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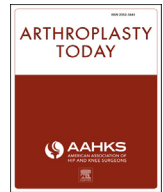
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Original Research

Is Cooled Radiofrequency Genicular Nerve Block and Ablation a Viable Option for the Treatment of Knee Osteoarthritis?

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ABSTRACT

Background: The purpose of this study was to determine demographic and psychosocial factors that influence the effectiveness of cooled radiofrequency genicular nerve ablation (C-RFA) and block in patients with chronic knee pain secondary to osteoarthritis (OA).

Methods: A retrospective review was completed including patients with knee OA who underwent genicular nerve ablation or block or both. Patient information collected included opioid use, psychological comorbidities, smoking history, body mass index, and medical comorbidities. Success was defined using the Osteoarthritis Research Society International criterion of greater than or equal to 50% reported pain relief from the procedure. Patients without a diagnosis of knee OA and patients with ipsilateral total knee arthroplasty were excluded. Patient factors were compared between (1) those that did or did not respond to the initial block and (2) those that did or did not respond to C-RFA.

Results: Of the 176 subjects that underwent genicular nerve block, 31.8% failed to respond to the procedure. Subjects that failed the initial block were significantly more likely to have psychological comorbidities, smoking history, and diabetes. Of the subjects that proceeded to genicular nerve ablation, 53.7% reported less than 50% pain relief, and 46.3% reported pain relief greater than or equal to 50% at the first follow-up visit. While the presence of psychological comorbidities, smoking, and diabetes were associated with first-stage block failures, these patient factors were not associated with second-stage ablation failures.

Conclusions: C-RFA may be an effective adjunct therapy as part of a multimodal pain regimen; however, individual patient characteristics must be considered.

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Introduction

Knee osteoarthritis (OA) has substantially increased in prevalence in developed nations since the postindustrial era; longer life expectancy, increased body mass index (BMI), and other independent variables have been implicated in this rise in prevalence [1]. Knee pain associated with OA has been shown to be an independent risk factor for early mortality, and, thus, reducing knee OA pain is a global health concern [2]. Generally, the treatment goals for knee OA include improving patient function and alleviating pain, initially with conservative therapy consisting of physical therapy, nonsteroidal anti-inflammatory medications, and intraarticular corticosteroid injection [3]. When conservative treatment fails to

meet these goals, surgical intervention with total knee arthroplasty (TKA) is an excellent option to improve patient function and relieve pain [3,4]. As estimated by Weinstein et al. [5], 52.2% of males and 50.6% of females who are diagnosed with symptomatic knee OA will undergo TKA during their lifetime.

Few options exist for patients who fail initial conservative treatment options and desire to postpone TKA or for those who are poor surgical candidates. Cooled radiofrequency genicular nerve ablation (C-RFA) has been introduced as a safe, minimally invasive alternative for these patients [6]. The procedure is performed using a thermal probe that is directed using fluoroscopy or ultrasound to well-described and validated bony landmarks in the paths of the genicular nerves [7]. A current is applied through the probe to induce a thermal injury to the targeted nerve, which, in turn, disrupts the neurosignaling of pain sensation from the knee capsule.

A patient initially undergoes a diagnostic genicular nerve block with local anesthetic. If the nerve block is successful in alleviating

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the patient's pain, cooled radiofrequency ablation is performed of the superior medial, superior lateral, and inferior medial genicular nerves. Ablation of the inferior lateral genicular nerves is frequently avoided because of their close proximity to the common peroneal nerve. Genicular nerve C-RFA has been shown to be effective in reducing chronic knee pain for up to 6 months [8–14]. This provides a potential long-term therapeutic option for patients with significant medical comorbidities and those who desire to delay or avoid TKA.

However, demographic factors that contribute to success or failure of genicular nerve C-RFA have not been fully elucidated. Predictors of success and failure have been studied in the use of radiofrequency ablation in other regions, namely the sacroiliac joint and lumbar and cervical facets. Increased age, higher baseline pain level, previous surgery, history of depression, and opioid use have been found to be associated with failure of the procedure [15]. The effect of psychosocial factors on pain perception in knee OA is well documented, but has not been studied in regard to genicular nerve ablation [16]. Understanding how these factors affect outcomes can assist the surgeon with making more targeted treatment decisions. The purpose of the present study was to determine the demographic and psychosocial factors that influence the effectiveness of genicular nerve block and C-RFA in patients with knee OA.

Material and methods

An institutional review board–approved retrospective chart review was completed using the Electronic Medical Record at our institution. Patients were initially identified by performing a search with corresponding Common Procedural Terminology codes (64,450, 64,640). Patients who had undergone genicular nerve block and C-RFA with a diagnosis of knee OA, defined by the American College of Rheumatology criteria [17], were included. Patients undergoing traditional radiofrequency nerve ablation, patients without a diagnosis of knee OA, patients undergoing ablation after TKA, and patients with insufficient charted data were excluded.

All patients underwent C-RFA or block between January 2015 and September 2017 at a single institution. C-RFA was performed by the interventional pain specialists at our institution. Local anesthesia consisted of 1% lidocaine at each ablation site. Three milliliters of 2% lidocaine without epinephrine was then injected at each site, and the cooled radiofrequency ablation was undertaken at 60°C for 2 minutes and 30 seconds at each site. After ablation, 1 mL of steroid solution containing 0.25% bupivacaine and 40 mg of Depo-Medrol was injected at each site.

Patient information collected included demographic information (age, sex, BMI), opioid medication use (defined as an active prescription for greater than 1 month before procedure), self-reported psychological comorbidities, smoking history, and medical comorbidities. Patient-reported percent pain relief immediately after the genicular nerve block was recorded using a Visual Analog Scale as percentage of pain relief (0%–100%) and was also recorded at the first follow-up after genicular nerve ablation (range 4 to 6 weeks). Success of the block or ablation was defined using Osteoarthritis Research Society International criteria of greater than 50% reported pain relief from the procedure [18].

Patient factors were compared between (1) those that did or did not respond to the initial block and (2) those that did or did not respond to C-RFA. Continuous variables were compared between responders and nonresponders using 2-tailed independent *t*-tests, and categorical variables were compared using Chi-square or Fisher exact as appropriate. An alpha level of $P < .05$ was considered statistically significant, and all analyses were performed using SPSS Statistics 24 (IBM, Armonk, NY). The prevalence of patients with >50% pain relief was also compared based on Kellgren-Lawrence Classification (K-L Classification) using chi-square and Fisher Exact tests as appropriate.

Table 1

Comparison of knee OA patients that did vs did not respond to genicular nerve block.

Patient variables	Responders	Nonresponders	P value
N, %	120, 68.2%	56, 31.8%	–
Age (N ± SD)	58 ± 12.3	55 ± 10.6	.603
BMI	38.7 ± 10.4	36.0 ± 9.0	.099
Tobacco use (N, %)	26, 31.0%	31, 69%	<.001
Sex (M, F)	53, 67	21, 35	.252
Mental health Dx (N, %)	36, 30%	30, 55%	.002
Diabetes mellitus (N, %)	28, 23%	41, 75%	<.001
Opioid use (ME ± SD)	21.1 ± 39.3	13.8 ± 37.3	.262

BMI, body mass index; F, female; M, male; ME, morphine equivalents; OA, osteoarthritis; SD, standard deviation.

Results

Genicular nerve block

One hundred seventy-six knees were identified that met inclusion criteria and underwent genicular nerve block (Table 1). Of those, 56 (31.8%) failed to experience greater than or equal to 50% pain relief on the initial block and did not proceed to undergo ablation. Subjects that failed the initial block were significantly more likely to have self-reported psychological comorbidities, including anxiety and depression ($P = .002$). Those who failed the block also had a greater proportion of patients with a smoking history ($P < .001$) and diabetes mellitus (DM) ($P < .001$) than those with successful blocks. There were no significant differences between the 2 groups in age, morphine milligram equivalent dosage, gender, or BMI.

Genicular nerve ablation

One hundred twenty knees with successful genicular nerve blocks underwent genicular nerve ablation. Follow-up data were unavailable for 25 subjects after ablation and were excluded from analysis (Fig. 1). Of the 95 knees with follow-up data 4 to 6 weeks after C-RFA ablation, 44 (46.3%) experienced greater than or equal

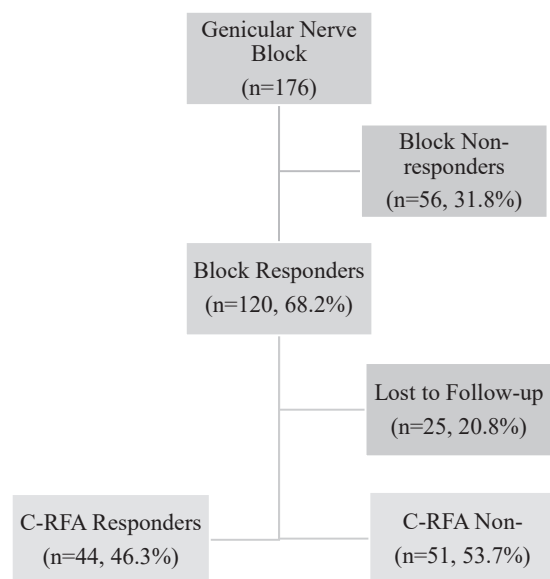


Figure 1. Patients undergoing cooled radiofrequency genicular nerve ablation (C-RFA) must first undergo a diagnostic genicular nerve block and experience at least 50% pain relief on a Visual Analog Scale. The figure outlines the response rate to block and C-RFA in our patient population.

to 50% pain relief, and 51 (53.7%) failed to experience greater than or equal to 50% pain relief. No significant differences were found in the demographic characteristics between those who failed and those who had successful ablation, including psychological comorbidities, smoking history, DM, gender, age, or opioid use (Table 2). The average percent pain improvement at the post-ablation follow-up was 36.7% (standard deviation, 36.2). Of all, 57.9% of subjects reported some reduction in pain, while 42.1% reported no reduction in pain. Repeat C-RFA was performed in 21 (18%) subjects. Follow-up data were available for 16 of the 21 repeat ablations, with 56% reporting greater than 50% pain relief. Of the patients reporting greater than 50% pain relief after repeat C-RFA, only 37.5% experienced greater than 50% pain relief after the first C-RFA. Significantly fewer patients with K-L grade 4 radiographic changes had >50% pain relief (11/38, 28.9%) when compared to both K-L grade 2 (13/21, 61.9%, $P = .03$) and K-L grade 3 (16/30, 53.3%, $P = .049$). There was no difference between K-L grade 2 and 3 ($P = .58$). When combining the K-L grade 2 and 3 patients, K-L grade 4 patients were significantly more likely to have pain relief <50% with genicular nerve ablation (odds ratio = 3.2, 95% confidence interval: 1.3 to 7.9, $P = .01$). No major adverse events were reported after the block or C-RFA procedures.

Discussion

Knee pain from OA is an increasing problem encountered by orthopedic surgeons. However, many patients are unable to find relief with conservative management or are poor candidates for TKA because of other medical comorbidities. Genicular nerve C-RFA offers a less invasive option that has been shown to be effective in treating OA knee pain for up to 6 months or longer [19]. However, demographic factors influencing the success of this procedure have not yet been fully elucidated. Knowledge of these factors is vital for the orthopaedist to appropriately select patients that may benefit from the procedure and to avoid delaying treatment of chronic knee pain in patients that are less likely to benefit from this procedure.

A large proportion (31.8%) of the patients undergoing diagnostic genicular nerve block failed to gain greater than 50% pain relief from the procedure. This appears to be consistent with previously reported literature; however, the true success rate of the block is yet to be established as most previous studies investigating genicular nerve C-RFA fail to report this number. Patients with self-reported psychological comorbidities, smoking history, and DM were significantly more likely to fail genicular nerve block. This suggests that these failures are less likely because of technical factors, but, rather, patient-specific peripheral and central pain processing.

Mounting evidence suggests that tobacco smoking plays a role in chronic pain processing. Jakobsson [20] demonstrated a greater

chronic pain intensity in smokers in a large population in Sweden. The exact mechanism of pain modulation in smokers is not fully established; however, Jakobsson suggested that it may be a combination of altered central pain processing and deranged local nociception due to microvascular constriction and tissue hypoxia. Shi et al. [21] noted several factors that contributed to the increased incidence of chronic pain in smokers. They note that chronic smoking leads to receptor desensitization and tolerance, and subsequent receptor upregulation, that may significantly alter the local processing within analgesic pathways. Moreover, chronic smoking causes downregulation of the stress response in the sympathetic system and hypothalamic-pituitary-adrenal axis, systems which generally decrease perception of pain, causing dysregulation of ventral pain processing. Shi et al. [21] additionally note that chronic smoking is associated with many psychosocial factors such as depression, low socioeconomic status, and chronic opioid use, which have been independently implicated in increased chronic pain. In addition to the physiologic effects of smoking, these factors play a complex role in the regulation of local and central pain processing.

The macroscopic and microscopic effects of hyperglycemia on peripheral and central nerve function are well established. Hyperglycemia leads to oxidative injury to peripheral nerves and small fibers causing dysregulation in local nociception [22]. It has been demonstrated that, on a microscopic level, hyperglycemia causes mitochondrial dysfunction, which plays a substantial role in peripheral neuropathies and local pain processing [23]. Thus, it is not surprising to find that patients with DM responded to the genicular nerve block with less success than patients without DM. Of note, we did not explore the individual profile of each patient's DM diagnosis, such as Hb-A1C or length of diagnosis; however, future studies should include these variables.

Less well known are the effects of mental health disorders on central pain processing. This is an active area of investigation, and studies have demonstrated a substantial link between mental health disorders and pain perception. Christensen et al. [24] demonstrated that a prior history of depression was determined to be a significant predictor of neurotomy failure in zygapophyseal joints. In addition, pain catastrophizing has been implicated as a link between increased chronic pain and mental health disorders [25–27]. Keefe et al. [25] demonstrated that higher catastrophizing scores in a cohort of patients with knee OA correlated to increased chronic pain behavior. Thus, this makes an argument for combined C-RFA and cognitive behavioral therapy for OA patients with psychological comorbidities, as their pain does not appear to be solely associated with local nociception, but, rather, deranged central pain processing. Future studies are needed to determine if mental health therapy does, in fact, have an impact on the outcome of genicular nerve block or C-RFA.

Our results demonstrate that patients with self-reported psychological comorbidities, smoking history, and DM were significantly more likely to fail genicular nerve block ($P = .002$, $<.001$, $<.001$), whereas these factors had no significant difference between those who failed or had success with genicular nerve C-RFA. We believe that this observation is due to selection bias in our ablation population. We submit that the reason our inability to demonstrate a significant influence of these factors on C-RFA failure is likely due to the fact that the block failure patients, with altered pain processing, were selectively eliminated from proceeding to C-RFA.

The utility of the genicular nerve block is still under investigation. The study by Reddy et al. [28] in 2016 attempted to create selection criteria for C-RFA. A threshold of 80% pain reduction from the block resulted in >90% pain reduction after ablation, improved self-reported functionality, and avoidance of surgery at 6-month follow-up. However, this study had a small population study of

Table 2

Comparison of knee OA patients that did vs did not respond to cooled radio frequency genicular nerve ablation.

Patient variables	Responders	Nonresponders	P value
N, %	44, 46.3%	53, 53.7%	—
Age (N ± SD)	58.9 ± 13.0	58.6 ± 13.8	.938
BMI	37.4 ± 10.5	40.1 ± 8.8	.179
Tobacco use (N, %)	8, 24.0%	12, 46.0%	.361
Sex (M, F)	20, 31	22, 22	.291
Mental health Dx (N, %)	16, 31.0%	11, 25.0%	.492
Diabetes mellitus (N, %)	11, 21.6%	8, 18.2%	.799
Opioid use (ME ± SD)	19.9 ± 37.0	24.6 ± 43.9	.589

BMI, body mass index; F, female; M, male; ME, morphine equivalents; OA, osteoarthritis; SD, standard deviation.

only 4 patients. Similarly, McCormick et al., 2017 [8], found >80% pain relief from the block was predictive of treatment success and reported a success rate of 35%. The present study used the 50% threshold as outlined by Osteoarthritis Research Society International and demonstrated a 46.3% success rate for ablation. Previous studies investigating the utility of higher cutoffs to define a successful block, mostly in cervical and lumbar RFA, have mostly demonstrated no improvement in outcomes [29]. Our results are in agreement with these previous studies in the spine. When applying 75 and 90% cutoff values to define success in the diagnostic block to our cohort, we find C-RFA success to be 42.9 and 44.9%, respectively.

We report a 46.3% C-RFA success rate. These results are less encouraging than those found in previous trials. Choi et al., 2011 [13], reported 59% of the RF group maintained 50% pain relief at 12 weeks. Seventy-four percent of the C-RFA group maintained QARS criteria at 6-month follow-up in the trial by Davis et al. in 2018 [9]. Despite our C-RFA success rate of 46.3%, we believe that our results, in combination with previously published literature, support genicular nerve C-RFA as a viable treatment option for some patients with knee OA.

An interesting finding of our study is that significantly fewer patients with K-L grade 4 radiographic changes had >50% pain relief when compared to both K-L grades 2 and 3. To our knowledge, no other study investigating the efficacy of C-RFA has stratified patients based on Kellgren-Lawrence Classification. This finding suggests that patients with more advanced radiographic OA may be less likely to benefit from C-RFA. However, further prospective randomized controlled studies are needed to further validate this finding.

This study was an analysis of effectiveness of genicular nerve block and C-RFA; we did not perform a cost analysis; however, with the current trend of cost-conscious medicine, one must take health-care expenditure into consideration. The process of this treatment requires multiple visits and, potentially, multiple procedures, which may increase cost. A recent study looking at the health-care expenditure before TKA reported that over half of the noninpatient costs associated with treatment of knee OA occur in the year before TKA and concluded that a significant reduction in treatment cost could be achieved if only treatments supported by Clinical Practice Guidelines were used [30]. Future studies are needed to determine the cost-effectiveness of C-RFA.

Limitations

The limitations of this study must be addressed. First, the lack of observed differences in patient factors between responders and nonresponders could potentially have been due to a lack of sufficient power. For this observational study, an a priori power analysis was not performed as we could not estimate the prevalence of those that would respond to the block or ablation, and there were no available data in the literature to support such an analysis. Using individual knees as subjects allows patients with bilateral knee pain and procedures to be doubly included, possibly affecting outcomes. However, we found that the distribution of C-RFA success vs failure in bilateral knee patients is comparable with the remainder of the cohort with 50% success and 50% failures. As a retrospective study, this study is subject to the lack of randomization and blinding inherent of retrospective studies. In addition, only one outcome measure, Visual Analog Scale, was used in this study. Analyzing more aspects of patient outcomes including functionality and quality of life would provide a more detailed view of treatment outcomes. Patient follow-up was limited to 6 weeks, as per the protocol of the pain management specialists at our institution. Furthermore, baseline pain scores were unavailable for our patient population. Differences in baseline pain scores may variably affect patient perspectives of pain reduction. Finally, our study may be

affected by selection bias secondary to the nature of our patient population. Many of the patients in this study have multiple medical comorbidities, including chronic pain, and were specifically selected to undergo C-RFA as a means to avoid the risks of arthroplasty and anesthesia. Thus, the results of this study may not be generalizable to healthier patients with primary knee OA.

Conclusions

Genicular nerve C-RFA is a potential therapeutic option for patients suffering chronic knee OA pain not responsive to conservative treatment or for patients unable to undergo TKA because of overwhelming medical comorbidities. However, patients with self-reported psychological comorbidities, DM, and tobacco smoking are less likely to benefit. The genicular nerve block may have utility in discerning patients who will not respond to ablation because of changes in pain processing. In conclusion, C-RFA is an effective adjunct therapy as part of a multimodal pain regimen for many patients with OA, but future studies are needed to fully elucidate why some patients fail to respond.

Conflict of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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