Knee Ablation Approaches

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KEYWORDS

• Radiofrequency ablation • Denervation • Osteoarthritis • Knee pain

KEY POINTS

- The convention targets for knee denervation are superomedial, superolateral, and inferomedial genicular nerves.
- These landmarks have been extensively examined for the anatomic basis.
- Literature supports the improvement in pain and function after the radiofrequency ablation of those three genicular targets in patients with chronic knee pain secondary to osteoarthritis.
- Ongoing investigation is needed to explore the optimal number, types, and configuration of lesions.

BACKGROUND

Osteoarthritis (OA) is well known to be one of the most prevalent conditions, with over 54 million people in the United States alone living with OA and an estimated productivity cost of work lost in the range of 17.5 billion dollars per year.[1,2] The knee joint continues to be the most common joint affected by OA, necessitating invasive intervention with a minimum of 60,000 total knee arthroplasties (TKAs) performed per year in Canada and an estimate of near 500,000 per year in the United States.[1] Despite its prevalence and impact, there is no cure for OA. Current conservative therapies target symptom management and pain relief and are known to have diminishing returns with repeat interventions.[3] These therapies include therapeutic exercise,[4] pharmacologic medications,[5,6] viscosupplementation,[7] corticosteroid,[8] and platelet-rich plasma (PRP).[9] Knee arthroplasty remains the treatment of choice for moderate to severe knee OA resistant to adequate nonsurgical management options; however, it carries surgical risks and adverse events that preclude or limit its availability to all

Authors' contribution: All the authors participated in the conception of the review, acquisition, analysis, interpretation of data, and drafting the article.
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Phys Med Rehabil Clin N Am ■ (2021) ■–■
https://doi.org/10.1016/j.pmr.2021.05.012
pmr.theclinics.com

patients, including those with significant comorbidities. Furthermore, a substantial proportion of patients continue to experience persistent pain, or functional restrictions after TKA, limiting its attractiveness as a definitive treatment option.[10,11]

Radiofrequency ablation (RFA) has been used by practitioners for more than half a century as a treatment for a multitude of chronic pains because of its ability to inhibit pain signals through the destruction or modulation of peripheral nerves with either high or pulsatile thermal energy, respectively.[12] In recent years, starting in 2011,[13] there has been increased interest in genicular nerve ablation to aid in pain management in either those who are not a surgical candidate for knee replacement or to prolong the function of the native knee before total joint arthroplasty. Since its initial publication describing RFA of three genicular nerves at the superomedial, inferomedial, and superolateral joints, there has been significant interest in describing and optimizing techniques to effectively denervate the sensory supply to the anterior knee joint. This review aims to summarize the available literature on the intervention of genicular nerve RFA, including different techniques and targets as well as clinical outcomes and potential complications. Clinical neuroanatomy relevant to knee RFA has been discussed in another chapter of this issue.

INDICATIONS (PATIENT SELECTION)

Genicular nerve RFA is offered to patients with moderate to severe symptomatic knee OA with grade II to IV Kellgren-Lawrence classification refractory to conservative treatment and not the surgical candidate for joint replacement due to significant comorbidities or reluctance to pursue the surgical option.

At the time of publication of this review, there is on-going research to determine the clinical effect of genicular nerve RFA on persistent knee pain after TKA and whether genicular nerve RFA before TKA facilitates pain management and/or rehabilitation. At the current time, there is inadequate evidence to determine the effect of genicular RFA in these patient populations. Although RFA provides pain relief for patients with pain related to OA, patients with unstable knee joints will not benefit from this procedure, and a surgical option should be considered.

TARGETS FOR DENERVATION AND TECHNIQUES

The current technique is based mostly on the original description by Choi and colleagues with slight modification.[13] The three targets that most practitioners believe are superomedial (SMGN), inferomedial (IMGN), and superolateral genicular nerves (SLGN). Since the original description of RFA in these three nerves, several anatomy studies evaluated the anatomic basis of these landmarks. These include one of the most comprehensive dissections with 3-dimensional documentation of all articular branches in the anterior knee capsule published by Tran and colleagues[14] (**Fig. 1**). So far, these publications support the anatomic landmark of these articular branches at the junction of diaphysis and epiphysis. Both Tran and colleagues[14] and Franco and colleagues[15] suggested having the needle placed slightly more posterior in the lateral plane for SMGN and SLGN. Most recently, Tran and colleagues also published an article validating the articular branches captured by the lesions in these three locations.[16] They confirmed that the superomedial and superolateral lesions capture the SLGN and SMGN, respectively. Interestingly, only the transverse deep branches of SMGN and SLGN are captured, and nerves to the posterior division of medial and lateral branches of nerve to vastus intermedius are also captured in the convention lesion (**Fig. 2**).

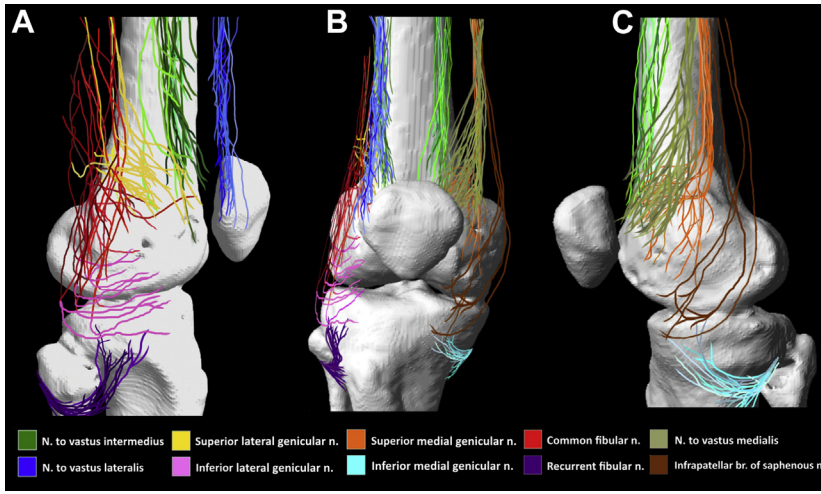

Fig. 1. Frequency map and distribution of the 10 articular branches of anterior knee capsule. N, n, nerve. (*Courtesy of* Philip Peng Educational Series.)

Recently, there are some additional landmarks suggested,[17,18] but the benefit of adding further site of ablation is still being investigated. Therefore, we only discuss the ablation technique for SMGN, SLGN, and IMGN, respectively.[16]

Both ultrasound (US) and fluoroscopy guidance techniques have been described for both diagnostic and ablation. Under fluoroscopy guidance, the patient is put in a supine position with a bolster or pillow to keep the knee in flexion. For the SMGN and SLGN, the target is the junction between epiphysis and diaphysis in the anteroposterior view and midpoint between anterior and posterior cortex in the lateral view. For the IMGN, the target is the junction between epiphysis and diaphysis deep to the medial collateral ligament (**Fig. 3**). Similarly, the targets for SMGN, SLGN, and IMGN are the same for the US-guided technique (**Figs. 4** and **5**). For diagnostic block, 1 mL of local anesthetic is administered to the target. For RFA, the radiofrequency (RF) needle is inserted instead. In some centers including the authors' center, a palisade lesion is preferred for the superior quadrants, especially the medial compartment given the configuration of the articular branches.

CLINICAL EFFECTIVENESS AND SAFETY

Since the first randomized trial[13] on genicular nerve RFA, there has been outpouring interest culminating in over 35 clinical studies and 15 randomized controlled trials that are all of moderate to high methodological quality.[19–21]

The clinical efficacy of genicular RFA is best exemplified with the largest double-blind, randomized control trial of cooled RFA (CRFA) compared with intra-articular steroid (IAS) in 151 patients with symptomatic knee OA (Kellgren and Lawrence [KL] grade 2–4).[22] Despite having similar preintervention numeric pain rating scores, the mean knee pain score was less in the CRFA group than in the IAS group at every follow-up interval, including 1, 3, and 6 months after the intervention. Mean improvement in the CFRA group at 1 and 6 months was 4.2 and 4.9 points, respectively, on a 10-point numeric rating scale (NRS) compared with 3.3 and 1.3 in the IAS group. Similarly, at 6 months, 74% and 22% in the CRFA group met successful outcome criteria

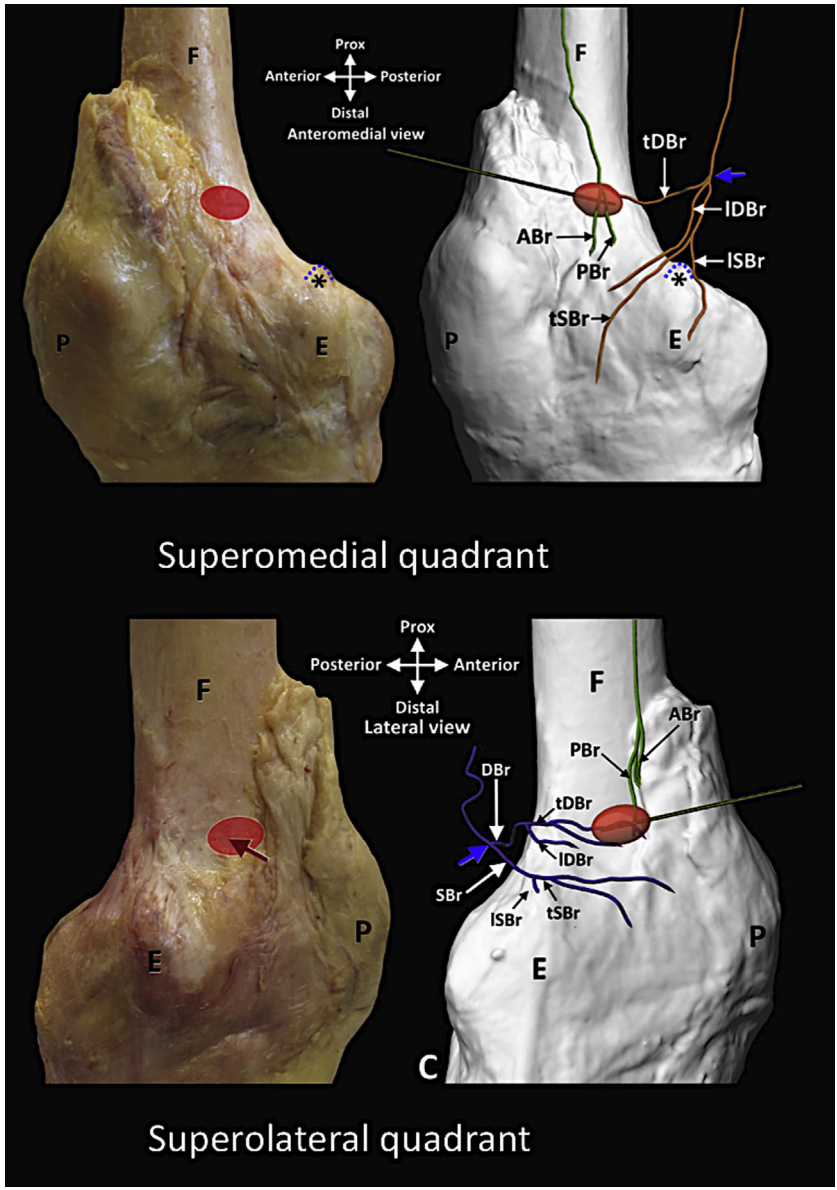

Fig. 2. Simulated lesion and the nerves capture. *Upper panel*, a conventional lesion in the superomedial quadrant captures the transverse deep branch (tDBr) of superomedial genicular nerve. It also captures the posterior division (PBr) of the medial branch of nerve to vastus intermedius. *Lower panel*, a conventional lesion in the superolateral quadrant captures the transverse deep branch (tDBr) of superolateral genicular nerve. It also captures the posterior division (PBr) of the lateral branch of nerve to vastus intermedius. *, adductor tubercle; ABr, anterior division of nerve to vastus intermedius medial branch; E, epicondyle; F, femur; lDBr, longitudinal deep branch; lSBr, longitudinal superficial branch; P, patella; tSBr, transverse superficial branch of superomedial genicular nerve. (*Courtesy of* Philip Peng Educational Series.)

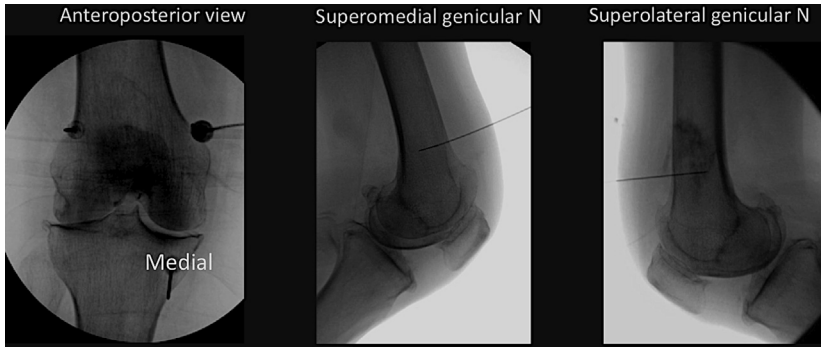

Fig. 3. Fluoroscopy view of the needles at the three targets of genicular nerves. (*Courtesy of* Philip Peng Educational Series.)

(>50% reduction in NRS score) and 100% pain relief, respectively, compared with only 25.9% and 4% in the IAS group. Similarly, to pain relief, where CFRA demonstrated improved and long-lasting improvement compared with IAS, functional outcomes demonstrated clinically and statistically significant improvements in the CRFA group compared with those in the IAS group.[22]

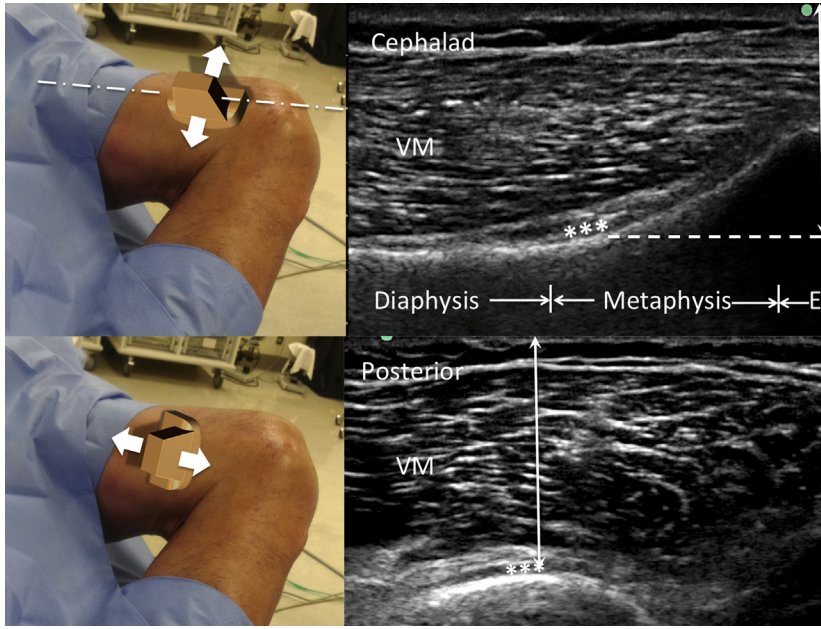

Fig. 4. Ultrasound image of the target for superomedial genicular nerve. The leg is put in external rotation of hip, and the orientation of the probe is in long axis of femur. The target is the fascial expansion (***) deep to the vastus medialis (VM) between diaphysis and epiphysis (*E*). The probe is then rotated 90° keeping the target at the same depth. This view allows in-plane insertion of needle from anterior to posterior orientation. (*Courtesy of* Philip Peng Educational Series.)

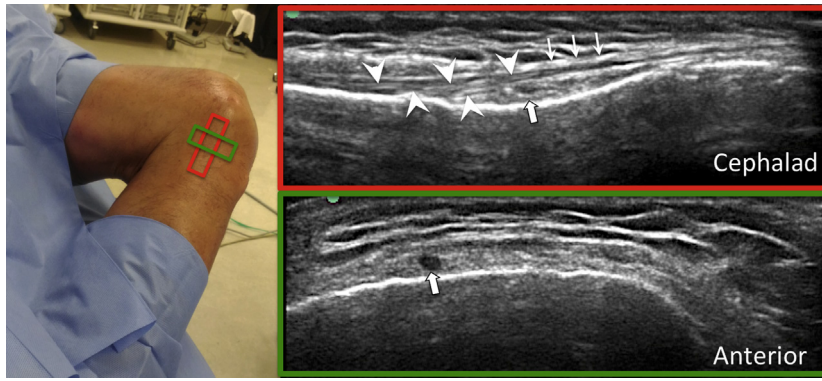

Fig. 5. Ultrasound image of the target for inferomedial genicular nerve. The initial position of the probe is over the medial collateral ligament (*red rectangle*). The inferior medial genicular nerve (IMGN) and vessel (*bold arrow*) is deep to the medial collateral ligament (*arrowheads*), which is deep to the crural fascia (*arrows*). The depth of the target is marked, and the probe is rotated 90° keeping the target at the same depth as the previous scan. The neurovascular bundle (*bold arrow*) was seen again. This view allows in-plane insertion of needle from anterior to posterior orientation. (*Courtesy of* Philip Peng Educational Series.)

The clinical efficacy of genicular RFA has been supported by multiple systematic reviews and meta-analyses.[19–21] Genicular RFA has demonstrated greater than 50% pain relief in 194 of 296 patients (65.5%) at 6 months when combining all available comparative studies or a pooled mean difference in the visual analog scale (VAS) of −4.196 when combining only US-guided RFA studies.[19–21] Similarly, 27 of 28 (96%) comparative studies demonstrated enhanced functionality from baseline up until 6 months[19] in those undergoing RFA or a pooled mean difference in the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) scores of 23.155 points when combining only US-guided RFA studies.[21]

The large majority of randomized controlled trials have final follow-ups at the 6-month postintervention period; however, long-term follow-up studies of these large, randomized trials have demonstrated sustained pain relief and improved function up to 24 months after the intervention.[23,24] At 18 and 24 months after the intervention, there was a demonstration of a significant decrease in NRS pain scores from 6.6 ± 1.6 at baseline to 3.1 ± 2.7(n = 25) and 3.6 ± 2.8 (n = 18) at 18 and 24 months, respectively, with 12 of 25 subjects reporting ≥50% pain relief at 18 months and 11 of 18 demonstrating ≥50% pain relief at 24 months from the baseline.[23] Similarly, there was a demonstration of prolonged functional improvement as measured by the Oxford Knee Score, with an overall mean change from baseline of 26.0 ± 9.6 points (Minimal clinically important difference = 5) at 18 months and 29.9 ± 10.4 points at 24 months.[23]

While the evidence supports the use of RFA in patients with chronic knee pain as a result of OA in the native knee, this procedure has not shown expected benefits in some scenarios: preoperative for those undergoing TKA or in those with persistent chronic TKA pain. A single-center sham-controlled prospective trial that assessed the efficacy of preoperative knee RF performed 2 to 6 weeks before TKA reported a lack of benefit in terms of postoperative pain, consumption of analgesics including opioid medications, and functional recovery.[25] The authors proposed a 26% nonresponder rate of this procedure and is probably explained by the variable course of genicular nerves and copresence of central sensitization with chronic advanced knee OA.[26] Similarly, RFA of the knee joint has not been rigorously tested in subacute

and chronic persistent knee pains after arthroplasty. A retrospective comparative study of US-guided knee RFA in chronic pains secondary to TKA or advanced knee OA (KL grade III-IV) in 23 patients reported comparable benefits (67% in TKA group and 88% in knee OA group of >50% improvement in VAS pain scores) in both the groups at 3 months.[27] A few isolated case reports of knee RF in acute posttraumatic pains[28] and acute postoperative TKA pains[29] have been published, although the clinical efficacy in these conditions remains to be established.

Comparison with Other Treatment Groups

Eight studies have compared genicular nerve RFA to common injection therapies including corticosteroid injection,[22,30,31] ozone injection,[32] hyaluronic acid (HA) injection,[33] PRP with sodium hyaluronate injection,[34] solely sodium hydrate injection,[35,36] and intra articular prolotherapy with erythropoietin and dextrose injection.[36]

All randomized control trials of RFA compared with corticosteroid injection have demonstrated significant improvements at all follow-ups for pain reduction; however, only 2 of 3 studies have demonstrated significant improvements in functional scores.[22,31,37] Similar to corticosteroid, RFA has demonstrated improvements in pain and functional scores when compared with PRP and hyaluronic acid in a randomized fashion, with the RFA group demonstrating significant improvements in VAS ($P<.05$) (RF: 4.28 ± 1.12 vs PRP + HA: 6.32 ± 1.18) and American Knee Society scores ($P<.05$) at all follow-ups.[34] Finally, compared with solely hyaluronic acid, RFA demonstrated significant improvements in VAS and function (WOMAC RF: 12.06 ± 4.03 vs HA: 59.93 ± 15.97) at all time points.[33–35]

Unfortunately, compared with nontraditional intra-articular injections, including erythropoietin plus dextrose injection and ozone injection, RFA has not demonstrated significant benefits.[32,36] The significance of these randomized control trials, despite being of moderate quality, necessitate further investigation because of the infrequent utilization of these intra-articular therapies for knee OA.[32,36]

Comparative Efficacy of US Vs Fluoroscopy-Guided Radiofrequency Ablation Techniques

Both fluoroscopy and US have been used as imaging modalities for guiding the needle to the target position. Knee RFA was initially performed using a fluoroscopy-guided approach.[13] Later, US was suggested as an alternate radiation-free office-based technique.[38] Several studies, both cadaveric and clinical, on the US-based approach for knee RFA asserted the adjacent location of genicular arteries as a surrogate marker for localization of genicular nerves to yield better outcomes.[39,40] Yet, subsequent cadaveric studies that investigated the relationship of genicular nerves and arteries did not find this assumption to be true.[41] Clinically, a couple of RCTs have compared the efficacy of pain relief in US and RFA techniques and reported similar outcomes with both techniques.[37,42] Each technique offers a unique set of advantages. Fluoroscopy guidance can easily identify the nerve targets as they run adjacent to the periosteum and offer better needle visualization regardless of tissue depth and needle gauze. In contrast, US guidance offers the benefit of an office-based cheaper alternative with no radiation exposure and improved safety due to better visualization of adjacent soft-tissue structures. The choice of technique should be based on the availability of set up and individual experience and comfort with the imaging modalities.

Complications/Adverse Events

Most publications regarding genicular nerve RFA have not demonstrated any significant adverse events related to the procedure. With the significant increase in the

procedure rate of genicular nerve RFA, there have been reports of rare, however, significant safety concerns.[42,43] Transient hypoesthesia,[44,45] numbness,[45] and periosteal touch allodynia[13] were reported in few studies and significantly improved within a few weeks after the procedure. Rare complications including vascular injury of the knee including large subcutaneous bleeding,[44] ecchymosis,[46] hematoma formation,[47] skin burns,[48] hemarthrosis, pes anserine tendon damage,[49] septic arthritis,[50] or pseudoaneurysm as well as osteonecrosis of the patella have been described in the literature.[42] Direct comparison of fluoroscopy and US-guided knee RFA was performed in two studies and did not report any adverse effects.[37,43]

Several clinicians argue Charcot's neuropathy is a possible catastrophic side effect of knee joint nerve ablation. Nevertheless, Charcot's neuropathy has never been reported as a complication after knee RFA, even in the studies with relatively more prolonged duration of follow-up.[23,46] The reasons for the non-occurrence of Charcot's neuropathy are twofold. First, the partial nerve supply to the joint is preserved with knee RFA as the articular sensory branches to the posterior joint is spared. Second, Charcot neuropathy develops in systemic conditions with inflammatory mediators that disrupt the homeostasis of bone mineralization, causing osteolysis.[51] Owing to the rarity of these adverse events and no description in large cohort studies, it is unknown what the true prevalence of these adverse events are, nor the procedural aspects that may increase or decrease the risk of these events.

SUMMARY

Knee RFA has quickly become one of the most promising interventions for those with knee pain secondary to OA because of its reproducible and prolonged effectiveness in reducing pain and improving function without violating the native knee joint, necessitating irreversible biomechanical changes or exposing patients to potentially serious adverse events. However, there continues to be debate regarding the true efficacy, optimal imaging technique, ideal targets, and lesion size and/or system.

Although numerous studies have been published since the original description by Choi and colleagues describing alternative descriptions of nerve supply to the anterior knee joint and potential targets for RFA, there has been no definitive evidence regarding the optimal number and location of targets.[13] Most of the published clinical studies have embraced the SMGN, IMGN, and SLGN as conventional landmarks following the first RCT[13] that adopted these landmarks. Tran and colleagues described the detailed course of articular branches in four quadrants.[14] Succeeding studies reported disparity in the sensory innervation of the knee joint,[14,52] and thereafter, a range of procedural targets to capture different nerve combinations for improvement of responder rate and magnitude of pain relief have been described.[17,18,53] The optimal location to target these nerves has also been argued based on the heterogeneity of the course of genicular nerves identified in cadaveric dissections with the suggestion of revised locations.[17,41] While there has been a suggestion to modify the conventional targets for genicular nerve ablation, clinical studies that have used conventional landmarks have reported excellent benefits.[22,48] Hence, despite the fact that recent anatomic studies may advocate a correlation of improved nerve capture with reduced arterial ablation using revised ablation points,[17,41] it remains to be determined if the correlation of these points yields either improved clinical efficacy or safety after genicular nerve RFA.

Several patient- and procedure-related factors have been debated to contribute to the success of knee RFA procedure. Clinical trials that enrolled patients with variable grades of knee OA from mild to severe (KL grade 1–4) have reported beneficial

outcomes.[19,20,22] There is a lack of precise data to predict if the success of knee RFA depends on the structural severity of knee RFA. While a study reported approximately 3 times better outcomes in those with a KL grade 3 or less than KL grade 4,[54] another study in advanced knee OA (KL grade 3–4) reported at least 32% improvement in pre-treatment pain scores at 1-year follow-up.[46] The variability in success rate could likely be owing to multiple nonstructural elements such as psychological comorbidities and central sensitization that contribute to determining subjective knee pain, and these factors should be carefully assessed before making a decision to offer this treatment. Diagnostic nerve blocks have not shown any value to determine the predictive outcome of genicular nerve RFA.[48] Furthermore, authors have reported a 64% success rate of knee RFA at 6 months without a proceeding diagnostic block.[46]

In summary, knee RFA has been demonstrated to be a promising intervention resulting in prolonged improvement in pain and function. Further investigation is needed to compare and optimize technical aspects of knee RFA, including the number of neuroablative lesions, needle location, imaging technique, lesion size, and the need and effectiveness for repeat interventions.

DISCLOSURE

P.W.H. Peng received equipment support from Sonosite Fujifilm Canada. The other authors declare nothing to disclose. The authors have not received funding for this work and have no conflicts of interest in the authorship or publication of this contribution.

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