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Genicular Nerve Radiofrequency Ablation

A Novel Approach to Symptomatic Knee Osteoarthritis

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Abstract

Knee osteoarthritis (OA) affects millions of Americans, and not every patient is amenable to surgery for a variety of reasons. Genicular nerve radiofrequency ablation (GNRFA) is emerging as an effective minimally invasive nonsurgical treatment option for symptomatic knee OA. GNRFA has been shown to provide consistent short-term (3 to 6 months), and sometimes longer, pain relief in patients with symptomatic knee OA or with pain syndrome following total knee arthroplasty. The data are limited to mostly smaller studies on the efficacy and safety of RFA in patients with symptomatic knee OA.

According to the Centers for Disease Control and Prevention (CDC), >54 million Americans have been diagnosed with some form of arthritis[1]. The most prevalent form of arthritis is osteoarthritis (OA), which can affect any joint in the body. There is no cure for OA. Factors attributed to the onset of OA include genetics, diet, obesity, sports, injury, and older age, to name just a few. Knee OA is especially prevalent and, depending on the severity, can contribute to pain, joint stiffness, disability, depression, insomnia, and a decrease in overall functional capacity[2]. Nonpharmacologic treatment of knee OA typically consists of weight loss, physical and aquatic therapy, medial compartment unloading, the use of lateral wedge insoles, platelet-rich plasma (PRP) injections, and the use of assistive devices. Pharmacologic treatment consists of hyaluronic acid and cortisone injections; nonsteroidal anti-inflammatory drugs (NSAIDs), including cyclooxygenase-2 (COX-2) inhibitors; opioid therapy; and glucosamine plus chondroitin. Conversely, in their clinical practice guideline (2nd edition), the American Academy of Orthopaedic Surgeons (AAOS) does not recommend the use of hyaluronic acid, PRP injections, or glucosamine plus chondroitin in the treatment of symptomatic knee OA.

However, a new analysis of 54 studies covering 16,427 patients found supporting evidence that glucosamine plus chondroitin is an effective treatment for symptomatic knee OA[3]. In addition, glucosamine plus chondroitin was found to be comparable with celecoxib (Celebrex) in reducing pain, swelling, and functional limitation over a period of 6 months in people with moderate-to-severe knee OA[4]. Surgical options consist of arthroscopy with lavage and/or debridement, valgus-producing proximal tibial osteotomy, and unicompartmental knee arthroplasty or total knee arthroplasty (TKA). Each of these treatment modalities has a different rate of success and is highly dependent on patient selection. One novel treatment that shows promise in the treatment of OA is genicular nerve radiofrequency ablation (GNRFA). But what is GNRFA, and is it effective in treating knee pain caused by OA?

GNRFA is described infrequently in the orthopaedic medical literature, and is rarely prescribed by orthopaedic surgeons for the treatment of symptomatic knee OA. Some have speculated that musculoskeletal pain that does not respond to traditional

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orthopaedic approaches (nonsurgical or surgical) should be evaluated for a neural origin[5]. RFA is a relatively new pain management intervention for patients with knee OA that is recalcitrant to nonoperative measures. In addition, patients who are not candidates for TKA because of comorbidities may find GNRFA to be a suitable alternative to surgery. GNRFA uses either thermal or cooled RFA with U.S. Food and Drug Administration (FDA)-approved probes. Conventional thermal RFA uses electric current to cauterize nervous tissue at between 80°C and 90° C for 90 to 120 seconds. Cooled RFA typically does not exceed 60°C and uses internally cooled radiofrequency probes in which water cools the probe tip, which enlarges the size of the lesion, thereby increasing the chance of completely denervating the tissue by overcoming the anatomic variability[6,7]. In essence, heat lesioning involves a spherical area of tissue destruction (burn) at the tip of the needle. The factors that contribute to the size and shape of the heat lesion include the needle diameter, the size of the electrode, and the active tip's position and orientation in the soft tissue[8]. A recent criticism of cooled RFA is that it produces a much larger heat lesion than conventional ablation, which may potentially cause thermal injury to unintended tissue[9].

In 2017, the FDA approved cooled RFA treatment for symptomatic knee OA[10]. GNRFA appears very promising, not only for knee OA but also for patients with persistent postoperative pain following TKA. While it is generally accepted that 90% of patients do well after TKA, 1 study demonstrated that approximately 20% do not[11]. With the 20% of patients who do poorly, there exists a continuum of pain that is not readily treated by conventional means. In light of the opioid pandemic, other methods need to be sought to treat patients with TKA pain syndrome, and GNRFA may be a good alternative.

Performing GNRFA

There are 6 genicular branches from the knee joint, called genicular nerves, including the inferior lateral, the inferior medial, the superior lateral, the middle, the superior medial, and the recurrent tibial genicular nerves[12]. The genicular nerves are sensory peripheral nerves that innervate the articular capsule of the knee joint[13]. The genicular nerves of the medial aspect of the knee are supplied from the tibial nerve, and the genicular nerves of the lateral aspect of the knee are supplied from the common peroneal nerve[14]. The genicular nerves are close in proximity to the 5 genicular arteries, which are the major blood supply to the knee joint[15]. The nerves targeted for ablation are outside of the capsule and include the superior lateral, the superior medial, and the inferior medial genicular nerves (Fig. 1). These 3 sensory nerves are thought to be primarily responsible for transmitting nociceptive pain signals from the knee to the brain. Ablation that is performed correctly should cause iatrogenic neural degeneration of these nerves without motor deficits[16]. RFA can be performed percutaneously using fluoroscopic or ultrasound guidance.

It is important to note that diagnostic-imaging quality is operator-dependent and subjective to interpretive error[17]. While there is a steep learning curve, little is known about the effects of case volume on the safety and efficacy of RFA[18]. The conventional GNRFA procedure is done in the physician's office or operating room, and typically starts with anesthetizing the skin, followed by a diagnostic nerve block with the use of a local anesthetic to better predict the success of ablation. If the patient reports minimally adequate pain relief of ≥50% for 24 hours, then motor and sensory stimulation is done for added safety prior to RFA. Ablation is performed using a 20 or 22-gauge needle with a 5, 10, or 15-mm active tip, a spinal needle, or a Venom needle (Stryker). Although RFA targets osseous landmarks, it may be difficult to isolate the exact anatomic location of 1 or more of the genicular nerves[19,20]. Previous research using cadaveric knee specimens has demonstrated a proposed anatomic roadmap and systematic approach for the placement of probes[20-22]. The ablation technique is performed adjacent to the periosteum. The procedure does not require general anesthesia and can be completed in 15 to 30 minutes under local sedation. Because the knee joint is innervated by a complex set of nerves (the obturator, the saphenous, the femoral, and the common peroneal and tibial nerves), patients may not experience complete pain relief with only GNRFA[23,24]. Peripheral nerve regrowth and regeneration may occur following ablation, leading to a recurrence of pain and the subsequent need for repeat neuronal ablation[25].

Long-Term Effectiveness of GNRFA Using Thermal, Cooled, and Pulsed Techniques

There is a dearth of large prospective randomized controlled trials (RCTs) on the therapeutic efficacy of GNRFA in the treatment of symptomatic knee OA. In addition, some of these studies used small sample sizes and a short follow-up duration, making it somewhat difficult to detect clinically relevant differences. The lack of large RCTs contributes to the difficulty of conducting a meta-analysis and calculating the appropriate effect size[26]. Some studies used a retrospective chart review without a power analysis to determine the number of charts needed for a particular study. Other studies used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and visual analog scale (VAS) scores to assess the dimensions of stiffness, pain, and function. While VAS and Likert responses are highly correlated for differentiating treatment modalities in patients with degenerative joint disease, the use of both of these scales together can lead to

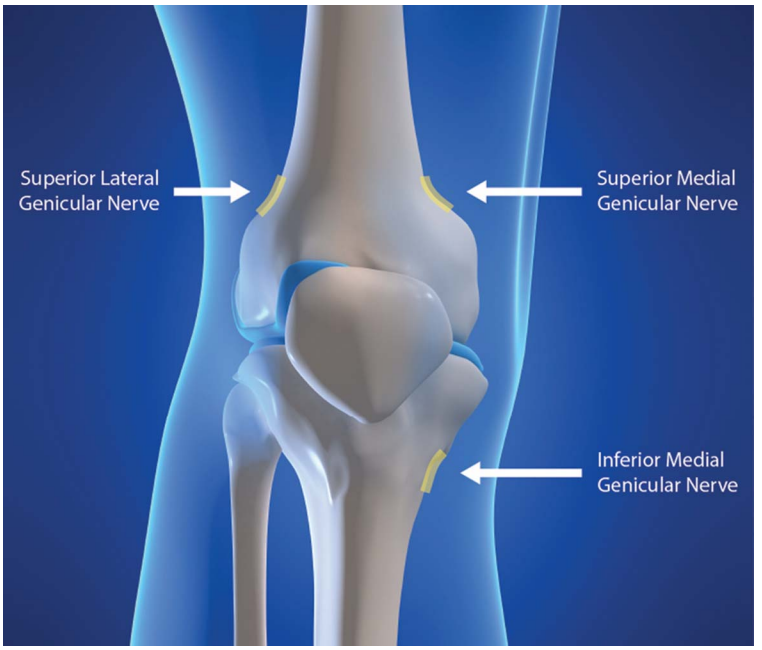

Fig. 1
Illustration of the genicular nerves targeted for ablation. (Reproduced with permission of Dr. Corey Hunter [http://ainsworthinstitute.com/genicular-neurotomy/]).

variability in the interpretation of study results[27-29]. The Kellgren and Lawrence system was used by most studies to classify the severity of arthritis. Patients with grade-3 or 4 OA, according to the Kellgren and Lawrence system, demonstrated clinical benefit from RFA[14,30,31]. However, research has shown that radiographic classification systems have only moderate, rather than very good, interobserver reliability for classifying tibiofemoral OA of the knee[32]. In addition, there is disagreement among researchers about the definition and grading of arthritic disease according to the original Kellgren and Lawrence classification system[33]. Nevertheless, the reviewed literature is intriguing and highlights the potential benefits of GNRFA.

One study reviewed 38 elderly patients with severe knee pain for 3 months who underwent GNRFA, which subsequently led to substantial pain reduction and functional improvement in 60% of elderly patients with knee arthritis[14]. In an RCT of 73 patients that compared the efficacy of intra-articular injections using a combination of bupivacaine, betamethasone, and morphine versus radiofrequency neurotomy, researchers observed no significant differences between the groups in terms of baseline VAS pain scores. However, the radiofrequency group experienced significant reductions in VAS pain scores in the first and third months ($p < 0.001$)[34]. A small double-blind, randomized study of 28 patients with persistent knee pain for >6 months following TKA compared radiofrequency neurolysis to local anesthetic and corticosteroid block of 3 genicular nerves, and concluded that both techniques improved disability, improved quality of life, decreased joint pain, and improved joint function during the first 3 to 6 months[35]. Limitations of the study included a small sample size, short duration, and the inclusion criteria of persistent knee pain for >6 months, which is not the currently accepted duration of postoperative pain following knee replacement. Kirdemir et al. applied RFA to 49 patients with a diagnosis of knee OA and a mean preprocedure VAS score of 8.9 ± 0.8; postprocedure, the VAS score was 4.73 ± 3.23, 3.89 ± 2.9, and 3.93 ± 2.95 at 1, 4, and 12 weeks, respectively[30]. The authors noted substantial functional improvement, pain reduction, and improved WOMAC scores following thermal ablation in a subset of elderly patients[30]. McCormick et al. enrolled 33 patients with knee OA in their study, and participants received cooled RFA; 35% of patients reported a ≥50% reduction in their pain scores[36], and 19% reported complete pain relief at their 6-month follow-up, demonstrating a modest success rate[36]. A prospective randomized multicenter study consisting of 151 patients comparing cooled RFA to intra-articular corticosteroid injections found that 74.1% of the cooled RFA patient group experienced improved function and at least a 50% reduction in knee pain at 6 months, which was maintained in over 65.4% of patients at 12 months[10,37]. In addition, at 6 months, 91.4% of the subjects in the cooled RFA group reported improvement in the global perceived effect when compared with patients in the injection group (23.9%)[10]. The authors concluded that GNRFA is superior to a single corticosteroid injection for managing osteoarthritic knee pain. A case series that reviewed the records of 9 patients with chronic

knee pain who underwent cooled RFA of the genicular nerves concluded that the majority of patients experienced a degree of pain relief and improved function at 1, 3, 6, and 12 months of follow-up[38].

Clinicians concerned about intimal injuries may want to consider the use of pulsed RFA. To my knowledge, the preliminary report by Kesikburun et al. is the only study to investigate the use of pulsed RFA of the genicular nerves to alleviate chronic knee pain[39]. According to that report, ultrasound-guided genicular nerve pulsed RFA was applied to 15 knees of 9 patients, and there was a significant ($p < 0.01$) reduction in VAS pain scores and improvement in the WOMAC scores[39]. However, because of the small sample size, the lack of a control group, and the short follow-up period, it is not possible to make meaningful conclusions regarding this study. Despite the lack of evidence, there appears to be a role for pulsed RFA. Unlike fluoroscopic or ultrasound-guided ablation, pulsed RFA does not cause any neuronal or tissue damage, and the temperature usually does not exceed 42°C[40]. Pulsed RFA uses a radiofrequency current that is delivered in short bursts (20 ms) and is followed by a silent phase, allowing the temperature to remain fairly consistent in order to avoid the neurodestructive range of >45°C[41].

Pulsed RFA is a painless modality that has been used to improve pain and function in a number of conditions, including mechanical back pain and knee OA. Akbas et al. studied the long-term efficacy of pulsed radiofrequency treatment on the saphenous nerve in 115 patients with chronic knee pain, and found that all patients showed improvement in their VAS and WOMAC scores after 10 days, 3 months, and 6 months ($p = 0.001$)[42]. Karaman et al. conducted a retrospective analysis and found substantial pain relief at the first and 6-month follow-ups after intra-articular pulsed RFA in 31 patients with knee OA[40]. The exact mechanism of how pulsed RFA reduces knee pain remains a mystery, but it has been postulated that the electromagnetic field, rather than the temperature, produces the overall analgesic effect[40,43]. To my knowledge, there are no long-term data on the effects of pulsed RFA on the genicular nerves for symptomatic knee OA. In addition, some payers consider ablation therapies such as pulsed RFA experimental, and therefore do not cover this treatment for certain conditions.

Risk Associated with GNRFA

Despite the vast array of complex vascular and neuronal networks of the knee and its supporting structures, to my knowledge, there is no reported case of iatrogenic vascular injury following GNRFA in the literature[44]. Consequently, the literature supports the assertion that GNRFA is a safe and minimally invasive therapy for patients with symptomatic knee OA and TKA pain syndrome. However, it is important to point out that conventional RFA may be associated with vascular injury[44]. In addition, cooled RFA, in rare cases, may be associated with third-degree skin burns at the site of the electrode. In 2014, Walega and Roussis reported the case of a full-thickness skin burn during a thoracic medial branch ablation using cooled RFA, which took nearly 5 months to heal[7]. There is also a risk of soft-tissue infection whenever the skin is breached; however, to my knowledge, no cases of infection have been reported. Lastly, heat lesioning may have unintended consequences, such as motor dysfunction, deafferentation pain, and possible neuritis[16]. This is not much of a concern with pulsed RFA.

Selection of Patients for GNRFA

There is no universally accepted criterion of candidacy for GNRFA. Patients who do not respond to nonoperative treatment and who respond well to the diagnostic genicular nerve block may be amenable to nerve ablation treatment. Clinicians should avoid recommending GNRFA treatment in patients who are pregnant, are morbidly obese, or have an acute injury, an unstable knee, abnormal patellofemoral tracking, uncontrolled diabetes mellitus, a bleeding disorder, an implantable defibrillator, a peripheral nerve stimulator, a pacemaker, or an active or latent knee infection.

Summary

Although there are limited studies on the efficacy and safety of RFA in patients with symptomatic knee OA, GNRFA appears to be a promising therapy for patients who had unsuccessful nonoperative management. GNRFA has been shown to consistently provide short-term (3 to 6 months), and sometimes longer, pain relief in patients with symptomatic knee OA or with pain syndrome following TKA. Thermal, cooled, and pulsed RFA techniques can be used to aid in genicular nerve neurotomy. Pulsed RFA appears to be the least risky technique of the 3, but may not have an advantage over cooled or conventional thermal ablation. Because of the paucity of noteworthy studies, it is unreasonable to recommend any specific RFA procedure modality for the treatment of knee OA. Nevertheless, GNRFA is gaining momentum in the medical community as an effective and safe alternative treatment for symptomatic knee OA in lieu of surgical intervention.

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