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Radiologists as clinicians: Radiological interventions for knee osteoarthritis

Radiologists can offer a number of image-guided percutaneous therapies in the treatment of knee osteoarthritis, including newer nonpharmacological options such as neuroablation, neuromodulation, and genicular artery embolization.

ABSTRACT: Knee osteoarthritis is often treated surgically (knee joint replacement) or nonsurgically (physiotherapy, pharmacological treatment). However, interventional radiologists can also offer a number of image-guided percutaneous therapies, including pharmacological treatments (intra-articular steroid, local anesthetic, and hyaluronic acid injections), biological options (platelet-rich plasma or mesenchymal stem cell injections), and newer nonpharmacological therapies (neuroablation, neuromodulation, and genicular artery embolization). Intra-articular steroid injection is the most widely used radiologically guided therapy; it provides pain relief and can help confirm the joint as the source of pain. However, platelet-rich plasma injection may provide greater pain relief and functional improvement compared with other intra-articular injections. Mesenchymal stem cell injections may improve pain, function, and cartilage volume, but the therapy is still under clinical investigation. Neuroablation and neuromodulation achieve pain reduction by targeting the sensory nerves of the knee joint. Radiofrequency ablation has been shown to be more effective than intra-articular steroid injections at treating knee osteoarthritis pain and function. Potential advantages of neuromodulation over conventional radiofrequency ablation include less intraprocedural pain and lower risk of thermal damage to adjacent structures. Genicular artery embolization aims to downregulate inflammation and its downstream effects by altering synovial blood flow; it is considered a promising therapy for osteoarthritis-associated knee pain.

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Knee osteoarthritis is a common disorder with increasing prevalence due to the aging population. Osteoarthritis has a complex pathophysiology with resultant disability and places a significant burden on the health care system and economy. Osteoarthritis is a common problem managed by both orthopaedic surgeons and rheumatologists, as well as family physicians in the community.

Although knee joint replacement therapy is commonly performed in more advanced cases and where conservative measures have failed, nonsurgical options are desirable for many patients, such as those with milder disease, those on surgical wait lists, and those who are unsuitable for surgery or prefer to avoid it. Nonsurgical treatment includes physiotherapy to strengthen joint-stabilizing muscles and pharmacological treatment (including acetaminophen and NSAIDs). Additionally, an increasing number of image-guided percutaneous therapies can be offered by interventional radiologists.

We review the current therapies for knee osteoarthritis that can be offered by the radiologist, as well as newer and potential future treatments, beginning with a guide to imaging workup for osteoarthritis, followed by a brief description of current and emerging imaging-guided interventions.

Radiological diagnosis

Radiographs

When clinical history and examination findings are consistent with osteoarthritis, a radiograph of the knee joint is often sufficient to confirm the diagnosis. A weight-bearing radiograph is advantageous when assessing the degree of osteoarthritis because it allows for better assessment of joint space loss. Osteoarthritis severity on radiographs can be graded

according to the Kellgren-Lawrence score, which assigns a grade to the degree of osteoarthritis-related change based on the presence of osteophytes, periarticular ossicles, joint space narrowing, subchondral sclerosis, pseudocystic areas (sometimes referred to as geodes), and altered shape of the bone ends.

MRI

For patients with appropriate demographics, typical symptoms, and radiographic findings of osteoarthritis, MRI is rarely useful and rarely adds further information compared with radiographs. Meniscus tears commonly coexist with knee osteoarthritis and do not appear to correlate with pain and function, which limits the value of using MRI to assess for meniscus tears in knee osteoarthritis. In instances where patients have atypical symptoms, normal radiographs, or locking of the knee, MRI may be beneficial to assess for internal derangement, flipped meniscal fragments, intra-articular osteochondral fragments, subchondral fracture, inflammatory arthritis, or earlier signs of degeneration. The assessment for inflammatory arthritis and synovitis is best achieved with administration of gadolinium to determine the degree of synovial thickening in the joint. There may also be a role for contrast MRI when assessing the degree of synovitis associated with osteoarthritis, as discussed in the section on geniculate artery embolization, since synovial inflammation can be a target for embolization.

CT scan

CT scan may be beneficial in cases of trauma and osteoarthritis to exclude fractures; to further assess abnormalities, such as bone lesions, seen on radiograph; or for preoperative planning when requested by the surgical team. Dual-energy CT is of value in the assessment of suspected gouty arthropathy because it can detect monosodium urate crystals in the knee joint or surrounding tendons and ligaments. Dual-energy CT can also aid radiologists in making more definitive diagnosis of equivocal findings that are suspicious for fractures by detecting surrounding bone marrow edema.

Ultrasonography

Ultrasonography has a limited role in the assessment of internal derangement of the knee joint due to the blockade of the acoustic waves by the surrounding bone. However, it is sensitive enough to detect joint effusions and juxta-articular knee joint cysts (e.g., Baker cysts), although confirming these entities is of dubious clinical benefit. Ultrasonography also has a role in the detection of synovitis. This involves measurements and comparison of synovial thickness and vascularity, assessed with color Doppler. Associated erosions in cases of inflammatory arthropathy may also be visualized. Limited views of the menisci, including meniscal tears, can be obtained, as well as visualization of marginal osteophytes; however, other modalities described previously remain superior in the detection of these abnormalities. In general, ultrasonography is a valuable tool when looking for soft tissue pathology around, rather than within, the knee joint. As such, it is not a first-line modality for osteoarthritis assessment. It remains an excellent modality for guiding aspiration of the knee joint in cases where infection or crystal arthropathy is suspected. Some centres use contrast-enhanced ultrasonography to assess for synovitis. Recent advances such as superb microvascular imaging (Canon Medical Systems) have allowed for detection rates of synovial vascularity in rheumatoid arthritis comparable to contrast-enhanced ultrasonography.

Image-guided percutaneous treatments

Radiologically guided therapy for knee osteoarthritis encompasses a variety of treatments, including drug delivery through image-guided joint injection, energy-based neuromodulation, and embolotherapy. The oldest and most widely performed is intra-articular steroid injection. Other options include hyaluronic acid and biological injections, radiofrequency nerve therapy, and genicular artery embolization. In general, these pain management therapies work best for mild to moderate knee osteoarthritis and are less effective for severe osteoarthritis.

Pre- and post-procedure pain scoring is key, both when using interventions to confirm the joint as the pain source and as a longer-term therapeutic option for the patient, because it establishes the potential value of repeat treatment in the future. Assessment of pain by the patient can be recorded according to a visual analog scale or graded from 0 to 10, both prior to and immediately after the procedure. Patients are also advised to score their pain daily following the procedure and record it in a pain diary so they can review it with their referring physician to assess the degree and duration of pain relief in the longer term.

For all image-guided procedures, the radiologist provides the patient with a basic description of the procedure and discusses expected outcomes and possible complications. For most procedures performed on the knee, it is preferred to have the patient lie supine. Local anesthetic is sufficient for analgesia in most cases. The radiologist may use ultrasonography or fluoroscopy guidance to ensure proper placement of the needle. Following the procedure, a simple dressing, such as a Band-Aid, is placed over the injection site.

Treatments can be divided into pharmacological, biological, and nonpharmacological.

Pharmacological treatments

Intra-articular steroid therapy: Intra-articular steroid injection for knee osteoarthritis is widely used for pain relief and can help confirm the joint as the source of pain. The mechanism of action is not fully understood but is believed to be due primarily to the anti-inflammatory role of steroids. Multiple steroid formulations for intra-articular joint injection are available, including triamcinolone, methylprednisolone, betamethasone, and dexamethasone.

Local anesthetic is usually injected alongside intra-articular steroids and is

responsible for immediate analgesic effects and short-term relief of pain. Depending on the local anesthetic that is used, the analgesic effect wanes within a few hours, while the steroid may take a few days to take effect. Therefore, patients may experience a transient discomfort in the interval between local anesthetic cessation and steroid activation. Increased activity during the analgesic period immediately following injection should therefore be discouraged to avoid a pain flare later. A single intra-articular steroid injection may last from 2 weeks to beyond 6 months and is variable among different patients.

Local complications related to the use of intra-articular steroids include transient pain flare, rash, and local skin changes (atrophy or pigmentation). Steroid-related pain flare affects up to 10% of patients and usually resolves within 5 days. More severe adverse effects are rarer but include rapidly progressive osteoarthritis, subchondral insufficiency fractures, and avascular necrosis.

Although intra-articular steroid injections are considered local therapy, systemic effects may occasionally be seen, such as hyperglycemia, Cushingoid symptoms, or osteoporosis; therefore, physicians need to advise diabetic patients to closely monitor glucose levels after injections. Generally, injection frequency should be limited to four treatments per year.

Local anesthetic as a single agent: Intra-articular local anesthetic injection alone is occasionally performed in patients for diagnostic rather than therapeutic purposes—for example, in cases of atypical pain or suspected referred pain from the hip joint to the knee. In these instances, the patient receives intra-articular local anesthetic and is instructed to perform the activities that would usually trigger their pain. Resolution of the pain after the injection confirms the knee as the source of the pain. A few local anesthetics, which have different half-lives and potentially chondrotoxic effects, can be used. The most commonly used short-acting local anesthetic is lidocaine; common long-acting local anesthetics are bupivacaine and ropivacaine. In our centre, we use ropivacaine 0.5% because it is a long-acting local anesthetic with the least chondrotoxic effect.

Hyaluronic acid: Hyaluronic acid is an important component of synovial fluid, secreted by the joint capsule, which lubricates the articular surfaces and acts as a shock absorber. Hyaluronic acid may also play a role in inflammatory cascade regulation, reduction of pain and cartilage degeneration, and cartilage regeneration.[1] In the synovial fluid of patients with knee osteoarthritis, hyaluronic acid levels are low.[2]

Pre- and post-procedure pain scoring is key, both when using interventions to confirm the joint as the pain source and as a longer-term therapeutic option for the patient, because it establishes the potential value of repeat treatment in the future.

Multiple hyaluronic acid preparations are available for intra-articular injection. Hyaluronic acid injections are typically performed as one injection or two to four spaced injections. Compared with intra-articular steroids, hyaluronic acid onset of action is typically delayed, with noticeable pain improvement starting after 3 to 4 weeks and lasting longer, for up to 6 months.[3-5]

Other clinical parameters, such as physical function, improve with hyaluronic acid injections compared with intra-articular steroids or placebo.[3,6] Some studies suggest there is a potential synergistic effect when steroids are combined with hyaluronic acid steroids, which results in greater and longer-lasting pain relief.[7] Obesity, the presence of large joint effusions, severe degenerative changes, and isolated severe patellofemoral degenerative changes may reduce the benefits associated with hyaluronic acid injections.[8] Complications associated with hyaluronic acid injections are usually self-limited and include injection site pain, swelling, and arthralgia, which usually subside within a few days of the procedure.[2,9]

Biological treatments

Platelet-rich plasma: Platelet-rich plasma is produced by withdrawing a blood sample from the patient on the day of the procedure. An anticoagulant is typically used. The blood then undergoes centrifugation to achieve a high platelet concentration. Concentrations used vary significantly: reports include 1.6 to18 times that of whole blood in commercially available kits, although some practices achieve 45 times baseline with manual protocols. Several other parameters are also variable, including recovery rate, viability rate, WBC levels, RBC levels, and pH. At the time of injection, the platelets may be activated with exogenous or autologous thrombin. Injections can be performed as a single injection or a series of injections. Antiplatelet agents and NSAIDs are usually withheld prior to blood sampling. The platelet-rich plasma mechanism of action is complex and poorly understood, but it is likely related to growth factors and cytokine regulation of the inflammatory process, with possible cartilage production and preservation, as well as promotion of hyaluronic acid production.[10]

Platelet-rich plasma injection may provide greater pain relief and functional improvement in 12 months compared with other intra-articular injections such as hyaluronic acid or steroids.[9,11] A meta-analysis of 20 randomized controlled trials showed that platelet-rich plasma was superior to hyaluronic acid in terms of short-term functional recovery, long-term pain relief, and physical function improvement.[11]

A larger meta-analysis of 30 randomized controlled trials that compared platelet-rich plasma to hyaluronic acid, steroid therapy, and placebo indicated that platelet-rich plasma had the best visual analog scale and

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores up to 12 months posttreatment.[9] Complications related to platelet-rich plasma injections are usually self-limited and similar to those of other injections, such as injection site pain, joint stiffness, and localized swelling/bruising. Platelet-rich plasma is contraindicated in patients with septicemia, anemia, thrombocytopenia, and hematological or skeletal malignancy.

Currently, platelet-rich plasma therapy for knee osteoarthritis is considered an off-label use and is not available in the public health care system in BC, though it is offered in some private facilities.

Mesenchymal stem cell therapy: Mesenchymal stem cell therapy has received much interest in recent years. Research has been conducted on applications for a wide variety of anatomical locations and pathologies, with the goal of promoting regeneration and restoration of function. Similarly, the intention of intra-articular injections of mesenchymal stem cells is symptomatic improvement through cartilage repair/regeneration via differentiation of mesenchymal stem cells into chondroblasts. Mesenchymal stem cells can be obtained from bone marrow or subcutaneous fat from the patient's body (autologous) or from amniotic membrane or fluid (allogenic). Initial reports suggested improved pain, function, and cartilage volume posttreatment with mesenchymal stem cell injections.[12-14] Adverse outcomes are usually minor, such as injection site pain and swelling, and tend to resolve within 1 week.[15] While of great potential interest for the future, this therapy is not currently offered in the public health care system in BC and is actively under clinical investigation.[16]

Nonpharmacological treatments

Nonpharmacological procedures are usually conducted in the tertiary centre setting and are best planned in conjunction with joint specialists. Geniculate artery embolization is currently performed at the Vancouver General Hospital, and neuromodulation is performed at the University of British Columbia Hospital.

Neuroablation and neuromodulation: These therapies aim to achieve pain reduction by targeting the sensory nerves of the knee joint. The most commonly used modality is radiofrequency ablation, although cryoablation and chemical ablation are also used. Prior to the day of the procedure, a preliminary diagnostic block of the geniculate nerves with lidocaine may be performed to assess pain alteration as a prognostic indicator of the potential success of ablation.

A recent systematic review concluded that radiofrequency ablation is more effective at treating knee osteoarthritis pain and function compared with intra-articular steroid injections, with pain relief clinically notable up to 24 months.

Neuroablation: The usual targets of neuroablation are three of the geniculate nerves (superior lateral, superior medial, and inferomedial); the inferolateral nerve (a branch of the common peroneal nerve) is spared to avoid risk of foot drop.[17] Nerve stimulation tests can also be performed to ensure no motor nerves are ablated.

In radiofrequency ablation, the target nerves are heated to 60 °C to 80 °C using continuous current to achieve tissue destruction and neurolysis and, therefore, pain relief through sensory neural destruction. There is potential for nerve regrowth and thus pain recurrence; however, the treatment can be repeated.

A recent systematic review concluded that radiofrequency ablation is more effective at treating knee osteoarthritis pain and function compared with intra-articular steroid injections, with pain relief clinically notable up to 24 months.[17] No serious adverse events were documented. Potential complications after radiofrequency ablation of genicular nerves are usually self-limited and include injection site pain, bruising, and temporary altered sensation (allodynia and hypoesthesia). Vascular complications such as genicular artery pseudoaneurysm or arteriovenous fistula are rare.

In contrast to radiofrequency ablation, cryoablation produces extremely low temperatures (as low as −40 °C) to achieve neurolysis with Wallerian degeneration of genicular nerves. The nerve sheath usually remains intact, so, as with radiofrequency ablation, there is the potential for pain recurrence though nerve regrowth, though the treatment can be repeated. Cryoablation has been less extensively studied in this setting than radiofrequency ablation; however, in a randomized, double-blind, sham-controlled trial of 180 patients, cryoablation reduced pain related to osteoarthritis for up to 150 days, with no serious adverse events related to the procedure.[18]

Neuromodulation: Neuromodulation, in contrast to neuroablation, involves little, if any, tissue damage. The principle is to use pulsed radiofrequency to improve pain through altered sensory nerve function rather than nerve destruction. Pulsed radiofrequency is used with short energy bursts, which keeps temperatures lower than conventional radiofrequency (under 42 °C) and below the threshold of permanent damage (45 °C to 50 °C).[19,20] Potential advantages of neuromodulation over conventional radiofrequency ablation include less intraprocedural pain and lower risk of thermal damage to adjacent structures.

The mechanism of action in neuromodulation is thought to relate to electric fields that induce transmembrane potentials that may result in cellular deformation and ion channel dysfunction, with resultant disruption of nerve conduction but without prolonged high-heat tissue damage.[19,21,22]

Neuromodulation can be performed using a three-needle genicular nerve technique, or by a single-probe intra-articular

technique to target intra-articular nerve endings. Intra-articular pulsed radiofrequency has shown clinically significant and reproducible pain relief in patients with knee osteoarthritis.[23,24] Pain reduction up to 12 months has been reported.[23-26] Studies that have targeted the three geniculate nerves have also reported pain reduction up to 12 months.[27-29]

Genicular artery embolization: Contrary to popular teaching, the presence of synovitis has been implicated in the pathogenesis and progression of osteoarthritis. Osteoarthritis has traditionally been considered a noninflammatory degenerative condition that arises from mechanical cartilaginous and osseous degeneration ("wear and tear"). More recent pathogenetic models of osteoarthritis focus on imbalances in cell signaling pathways within the joint favoring pro-inflammatory cytokines, which induce chronic synovitis, neovessel formation (angiogenesis), and alterations in chondrocyte function. By facilitating the distribution of pro-inflammatory cytokines within the local microenvironment, angiogenesis is believed to play a critical role in the maintenance and propagation of inflammation within the joint. Angiogenesis also induces the genesis of parallel sensory/pain fibres, which become sensitized in the local hypoxic, inflamed, and mechanically stressed environment. The milieu of structural and physiologic events leads to neovessels that may serve as a treatment target for osteoarthritis and osteoarthritis-related pain.[30]

Originally described in 2015 by Okuno and colleagues, genicular artery embolization is a minimally invasive procedure that involves selective catheterization and embolization of the genicular arteries that perfuse the knee capsule, resulting in alterations to synovial blood flow that are thought to downregulate inflammation and its downstream effects.[31] Phase I to IIB clinical trials have established genicular artery embolization as a promising therapy for osteoarthritis-associated knee pain.

In a recent meta-analysis of 11 publications that investigated the outcomes of genicular artery embolization in mild to moderate knee osteoarthritis (225 patients, 268 knees), the procedure was associated with rapid and sustained improvements in knee pain reported by visual analog scale (54% and 80% improvement within the first week and at 2-year follow-up, respectively).[32] Genicular artery embolization also resulted in improvement in functional status (58% and 85% improvement in WOMAC scores within the first week and at 2-year follow-up, respectively) and in the number of patients who employed other analgesic strategies (27%, 65%, and 73% reduction in the use of opioids, NSAIDs, and intra-articular hyaluronic acid injections, respectively). Sustained pain reduction has not been achieved after genicular artery embolization in cases of severe osteoarthritis.[33]

As our understanding of the disease processes of osteoarthritis of the knee increases, so does the potential for exciting new diagnostic and therapeutic options.

No severe or life-threatening adverse events have been reported for genicular artery embolization. Rates of minor adverse events may be as high as 25% and include transient, self-resolving complications such as local skin discoloration, puncture site hematoma, plantar paresthesia, and mild fever.[34] The most common minor adverse event, skin discoloration, is thought to reflect mild transient skin ischemia and has been successfully reduced by using ice packs applied intraprocedurally over the knee to temporarily constrict cutaneous vessels and divert blood flow.[34]

Several major randomized controlled trials designed to further explore the efficacy, prognosticators, and long-term outcomes of genicular artery embolization are currently underway.

Referral procedures and pathways

For most of the percutaneous therapies we have described, referrals can be made directly to radiology by any physician, including joint specialists and family practitioners, where these therapies are available in BC. Weight-bearing knee radiographs are very helpful for radiology triage, along with a brief description of symptoms, an indication of the working clinical diagnosis, and dates and types of previous treatments. This information is reviewed by the radiologist prior to injection.

For injections, the injectate (e.g., local anesthetic, steroid, hyaluronic acid) should be generally specified by the referring doctor. Doses are typically decided by the radiologist. These procedures are available in most hospital settings.

Neuromodulation referrals can be made to the radiology department at UBC Hospital. Inquiries can be made to other centres regarding the availability of this procedure.

Geniculate artery embolization is an area with ongoing clinical trials, which benefits from specialist clinical assessment. Referrals can be made to Dr Maziar Badii at the Artus Health Centre.

Conclusion

As our understanding of the disease processes of osteoarthritis of the knee increases, so does the potential for exciting new diagnostic and therapeutic options. A variety of image-guided percutaneous therapies are currently available, including pharmacological and nonpharmacological options. Corticosteroids and hyaluronate are currently the most widely used and are popular in BC. Biologics such as platelet-rich plasma and mesenchymal stem cells show promising results, with a growing evidence base, though they are not currently available in the public health care system in BC. Nonpharmacological options include geniculate artery embolization and neuromodulation, which have the potential to offer longer-term pain relief than traditional corticosteroid injection. ■

Competing interests

None declared.

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