee being the most common site in many studies.[5–7] OA is a leading cause of disability, with its prevalence increasing worldwide.[4,8–10] OA can affect all thee compartments of the knee joint: the medial tibiofemoral, the lateral tibiofemoral, and the patellofemoral compartment.[11,12] Pathogenesis of OA results from an interplay of biomechanical, inflammatory, and metabolic factors that contribute to cartilage damage, synovitis, and various subchondral bone abnormalities.[11–15] The global prevalence of knee OA is 16.0% in individuals aged 15 and older and 22.9% in individuals aged 40 and older. The global incidence of knee OA was 203 per 10,000 person-years in individuals aged 20 and older.[7] Both the prevalence and incidence increase with age.[11] Knee pain, functional loss, and the accompanying psychological burden may lead to substantial disability and major socio-economic costs, which were estimated at over $140,000 per person in the United States in 2013.[16–19] Risk factors of OA include advanced age (especially those >55 years), obesity, female sex, previous knee injury, and occupational factors.[8,11] The 10%–15% are attributed to trauma.[20] The incidence of knee OA is expected to increase because of the aging of the population and an increase in obesity.[10,11,21] Around 50% of the population first diagnosed with symptomatic knee OA are estimated to eventually undergo surgical treatment in the form of a total knee arthroplasty (TKA) which comprises the highest percentage of direct medical costs.[11,22] Between 10% and 35% of patients undergoing TKA experience persistent pain, with 15% reporting that pain has a high impact.[23–28]

METHODOLOGY

The paper includes peer-reviewed literature found by a search conducted in February 2024 using the terms "knee" AND "pain" AND "osteoarthritis" in PubMed and Cochrane databases (Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews). Only studies pertaining to chronic knee pain were included. Since this is the first review of interventional pain medicine on chronic knee pain, there were no limitations in the time frame for the literature search, and all types of original studies (randomized and non-randomized trials, prospective and observational trials, and case series and case reports) and reviews were included. Based on this initial search, the main domains relevant to the topic were identified. Afterward, multiple searches were performed based on the selected domains (eg, prevalence, diagnosis, pharmacological treatments, and interventional treatments). The literature search on interventional pain management techniques included the following terms: "Intra-articular corticosteroid injections" OR (("steroid" OR "corticosteroid") AND "injection"); "Intra-articular hyaluronic acid injection"

OR ((“hyaluronic” OR “hyaluronic acid” OR “visco-supplementation”) AND “injection”); “Intra-articular injections with platelet rich plasma” OR (“platelet rich plasma” AND “injection”); (“radiofrequency” OR “pulsed radiofrequency” OR “conventional radiofrequency” OR “cooled radiofrequency”) AND “genicular nerves”; (“chemical ablation” OR “phenol” OR “alcohol” OR “neurolysis”) AND “genicular nerves.” The initial literature search and screening of articles were performed by two authors AB and TV. In addition to the literature search, the included papers were screened for relevant articles and the authors of the manuscript proposed other important missing articles. The data were gathered and summarized per specific domain.

The group of authors included in this paper then determined whether each intervention should be recommended or not. The author team was chosen based on their expertise in the topic of chronic knee pain and consists of anesthetists and surgeons with broad international representation. Based on the summarized data, a table with each recommendation was composed together with a treatment algorithm for chronic knee pain. The possible grades of recommendation were “not recommended,” “not enough evidence for recommendation outside of a study setting,” “conditionally recommended,” “recommended,” and “highly recommended.” These recommendations were based on a critical evaluation of the literature focusing on the quality of the trials, the relevance of the intervention to the current clinical practice, the balance between the invasiveness of the intervention and the effect size, and the balance between the risk of adverse events and the effect size of the intervention. These recommendations were sent to the author team for review and a modified Delphi approach was used to achieve consensus.[29] This included multiple rounds of comments via email followed by video meetings. During the video meetings, the comments were addressed, disagreements resolved, and a consensus was forged. This same process was repeated for the technique section. Finally, the manuscript for publication was prepared and submitted to the author team for approval.

DIAGNOSIS

History

Patients with knee OA commonly present with insidious, chronic knee pain that is gradually worsening. Pain caused by knee OA is predominantly nociceptive with nociplastic characteristics occurring in approximately 35% of patients, and neuropathic qualities occasionally present in severely diseased knees.[11,30] Although pain is the most prominent symptom, patients with OA can experience reduced knee function, muscle weakness, morning stiffness, joint instability, and psychological distress. Knee pain due to OA is usually mechanical and worsens with activity due to the weight-bearing capacity of the joint.[31,32] While pain may be absent during the early stages, symptomatic OA pain is typically described as sharp and fluctuating depending on the activity level. Moderate knee OA is often described as constant pain and joint stiffness that affect daily activities. Severe knee OA can result in significant disability, function restriction, and decreased quality of life. Patients often report flare-ups for up to 72 h that include swelling, increased warmth, worsening pain, and functional limitations.[33] Burning electrical pain, paresthesia, hypoesthesia, hyperalgesia, and allodynia over the diseased joint are all characteristics of nociplastic and occasionally neuropathic pain. Multiple joint pain, morning stiffness that lasts longer than 30 min and other accompanying systemic symptoms in a patient with knee pain should prompt a rheumatology consultation to rule out rheumatoid arthritis and other arthropathies. Other red flags such as fever, a history of trauma, osteoporosis, cancer, deep vein thrombosis, or peripheral vascular disease can point toward a serious differential diagnosis and require further investigations and imaging.

Physical examination

A standard musculoskeletal and neurological examination is required for the diagnosis of knee OA.[34,35] A comparison of the diseased knee to the contralateral knee facilitates examination. First, the appearance of the knee is inspected for redness, edema, muscle atrophy, and trophic changes. Mild warmth, edema, and redness are compatible with OA while marked signs of inflammation should prompt tests for infectious or inflammatory arthritis.[31] Second, the flexed knee is palpated for bony enlargements, crepitus, and tenderness along the joint line, patella, tibial and femoral condyles, fibular head, and tibial tuberosity. Patients should be evaluated for the presence of knee joint effusion in a maximally extended knee. The following extra-articular knee compartments should also be examined and palpated: the quadriceps tendon, the patellar tendon, the iliotibial band on the lateral side of the knee, and the posterior knee fossa. Pain where the iliotibial band crosses the lateral knee is characteristic of iliotibial band syndrome, especially in runners. Discomfort at the popliteal fossa could indicate the presence of popliteal cysts (eg, Baker's cyst). Tenderness around the knee could also indicate the presence of inflamed bursae, the most important of which are the supra-, pre-, and infra-patellar bursa and the bursa surrounding the pes anserine. Third, the patient's gait, standing and walking knee alignment (varus and valgus), active and passive range of motion, and stability of the knee joint are evaluated. Examinations used to assess joint stability are the valgus and varus stress tests that evaluate medial and lateral instability respectively; the Lachman test; and the anterior and posterior

drawer tests to assess anterior and posterior knee stability problems due to anterior and posterior cruciate ligament injuries. A knee compression-rotation test is used to detect damaged meniscus. In general, the medial compartment tends to deteriorate faster than the patellofemoral and lateral compartments absent asymmetrical stressors (eg, valgus deformity predisposing to lateral compartment OA).[36]

It is important that radicular pain is excluded as the cause of the knee pain. Radicular pain resulting from compression of the L3, L4, and L5 spinal nerve roots can result in anterior (or lateral for L5 radiculopathies) knee pain while S1 and S2 nerve root compression can lead to posterior knee pain. Evaluation of the patellar reflex and the femoral stretch test can determine the integrity of the L3 and L4 nerve roots.[37] Allodynia and hypoesthesia to touch and prick of the knee should be also evaluated to identify neuropathic pain. Questionnaires such as the Douleur neuropathique 4 (DN4) and PainDETECT questionnaire can be used to determine the probability of non-nociceptive pain.[30] Due to changes in gait biomechanics, other (extra-articular) structures such as the attachment of the patella tendon and hamstring muscles at the tibia can become painful due to relative overuse resulting from altered locomotion.[38] Lastly, trophic, sudomotor, vasomotor, or sensory changes in the joint should raise the possibility of complex regional pain syndrome (CRPS).[39]

Technical investigations

A diagnosis of knee OA does not require radiography. The American College of Rheumatology (ACR) outlines three different means to diagnose knee OA. The use of history and physical exam alone requires chronic knee pain and at least three of the following criteria: age >50 years, <30 min morning stiffness, crepitus with motion, bony tenderness, bony enlargement, and no palpable synovial warmth. This is the most sensitive way to diagnose knee OA, but the least specific (sensitivity 95% and specificity 69%). The addition of radiographic abnormalities (eg, subchondral sclerosis) to history and physical requires pain in the knee, osteophytes, and at least one of the following: age >50 years, <30 min morning stiffness, and crepitus with motion. This method only slightly reduces the sensitivity to 91% but significantly improves the specificity to 86%. Finally, combining history and physical exam with labs (eg, erythrocyte sedimentation rate <40 mm/h, rheumatoid factor <1:40, and synovial fluid signs consistent with OA provides an intermediate sensitivity and specificity of 92% and 75%, respectively).[40]

As noted above, typical clinical OA findings are sufficient for diagnosis according to the ACR diagnostic criteria and EURLAR recommendations for diagnosis of knee OA.[31,40,41] Whereas disease modification is probably only possible at early stages of OA, because patients often experience minimal symptoms at this time, the ACR diagnostic criteria are frequently not sufficiently sensitive to detect all cases of knee pain secondary to degenerative etiologies.[42] The diagnosis of OA is more reliable if more affirmative signs of OA are present.[43] These include risk factors, symptoms, and physical examination. Additional testing in the form of imaging (radiography, magnetic resonance imaging (MRI), and bone scintigraphy), laboratory testing and synovial fluid analysis should be considered in young patients with symptoms of OA, knee joint instability, recent traumatic event, persistent post-operative pain, systemic symptoms, and when there is a need to rule out joint infection, inflammatory arthritis, or malignancy.[41]

Knee radiography, the gold standard imaging for knee OA, can identify the affected knee compartment: medial or lateral tibiofemoral (weight-bearing) arthrosis and patellofemoral arthrosis. Based on radiologic findings, the severity of tibiofemoral arthrosis is graded using the Kellgren–Lawrence (KL) grading scale from 0 to IV.[44] KL grade I indicates minimal radiological findings of OA while KL grade IV indicates severe OA with large osteophytes, marked narrowing of the joint space, severe sclerosis, and definite deformity of bone ends. Radiographic changes become more common after 1–2 years of symptoms.[45,46] Compared to plain radiography, MRI has a higher sensitivity for identifying earlier stages of OA that include only cartilage defects and subchondral bone lesions, and as such might aid in the early detection of knee OA.[31,47]

It is widely assumed that treatments such as lifestyle changes or efforts aimed at reducing load bearing and improving gait mechanics such as kinesiotaping are mainly useful at an early stage of OA when there is no or little pain, in an attempt to modify the disease course. From this perspective, there is an ongoing discussion on the function of pain as a protective mechanism to offload mechanical burdens and prevent further structural damage. If a treatment adequately reduces pain, this could theoretically lead to an increased rate of structural degeneration. However, aside from extreme levels of activities that unduly stress the knee joint, studies have consistently found that higher activity levels either have no significant effect or in the case of otherwise sedentary patients, possibly a protective effect on radiographic joint degeneration.[48] Further research is still needed to explore the effects of physical activity versus a sedentary lifestyle on pain.[49]

Radiographic changes in the knee should be carefully interpreted as knee symptoms tend to exhibit a poor-to-moderate correlation with the severity of radiographically observed joint alterations.[47] The proportion of patients with knee pain suffering from radiographically-confirmed OA ranges between 15% and 76%, with 15%–81% of patients with radiographically-confirmed knee OA experiencing knee pain.[50] In one systematic review,

most but not all studies, found a positive correlation between effusion and synovitis and knee pain, with another study finding that up to 25% of patients with KL grade IV did not experience knee pain.[51,52]

Differential diagnosis

The differential diagnosis of chronic knee pain depends largely on clinical presentation, medical history, imaging, and sometimes labs. Knee OA can be divided into primary and secondary OA. Whereas primary OA is a result of idiopathic degenerative processes, secondary OA occurs secondary to trauma, and other bone and joint disorders such as rheumatoid arthritis, arthropathies, and infections.[41] Post-traumatic knee pain is preceded by trauma which can be acute, prolonged over extended periods (eg, distance runners), and occur secondary to an acute traumatic event that predisposes the knee to increased stress and motion (eg, ligamentous and meniscal injuries). When preceded or accompanied by trauma, surgery, or an intervention, CRPS may ensue.[39] Radicular back pain is characterized by pain involving a specific dermatome and typically occurs with concomitant sensory and/ or motor deficits.

Differential diagnosis of chronic knee pain:

- OA
  - Primary OA
  - Secondary OA: OA enhanced by other factors such as trauma, other bone and joint disorders such as rheumatoid arthritis, arthropathies, and infections[22]
  - Patella malposition or mal-tracking[53]
  - Malalignment
  - Post-meniscectomy pain (degenerative or traumatic)
  - Osteochondritis dissecans (OCD)
- Persistent post-surgical knee pain
  - Mechanical problems (eg, prothesis malalignment, mal-sizing, component dislodgement, periprosthetic fractures, and ligament instability)
  - Joint infection
  - Inappropriate surgery (eg, joint replacement when OA was not the primary cause)
  - Inflammatory or allergic response to implanted material (metal allergy)
  - Nociplastic pain
  - Neuropathic pain (eg, due to surgical damage to the infrapatellar branch of the saphenous nerve)
  - CRPS
  - Idiopathic
- Post-traumatic knee pain
  - Fracture
  - Soft tissue trauma and peri-articular disorders (eg, ligament tear, meniscal tear, and cartilage defect)
- Referred knee pain
  - Radicular pain
  - Hip pain
- Infection of periarticular tissue (eg, bursitis and tendinitis)
- Infectious arthritis
- Inflammatory arthritis (eg, rheumatoid arthritis and psoriatic arthritis)
- Crystal arthropathy (eg, gout)
- Malignant knee pain

TREATMENT OPTIONS

The treatment of knee OA should be comprehensive and multimodal. A combination of education, physiotherapy, weight management, and medical treatment is indicated for most OA patients.[41,54–56] Treatment of knee OA is primarily symptomatic, aimed at relieving pain and improving functionality.[56] The importance of changes in lifestyle, self-efficacy, and a proactive approach to knee pain should be stressed. Minimally invasive treatments such as intra-articular infiltrations or nerve treatment are indicated when the previously mentioned approaches are insufficient. Surgical interventions should be performed when symptoms are refractory to conservative treatment.[57,58] We will further discuss pharmacological therapies, and the five minimally invasive treatments with the most supporting literature in knee OA: the intra-articular injection of corticosteroids, intra-articular injection of hyaluronic acid, intra-articular injection of platelet-rich plasma, radiofrequency treatment, and chemical ablation of the genicular nerves. We will discuss evidence of treatments from systematic reviews and results from distinguished individual trials addressing important clinical topics when aggregated data in systematic reviews is lacking.

Treatment of chronic knee OA can be classified into

1. Conservative treatment
   - 1.1. Non-interventional
     - 1.1.1. Non-pharmacological (education, physiotherapy, braces, dietary weight management, lifestyle changes, kinesiotaping, and cranes)
     - 1.1.2. Pharmacological (NSAIDs, paracetamol, duloxetine, tramadol, and topical capsaicin)
   - 1.2. Minimally invasive interventional management
     - 1.2.1. Pharmacological intra-articular infiltrations
       - 1.2.1.1. Intra-articular corticosteroid injection (IACS)
       - 1.2.1.2. Intra-articular hyaluronic acid injection (IAHA)
       - 1.2.1.3. Intra-articular injection with platelet-rich plasma (PRP)
     - 1.2.2. Non-pharmacological interventions:

1.2.2.1. Nerve block (RF, cryotherapy and chemical neurolysis)
1.2.3. Other (eg, genicular artery embolization, stem cells, dextrose or hypertonic saline injection (prolotherapy), and ozone)
2. Surgical treatment
3. Neurostimulation
3.1. Peripheral nerve stimulation
3.2. Spinal cord stimulation

Conservative management

Non-pharmacological care

Non-pharmacological care is considered essential to all OA patients. Patients should be educated on disease pathology, progression, and treatment modalities. Physiotherapy in the form of structured land-based exercise programs, aquatic exercise which mitigates the effect of gravity and may be particularly beneficial in overweight patients, use of gait aids, and self-management programs are considered safe and efficacious. A Cochrane systematic review comparing the effect of land-based therapeutic exercise with different comparators in OA patients showed that exercise significantly diminishes pain and improves physical function in the intermediate term without additional harm or accelerated disease progression.[59] While the importance of non-pharmacological care is supported by scientific research and expert opinion, the implementation of education, physiotherapy, weight loss, and self-management programs in clinical practice is often suboptimal.[60] Nationwide initiatives on neuromuscular exercise such as the Good Life with osteoArthritis in Denmark (GLA:D) can improve pain and quality of life of knee OA patients.[61] Transcutaneous electrical nerve stimulation (TENS) is another non-invasive technique that could be considered in some knee OA patients with neuropathic-like or nociplastic symptoms; however, the level of evidence is low.[62]

Pharmacological treatments

Pharmacological treatments are deemed suitable for most OA patients; however, attention should be paid to patients with comorbidities due to possible adverse effects, drug interactions, and complications. Topical or oral non-inflammatory drugs (NSAIDs) and paracetamol are first-line pharmacological treatments for knee OA. The effect of NSAIDs is superior to paracetamol with a number needed-to-treat (NNT) of between 4.5 and 9.8 for topical and oral NSAIDs and 4 ONSAID16 for paracetamol.[63–65] Cyclooxygenase-2 inhibitors or topical NSAIDs can be used in patients suffering from frailty, and gastrointestinal comorbidities due to fewer adverse effects.[55,56,63] Duloxetine is the only anti-depressant that is recommended as a second-line treatment for knee OA.[66,67] However, other antidepressants can be considered in patients with depressive symptoms or widespread pain disorders after careful patient selection, with tricyclic antidepressants having greater efficacy, albeit with more side effects, than serotonin-specific reuptake inhibitors.[54,66] Topical capsaicin can be considered despite studies reporting a small effect size.[54] High doses of pure mu agonists should only be considered for non-malignant knee pain on a case-to-case basis after carefully weighing the risks and benefits, with predefined benchmarks for success and an exit strategy.[68] Mixed-action opioids such as tramadol can be considered, but there is moderate-quality evidence that tramadol has no important benefit on pain due to OA.[54,69] Glucosamine, chondroitin, and biologicals (eg, anti-NGF/TNF antibody therapy) are not recommended for use in patients with knee OA.[54,70] Presently, no disease-modifying drugs are approved for OA.[54,70]

Interventional pain management

Intra-articular corticosteroid injections (IACS)

Intra-articular (IA) injections with corticosteroids have been extensively used in knee OA for over 50 years and should be considered when the previously mentioned treatments are exhausted. Corticosteroids, being strong anti-inflammatory agents, are hypothesized to reverse intra-articular (synovial) and extra-articular inflammation involving the degenerative joint, especially during an OA flare.[71] Corticosteroids available for intra-articular injection are present in a crystalline and non-crystalline form. The most frequently used corticosteroids and their corresponding dosage are the crystalline triamcinolone 20–40 mg, the non-crystalline prednisolone 50 mg, and methylprednisolone 40–120 mg.

IACS injections are shown to be more effective for pain reduction and improvement in functionality compared to placebo or no intervention in knee OA according to three recent systematic reviews and meta-analyses.[72–74] The effect size is small to moderate with a peak effect occurring around 2–4 weeks depending on the formulation.[71] The NNT for IACS injection in knee OA ranges from 8 to 10.[72,73] The duration of the effect of IACS seems to be limited to the short-term, as a meta-analysis found no analgesic effect at 6 months.[72] Compared to active treatment with IA hyaluronic acid or physiotherapy, IACS injections showed no statistically significant effect 6 weeks after treatment in knee OA patients.[74] Recurrent IACS do not provide additional symptom relief compared with other injectables at mid- and long-term follow-up.[75] Concomitant injection with viscosupplementation or local anesthetics has not been shown to increase the effect of the treatment, though the

addition of corticosteroids to hyaluronic acid has been shown in multiple studies to be superior to hyaluronic acid alone.[72,76,77] A higher equivalent dose than 40 mg of methylprednisolone does not increase the treatment effect.[72] Repeated injections have been shown in clinical trials to decrease cartilage volume.[78] There is insufficient data to advise the use of a specific short-acting or long-acting corticosteroid preparation.

Intra-articular hyaluronic acid (IAHA) injection

Hyaluronic acid (HA) is a non-sulfated glycosaminoglycan that is an important component of healthy articular cartilage and synovial fluid.[3,79] The hypothesized mechanism of action of viscosupplementation is through anti-inflammatory, anabolic, analgesic, and chondroprotective mechanisms; however, the physiological effect of HA has not been fully elucidated.[71,79] Injection of IAHA could improve pain and joint function by increasing lubrication during articulation and restoring the viscoelasticity of synovial hyaluronan.[70] Viscosupplements are available in different formulations (hyaluronan and hylan), different molecular weights (high [>1.5 million Da] and low molecular weights, and in different molecular structures [linear, cross-linked, or both]).[80] Despite conflicting clinical results, differences in HA molecular weight are hypothesized to result in differences in biological activity, with high molecular IAHA generally favored.[81,82] Although a growing trend is to perform a single IAHA injection, injection schedules per patient reported in studies vary from 1 to 5 injections.[71]

The clinical effect of IAHA in knee OA is controversial. Two meta-analyses comparing viscosupplementation to placebo or no intervention showed a small and non-clinically meaningful benefit for IAHA with an increased risk of adverse events, while another meta-analysis found significant improvement for pain and function compared to placebo up to 24 weeks.[83–85] A meta-analysis comparing IAHA with IACS reported a stronger effect for IACS up to 4 weeks, equal efficacy at 4–8 weeks, and higher efficacy of IAHA past 8 weeks. A network meta-analysis of different treatments for knee OA reported that IAHA leads to statistically significant improvement in pain and that IAHA was more effective than all conservative knee OA treatments including IACS.[86] The systematic reviews should be viewed with caution as most of the included trials were found to have low methodological quality, high heterogeneity, and were sponsored by industry.[87] If effective, IAHA reaches its peak effect at 4–8 weeks and the effect is detectable until 24 weeks.[84] Regarding repeated IAHA injections, a study by Ha et al.[88] comparing a single to three IAHA injections in knee OA resulted in non-inferiority of a single IAHA. When IAHA injections are effective, how long to continue these injections in clinical practice is unknown. When comparing low- and high-molecular weight IAHA injections, subgroup analyses in systematic reviews are inconclusive. In a randomized, double-blind study comparing low- and high-molecular weight IAHA injections, Gigis et al.[89] reported that both lead to similar symptom reduction. A systematic review of 7 RCTs and 10 cohort studies examined the effect of repeat IAHA injections. The number of injections per treatment course varied from 1 to 5, with the number of repeat courses also ranging from 1 to 5 and follow-up periods varying between 26 and 174 weeks. All studies showed significant improvement in pain after the first course of HA. After a repeat injection series, pain reduction remained significant compared to baseline.[90] The high degree of heterogeneity between studies should be considered when interpreting these results. The long-term follow-up of knee OA patients treated with IAHA does not indicate evidence for acceleration of knee OA progression, but future studies should address the potential for disease-modifying effects.[87]

Intra-articular injections with platelet-rich plasma

Platelet-rich plasma (PRP) is a highly concentrated volume of platelets derived from centrifugation of autologous blood. Both plasma and platelets in PRP contain growth factors that can aid healing and tissue regeneration.[91,92] PRP can be prepared by different methods (single-spinning method, double-spinning method, or selective blood filtration). Based on the leukocyte and fibrin content, PRP is classified into pure PRP, leukocyte-rich PRP, pure platelet-rich fibrin, and leukocyte- and platelet-rich fibrin.[91] Although some leukocytes can secrete growth cytokines, IA-injected leucocytes can also increase oxidative stress and inflammation, mitigating any clinical effect.[93] The PRP solution can also be exogenously activated. IA PRP is on average injected three times with 1, 2 or 3 weeks intervals separating treatments.[94]

Evidence for the clinical effect of IA PRP infiltrations is mixed. Compared to placebo or no treatment, two systematic reviews reported a significant positive effect on pain.[94,95] When compared to hyaluronic acid, there is moderate evidence that PRP is more effective for pain and function than IAHA.[94–99] Four systematic reviews found that PRP might be more effective in reducing pain and function for up to 9 months compared with IACS.[95,99–101] Although the aforementioned research tended to show favorable results for IA PRP, it must be noted that the quality of data is low, and the included studies exhibited extensive heterogeneity. No knee OA guideline currently recommends PRP.

The heterogeneity of the studies is evident in the volume of plasma injected, method of PRP preparation,

use of exogenous PRP activation, and frequency of injections. A direct comparison between single- versus double-spinned PRP by Filardo et al.[102] showed no statistical difference between preparation methods. Despite an absence of randomized, comparative-effectiveness studies, systematic reviews have concluded that exogenously-activated PRP is more effective than non-activated PRP,[103] and that leukocyte-poor PRP may be superior to leukocyte-rich PRP for knee OA.[96] A systematic review that evaluated cartilage degeneration in knee OA patients up to 12 months after PRP treatment concluded that PRP does not result in disease modification or an increase in degeneration compared to the expected OA progression.[99,104,105] There is no substantial evidence that simultaneous injection of PRP with hyaluronic acid or mesenchymal stem cells improves the clinical effect.[106–111] There is corroborating evidence that multiple PRP injections may be more beneficial than a single injection.[92,112]

Radiofrequency of genicular nerves

Radiofrequency (RF) treatment of the genicular nerves aims to interrupt pain signal transmission from the sensory genicular nerves by means of a thermal lesion.[113,114] RF treatment can be performed using three main different RF modalities: conventional RF with various iterations intended to enhance lesion size, cooled RF, and pulsed RF. In bipolar RF, symmetrically placed electrodes are positioned around the targeted area. Both electrodes serve as a conduit for electrical current which results in larger lesions when compared to conventional RF.[115] The targeted genicular nerves are branches of the femoral, obturator, and sciatic nerves that innervate the anterior part of the knee. The superomedial, the superolateral, and the inferomedial genicular nerve are the traditional targets of RF treatment based on the inaugural sham-controlled trial by Choi et al. There is an ongoing discussion as to whether targeting more nerves could increase outcomes as there are over 10 sensory nerves supplying nociceptive input from the anterior knee joint.[116–119] Figures 1 and 2 display the anatomical variations of the genicular nerves that innervate the anterior knee and possible targets for the RF procedure for each nerve.

When results from all clinical studies are evaluated, regardless of the RFA modality employed, successful outcomes have been reported in between 30% and 74% of OA patients at 6 months.[120–126] When RF of the genicular nerves is compared to intra-articular injections in knee OA, the results from systematic reviews are contradictory. One reported the probability of benefit after RF to be 4.5 times higher compared to IACS and 1.8 times higher compared to IAHA, while another showed no significant difference in effect between IA injections, RF ablation,

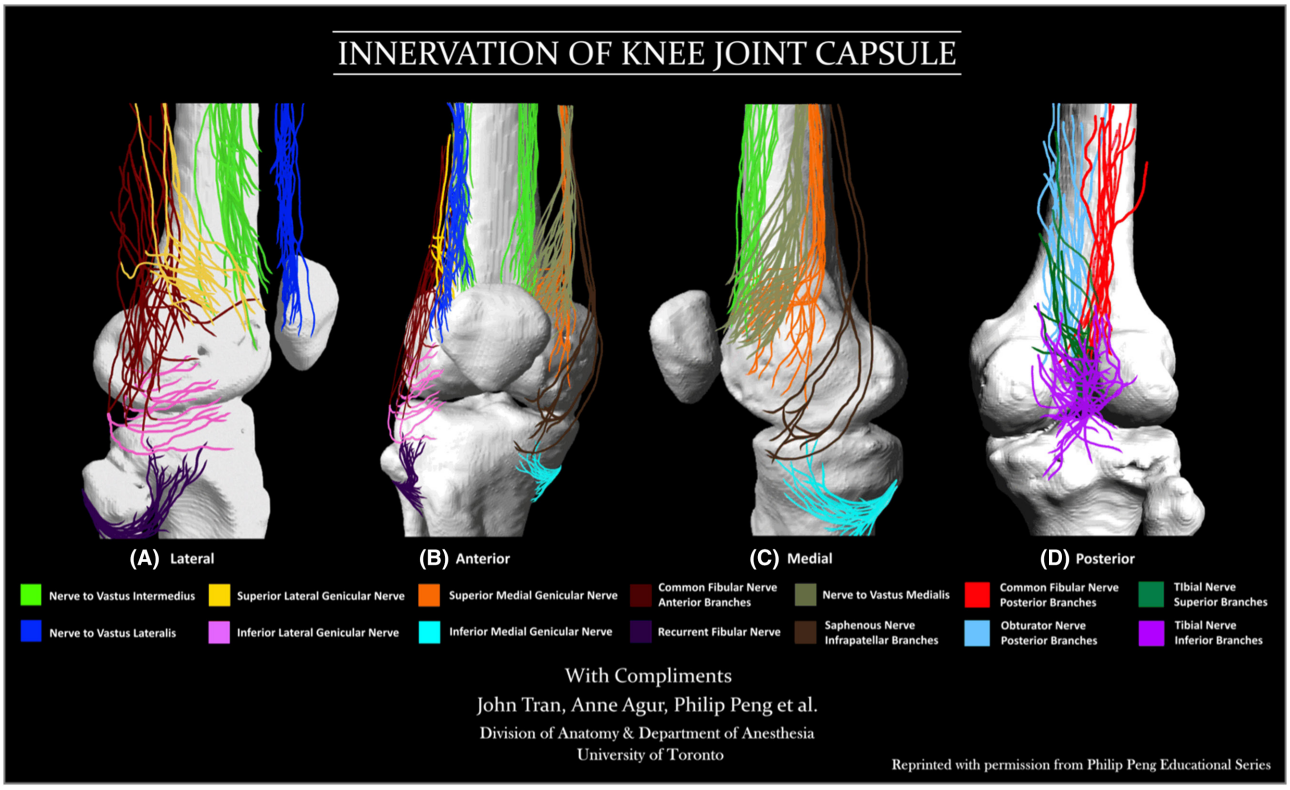

FIGURE 1 Anatomical variations of the genicular nerves that innervate the knee joint capsule—reproduced with permission of Philip Peng Educational Series[168] A. Lateral view. B. Anterior view. C. Medial view D. Posterior view.[168,176]

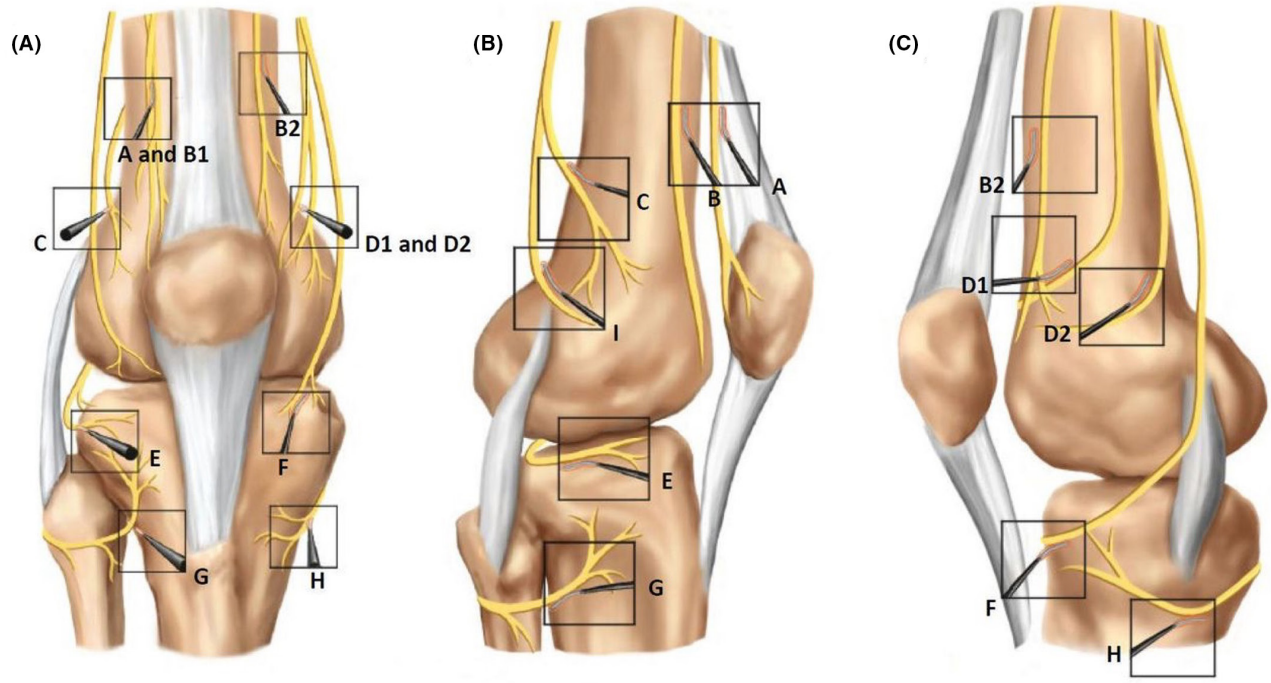

FIGURE 2 Innervation of the anterior knee capsule including possible target points for radiofrequency ablation—reproduced with permission of McCormick et al.[133] (A) Anterior view, (B) lateral view, and (C) medial view. (A) Nerve to vastus lateralis, (B1) Lateral branch of nerve to vastus intermedius, (B2) Medial branch nerve to vastus intermedius, (C) Superior lateral genicular nerve, (D1) Nerve to vastus medialis, (D2) Superior medial genicular nerve, (E) Inferior lateral genicular nerve, (F) Infrapatellar branch of saphenous, (G) Recurrent fibular nerve, (H) Inferior medial genicular nerve, and (I) Terminal articular branch of the common fibular nerve.

and genicular artery embolization.[125,127] There seem to be differences in the efficacy between the three RF modalities. Conventional RF treatment was shown to be superior to pulsed RF in OA knee pain in an RCT, which is consistent with comparisons for other joints.[128,129] Studies suggest that cooled RF may provide advantages over conventional RF but the incremental benefit is small. Cooled RF, which creates larger lesions and thus a greater likelihood of accurate denervation, could theoretically produce better and more prolonged pain relief compared to conventional RF based on a large cohort study.[130] The same study also demonstrated that larger needle size and thus larger lesion size was associated with longer pain relief. Conversely, although cooled RF provided better symptom control in a pilot RCT in patients with persistent postsurgical pain, it did not provide meaningfully better outcomes in OA patients.[131,132] More studies are needed to support the routine use of the more expensive and resource-intensive cooled RF technique.

Concerning the number of targeted nerves, there is a theoretical advantage of lesioning more than 3 nerves. Most studies up to now targeted three traditional genicular nerves, but there are studies that advocate targeting more nerves.[133] Three retrospective studies examining factors associated with outcome demonstrated that greater KL grade, not being on opioids and adjuvant analgesics, not having psychiatric co-morbidities, and targeting more than 3 nerves foreshadowed positive RFA outcomes.[117,134,135] Furthermore, the study by Malaithong et al.[115] found no significant differences up to 12 months between the group that received local anesthetic and steroid injections with sham-RFA and the group with local anesthetic and steroid plus bipolar-RFA targeting three genicular nerves. Both groups experienced significant reductions in pain. It should be noted that, unlike medial branch blocks before facet joint RFA, there appear to be some patients whose pain relief from genicular nerve blocks with steroids is sustained.[136–138] A study by Kose et al. randomized a total of 80 patients to receive either conventional RF of the three traditional nerves or conventional RF of three traditional nerves together with pulsed RF of the infrapatellar and recurrent fibular nerves. Both techniques provided pain reduction and functional improvement up to 6 months after the procedure but the 5-nerve-targeted group showed significant improvement compared with the 3-nerve-targeted group, though the 95% confidence intervals overlapped.[139]

Because of methodological flaws in existing studies comparing different nerve-targeting strategies, large comparative-effectiveness trials comparing the current standard 3-nerve technique to more aggressive ones are needed to determine optimal lesioning parameters.

Chemical ablation of genicular nerves

Ablation of genicular nerves can also be performed with chemical agents.[140–144] The use of alcohol (50%–100%) or phenol (6%–9%) are both described to perform neurolytic blocks.

Alcohol neurolysis of genicular nerves was only described in a case report and series.[142,143] Both studies reported pain reduction, respectively at 6 weeks and 6 months follow-up.

The phenolisation of genicular nerves was described in a prospective cohort study.[140] Forty-three patients underwent an ultrasound-guided injection of 1.5 mL phenol at each target. At 6 months follow-up, about 50% of patients had ≥50% pain reduction. Yildiz et al. randomized 64 patients into conventional RF or neurolysis with phenol 6%. There were no significant differences between the groups up to three months follow-up.[144] There are currently several ongoing studies using chemical neurolysis to target a larger number of genicular nerves.

In conclusion, only a small number of studies currently describe the use of chemical neurolysis of the genicular nerves. More research on the clinical effectiveness of chemical neurolysis is still needed.

Surgery

Whereas mild knee OA is generally well-managed by conservative treatments, a large number of patients experience inadequate pain and symptom relief as reported by the Study of Osteoarthritis Real World Therapies (SORT), a prospective observational study conducted in six European countries in 2015.[145] Patients with longer disease duration, bilateral knee OA, greater opioid use, and higher prevalence of co-morbidities are more likely to experience pain refractory to conventional treatments. It is estimated that 50% percent of patients diagnosed with symptomatic knee OA will undergo TKA procedure in their lifetime.[22] Currently the International Cartilage Repair and Joint Preservation Society (ICRS) focuses on joint-preserving treatments to postpone joint replacement, which typically lasts between 10 and up to 20 years. Surgery to unload joints (eg, joint distraction or osteotomy) and repair OCD have been shown to favorably alter biomechanics and improve symptoms.[146,147]

Surgery is indicated in patients with osteoarthritis refractory to conservative treatment. Surgical procedures performed for knee OA are[57,58]

1. Arthroscopic debridement (synovectomy, meniscectomy, loose body removal, etc.)
2. (Osteo)chondral repair
3. Joint distraction
4. Subchondroplasty
5. Osteotomy around the knee
6. Knee arthroplasty (unicondylar or bicompartmental knee arthroplasty, total knee arthroplasty, or revisions thereof)
7. Meniscus replacement/repair
8. Ligament repair (eg, anterior cruciate ligament repair and medial collateral ligament repair)

Arthroscopy of the knee which was extensively performed before randomized controlled trials found evidence for a lack of effect, may lead to worse short-term outcomes and does not inhibit disease progression.[148] Osteochondral repair aims to repair damaged articular cartilage in early OA. The results are promising, but the technique is currently limited to study settings.[149] Early correction of mechanical factors (mal-tracking patella, malalignment, etc.) before they lead to deleterious (osteo) chondral structural changes should be pursued whenever possible to delay the development of OA and following joint replacement at a young age.[150] During osteotomy, the bones forming the knee joint are realigned to "unload" the damaged cartilage. Total or partial knee arthroplasty (TKA) is the treatment of choice in refractive end-stage knee OA. TKA is successful in diminishing pain and increasing functionality; however, 20% of the patients are dissatisfied postoperatively and many develop PPSP.[26–28]

Neurostimulation (central and peripheral)

Peripheral nerve stimulation (PNS) involves using electrical pulses from a peripherally positioned electrode to inhibit nociceptive input from small-diameter nerve fibers.[151] PNS of the femoral and the sciatic nerve have been reported to be effective in small trials for refractory postoperative and neuropathic knee pain.[152] Evidence of the clinical effect of PNS for osteoarthritis of the knee is based on case series and thus systematic use is not recommended outside of the study setting.[153,154]

Spinal cord stimulation (SCS) and dorsal root ganglion (DRG) stimulation are two forms of central neurostimulation wherein an implanted pulse generator produces electrical stimulation directly at the spinal cord level or at the nerve root with the aim of reducing pain intensity. Literature on SCS and DRG stimulation describes the successful use of these techniques in severe refractory neuropathic knee pain due to pain after arthroplasty, post-traumatic pain, and CRPS.[152,155] There are no trials on the use of SCS and DRG stimulation for chronic knee pain due to osteoarthritis.

Evidence for interventional management

The summary of evidence for interventional management of chronic knee OA is provided in Table 1.

TABLE 1 Summary of evidence for interventional management of chronic knee OA.

Technique	Conclusion	Recommendation in clinical practice
Intra-articular corticosteroid injections	Studies have demonstrated short-term efficacy in knee OA[72–74,156]	Recommended
Intra-articular hyaluronic acid injection	Studies failed to establish a benefit, and harm may be associated with these injections, therefore the conditional recommendation against is made. This is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit[83–85,156]	Conditionally recommended
Intra-articular platelet-rich plasma	Research tended to show favorable results for IA PRP, although it must be noted that the quality of data is low, and the included studies exhibited extensive heterogeneity. No knee OA guideline currently recommends PRP[94–101,156]	Not enough evidence for recommendation outside of a study setting
Radiofrequency of the genicular nerves	Studies have demonstrated the efficacy of conventional and cooled RF in knee OA[113,125,128–130,157,158]	Recommended
Chemical ablation of the genicular nerves	Only a small number of studies currently describe the use of chemical neurolysis of the genicular nerves. More research on the clinical effectiveness of chemical neurolysis is still needed[140–144]	Not enough evidence for recommendation outside of a study setting
Spinal cord/dorsal root ganglion stimulation	There are no trials on the use of SCS and DRG stimulation for chronic knee pain due to osteoarthritis	Not enough evidence for recommendation outside of a study setting

SIDE EFFECTS AND COMPLICATIONS OF INTERVENTIONAL PAIN MANAGEMENT

Intra-articular corticosteroid injections (IACS)

IA corticosteroid injection has been reported to lead to the following adverse events: transient local pain and swelling; septic arthritis; acute corticosteroid-microcrystalline joint flare; hemarthrosis; and systemic reactions due to absorption of corticosteroids including facial flush, hyperglycemia, and high blood pressure.[156] The incidence of adverse events due to IACS is low and serious adverse events are rare.[72,156] Long-term adverse effects of IACS are controversial. Although the anti-inflammatory effect of corticosteroids might theoretically slow disease progression, there is evidence of time- and dose-dependent deleterious effects of corticosteroids possibly resulting in cartilage damage and chondrotoxicity.[157] A Cochrane systematic review from 2015 reported that there was no evidence of an effect of corticosteroids on joint space narrowing compared to sham or no interventions for up to 6 months; however, this conclusion was based on a single RCT.[72] McAlindon et al. published the results of a randomized, double-blind study in 140 patients with knee OA patients that found that IACS was associated with significantly greater cartilage volume loss compared to sham injections on magnetic resonance imaging at 2-year follow-up, while Latourte et al. reported that IACS injections did not significantly increase the 5-year incidence of total knee replacement or radiographic worsening in knee OA.[78,158] Future studies should address the long-term safety of IACS.

Intra-articular hyaluronic acid (IAHA) injection

IAHA has a low rate of adverse effects.[80,86,156,159] Despite a higher number of serious adverse events and adverse event-related study withdrawal in the systematic reviews by Rutjes et al. and Pereira et al.[59,76] the most frequent adverse events are short-term knee pain, swelling, arthralgia, and effusion. The network meta-analysis by Bannuru et al.[156] found similar adverse event rates for all IA injections. Unlike IACS, there are no systemic effects of IAHA.

Intra-articular injections with platelet-rich plasma

Literature on PRP asserts that IA PRP is not linked to any major safety issue and that adverse events are mild.[71,94,107,109] Frequently reported adverse events, similar to IACS and IAHA, are infection, bleeding, bruising, peripheral nerve injury, and temporary exacerbation of pain typically lasting from 2 to 7 days.[156]

Radiofrequency of genicular nerves

Systematic reviews report the RF intervention to be safe with limited non-severe adverse events.[125,126,160,161]

Frequent adverse events are postoperative pain (transient neuritis), hypoesthesia, and bruising. Other possible adverse events are allergic reactions, knee hematoma, infection, and soft tissue damage including skin burns if the RF cannula is positioned incorrectly.[162]

TECHNIQUES

IACS injection

There is considerable heterogeneity in the dosage and volume of injection, with most studies reporting the use of an equivalent dose of 40 mg prednisolone and a volume of 2–6 mL of injectate.[72] One randomized study found no differences in any outcome measures when comparing 40 and 80 mg of triamcinolone. We describe an ultrasound-guided procedure using the suprapatellar approach as this technique results in a high rate of intraarticular spread even in the presence of knee effusions.[163]

The patient is placed in the supine position with the knee flexed 30°. A high-frequency linear ultrasound probe is placed on the patella in the transverse position and is gently slid proximally to visualize the quadriceps tendon. Subclinical knee joint effusions can be visible under the quadriceps and suprapatellar fat pad. The target point is the suprapatellar bursa between the suprapatellar fat pad and the prefemoral fat pad. The insertion point of the needle should be lateral to the probe so that the in-plane trajectory does not pass through the quadriceps tendon. After subcutaneous infiltration of local anesthetic, a 22–25-gauge needle is inserted into the joint recession or effusion. In case of excessive joint effusion, fluid can also be aspirated. Last, the volume of corticosteroid is injected with minimal resistance.

IAHA injection

The technique used for IAHA injections is similar to the IACS injections. Correct positioning of the needle in the intra-articular compartment is essential for an IAHA injection as injection of hyaluronic acid into the periarticular compartment results in little therapeutical effect. Studies report injection volumes ranging from 0.5 to 6.0 mL and concentrations varying from 0.8 to 30 mg/mL.[79]

IA PRP injection

The technique of IA PRP injection is similar to the IA injection technique for IACS and IAHA.

Intraarticular injections are performed in a "blinded" manner or using fluoroscopic or ultrasound guidance. Studies have found failure rates ranging between less than 5%–30% for landmark-guided injections.[164,165] Image-guided procedures may result in larger effect sizes as shown by one large long-term cohort where patients who were treated with ultrasound-guided viscosupplementation were significantly less likely to undergo knee arthroplasty compared to patients treated with landmark-guided injections.[166] Compared to fluoroscopy, an ultrasound-guided procedure can ensure intra-articular needle placement without radiation, but unlike fluoroscopy cannot evaluate joint degeneration or identify capsular tears.[72]

RF of the genicular nerves

We describe here the technique for targeting three traditional genicular nerves: the superomedial (SMGN), the superolateral (SLGN), and the inferomedial genicular nerve (IMGN), as well as the technique to target the additional nerves. Whereas the described technique incorporates updated knowledge from recent anatomic studies evaluating the locations and trajectories of the genicular nerves, a number of different approaches to the genicular nerves are described in the literature, with no studies comparing effectiveness.[119,167–170] Currently, the optimal targets for the US- or fluoroscopically-guided technique are the subject of debate and similar to all new techniques it will likely go through adaptations as new insights from scientific evidence emerge. The following description is based on the expert opinion of the author team and aims to present a roadmap for the clinician.

Anatomical variations of the genicular nerves are illustrated in Figure 1. Figure 2 shows the innervation of the anterior knee capsule.

The patient is placed in a supine position with the index knee flexed 10–15° by placing a cushion in the popliteal fossa. The patient can be monitored using pulse oximetry and if indicated, lightly sedated. The three genicular nerves are targeted using a high-frequency linear ultrasound probe or fluoroscopy under sterile conditions. Ultrasound- and fluoroscopically-guided RF needle placement have resulted in similar effectiveness.[171,172] Although an ultrasound-guided procedure does not expose the patient and operator to radiation and enables visualization of soft tissues, gauging depth (especially in obese patients) is difficult, and aligning the electrodes parallel to the target nerve trajectories is easier with fluoroscopy. Therefore, which imaging guidance is preferred depends on the experience of the operator.

A prognostic block is sometimes performed prior to RF, though both direct (randomized trials) and indirect (comparisons of outcomes between studies that have used and not used prognostic blocks) evidence demonstrates consistently >80% response rates and no improvement in outcomes.[173,174] When blocks are used, the cut-off for designating a block as positive has generally been ≥50% pain relief, though one study found that using an 80% threshold resulted in a higher proportion

of successful procedures.[117,125,174] The prognostic block is usually performed with volumes not exceeding 1 mL of local anesthetic per genicular nerve. Due to the questionable prognostic effect and patient discomfort associated with the blocks, we presently advise against the routine use of a prognostic block.

RF cannula placement for ultrasound-guided RF

SMGN: The transducer is placed in a coronal orientation over the medial epicondyle of the femur and repositioned between the epiphysis and diaphysis of the femur. The target point is at the posterior half of the femur. After visualization of the target point, the transducer is then turned 90° into the transverse plane, and the RF cannula is inserted after local anesthetic infiltration to skin and soft tissues and advanced in an "in-plane" approach until contact is made with the bony cortex at the posterior half of the femur.

IMGN: The transducer is placed in a coronal orientation over the medial tibial epiphysis and diaphysis, the inferomedial genicular artery, and the medial collateral ligament. If the IM genicular artery is visualized below the medial collateral ligament and above the bony cortex, the RF cannula is directed next to the artery; otherwise, the target point is the junction between the epiphysis and diaphysis under the medial collateral ligament. After visualization of the target point an out-of-plane entry point for the needle is used. The transducer is then turned 90° into the transverse plane and the RF cannula is inserted after local anesthetic infiltration of skin and soft tissues, and advanced using an "in-plane" approach until contact is made with the bony cortex at the center of the tibia.

SLGN: The transducer is placed in a coronal orientation over the femoral lateral epicondyle at the junction between the epiphysis and diaphysis. The target point is the posterior half of the junction between the epiphysis and diaphysis of the femur. The transducer is centered on short axis of the femur to visualize this target point. After the skin and soft tissue are anesthetized with lidocaine, the cannula is advanced using an anterior-to-posterior "in-plane" approach in the oblique plane until contact is made with the posterior half of the bony cortex of the femur.

RF cannula placement for fluoroscopically-guided RF

The traditional target points for the fluoroscopically-guided procedure are similar to those used for ultrasound.

For the SMGN, IMGN, and SLGN, the cannulas are introduced under true AP fluoroscopic views of the tibiofemoral joint using a "co-axial (tunnel-view) technique." For the SMGN and the SLGN, the introducers are inserted medial and lateral to the junction of the femoral shaft and condyles, respectively, and advanced to between 50% and 100% across the depth of the femoral shaft. For the IMGN, the cannula is inserted medial to the junction of the medial tibial condyle and the shaft and advanced to 25%–75% depth across the tibial shaft.

More nerves are recommended with the fluoroscopically-guided approach and research on the outcomes incorporating those new targets is ongoing.

Once the cannula position is confirmed in multiple views, an RF electrode is inserted into the cannula. Sensory stimulation (50 Hz) is applied and should ideally produce paresthesia at a threshold of 0.5 V or less, but this is not always reproducible. The absence of fasciculations below 1 V is observed after motor stimulation at 2 Hz, confirming sufficient distance to relevant motor branches, particularly for the ILGN and recurrent fibular nerve. If no sensory stimulation threshold is obtained at this position, the electrode can be repositioned until this is achieved.

For conventional RF, 100 mm long, large electrodes (eg, 18G) with longer (eg, 10 mm) active tips are often used to increase nerve capture rates although this could cause increased patient discomfort during the procedure. During cooled RF, a 100 mm long, 17G RF introducer with an 18 G cooled electrode containing a 4 mm active tip is used.

SUMMARY OF TREATMENT RECOMMENDATIONS

We recommend the following for patients with chronic knee pain due to osteoarthritis:

- All patients should be advised to engage in physiotherapy, perform aquatic and land-based exercises, use gait aids, participate in weight management and nutritional programs if indicated, consider self-management groups, and utilize pharmacological treatments.
- Knee osteoarthritis patients should undergo trials with the following medications unless contraindicated: paracetamol, topical or oral NSAIDs, and duloxetine. Opioids are not routinely recommended for chronic non-malignant knee pain. Mixed-action opioids such as tramadol, tapentadol, and buprenorphine in those with high-impact pain can be considered.
- Intra-articular infiltrations with corticosteroids are recommended for short-term pain relief in knee OA patients. Other injections such as hyaluronic acid, PRP, stem cells, and so on are not recommended, only in trial settings and not on a regular basis but may be considered in some circumstances.
- Conventional and cooled radiofrequency treatment of the genicular nerves is recommended in patients suffering from therapy-resistant knee pain due to OA if the pain is moderate to severe and KL grade is II–IV.

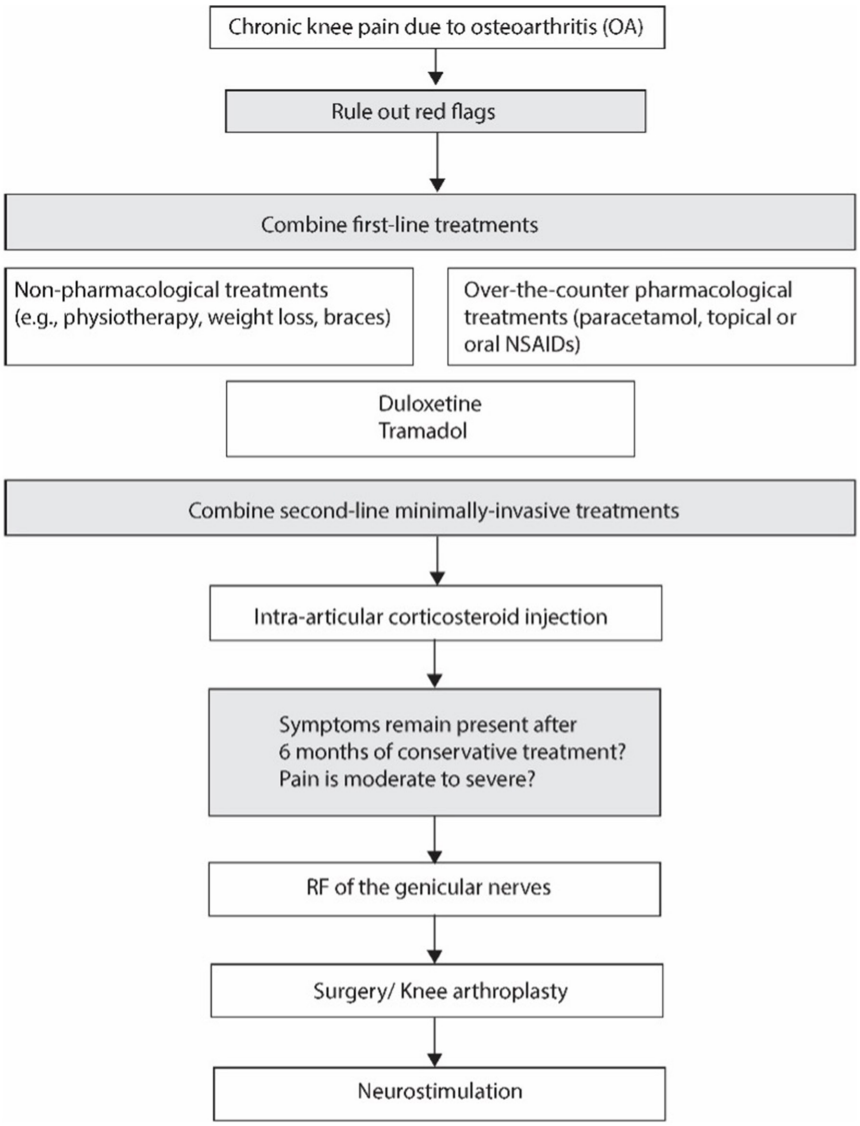

FIGURE 3 Clinical practice algorithm for treatment of chronic knee pain due to osteoarthritis. NSAID, Non-steroidal anti-inflammatory drugs; OA, osteoarthritis; RF, radiofrequency.

- A close collaboration between the surgical team and the pain/anesthesiology team is recommended to evaluate joint-preserving and joint-replacement options including using the recommendations outlined above, and implement individualized therapy plans in an iterative process.

These recommendations are summarized in the algorithm for the treatment of chronic knee pain due to OA in Figure 3. This algorithm is built on the updated ESCEO algorithm for the treatment of knee OA and is further extended to include RF of the genicular nerves and neurostimulation.[175]

AUTHOR CONTRIBUTIONS

Thibaut Vanneste (TV) and Amy Belba (AB) performed the literature search, reviewed the literature, and wrote the article. Gezina T.M.L. Oei reviewed and adapted the article with supplementary publications. Pieter Emans provided input on the diagnostic process and revised the article. Loic Fonkoue provided input on the anatomy and revised the article. Leonardo Kapural, Philip Peng, and Steven P. Cohen thoroughly reviewed the article and edited the paper. Jan Willem Kallewaard, Micha Sommer, and Bert Vanneste reviewed the article and provided additional input on treatment options and techniques. Jan Van Zundert controlled the paper, provided comments, and had full responsibility.

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DATA AVAILABILITY STATEMENT

Data sharing is not applicable, as no new data were created or analyzed in this study.

PATIENTS CONSENT

No patient information was retrieved or analyzed; all information is derived from published literature. Therefore, no patient consent was needed.

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