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Long-term clinical outcomes of genicular nerve radiofrequency ablation for chronic knee pain using a three-tined electrode for expanded nerve capture

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ABSTRACT

Objective: Genicular nerve radiofrequency ablation (GNRFA) is an effective treatment option for chronic knee pain in native knee osteoarthritis and total knee arthroplasty (TKA) patients. Recent dissections have revealed significant variability in typical genicular nerve targets and other sensory nerves not included in previous studies. Early, short-term results suggest that more complete sensory denervation with GNRFA may result in more significant pain reduction; however, no long-term clinical outcome exists. We aim to present long-term clinical outcomes after an expanded GNRFA technique with a three-tined radiofrequency cannula.

Methods: Eleven consecutive patients with ≥6 months of knee pain underwent an expanded GNRFA protocol targeting the superomedial (SMGN), superolateral (SLGN), inferomedial genicular nerves (IMGN), in addition to the nerves to vastus medialis (NVM), lateralis (NVL), and intermedius (NVI). Long-term pain and impression of change outcomes were collected in a cross-sectional fashion.

Results: At ≥18 months (mean 24 months) post-GNRFA, 91% (95% CI = 59, 100%), 73% (95% CI = 46, 99%), and 9% (95% CI = 0, 26%) of patients reported ≥50%, ≥80%, and 100% pain relief, respectively. Additionally, 27% (95% CI = 1, 54%) and 64% (95% CI = 35, 92%) of individuals reported a PGIC score of 6 ("much improved") and 7 ("very much improved"), respectively. The proportion of individuals who reported the MCID for the PGIC (score of ≥6) was 91% (95% CI = 59, 100%). There were no adverse events reported amongst the patients in this cohort. No patients progressed to surgery.

Conclusion: This single-arm cohort suggests that an expanded GNRFA protocol targeting SMGN, SLGN, IMGN, NVM, NVL, and NVI nerves with a three-tined electrode, resulted in significant long-term (≥18 months) improvements in pain and patient-perceived global improvement. Large, head-to-head trials are needed to establish whether this GNRFA protocol is superior to those used in previous clinical studies and those currently used more commonly in practice.

1. Introduction

Chronic knee pain from osteoarthritis is a prevalent problem afflicting millions of people throughout the world [1]. Despite both non-surgical and surgical treatments options, many individuals continue to suffer from daily persistent knee pain and impaired function. Unfortunately, many individuals fail conservative treatment options and cannot undergo a total knee arthroplasty (TKA), due to patient preference or being deemed ineligible by an orthopedic surgeon because of age or medical comorbidities, and up to 20% of post-TKA patients have continued pain [2,3]. Multiple prospective trials and systematic reviews have now demonstrated the effectiveness of genicular nerve radiofrequency

Abbreviations: Genicular nerve radiofrequency ablation, (GNRFA); superomedial genicular nerve, (SMGN); superolateral genicular nerve, (SLGN); inferomedial genicular nerve, (IMGN); nerve to vastus medialis, (NVM); nerve to vastus lateralis, (NVL); nerve to vastus intermedius, (NVI); recurrent fibular nerve, (RFN); patient global impression of change, (PGIC); Kellgren-Lawrence osteoarthritis score grade, (KL).

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ablation (GNRFA) for reducing chronic knee pain in patients with native knee osteoarthritis and after a total knee arthroplasty (TKA) [4–9]. GNRFA is a minimally invasive percutaneous procedure that utilizes thermal energy to coagulate sensory nerves that innervate the anterior knee capsule, thereby interrupting nociception. Based on early cadaveric studies, GNRFA has traditionally targeted the superior medial (SMGN), superior lateral (SLGN), and inferior medial (IMGN) genicular nerves. However, more meticulous dissections have revealed significant variability in these targets and additional sensory nerves which innervate the anterior capsule [10,11]. Early data indicates that more complete sensory denervation results in greater reductions in pain after GNRFA [12,13]. As such, we have previously proposed protocols to account for the variability of the SMGN, SLGN, and IMGN, as well as additionally targeting the recurrent fibular nerve (RFN) and nerves to vastus medialis (NVM), vastus lateralis (NVL), and vastus intermedius (NVI) [14–16].

We previously reported outcomes of 11 consecutively treated patients using an expanded denervation technique with an expandable three-tined radiofrequency cannula at the SMGN, SLGN, IMGN, NVM, NVL, and NVI [13]. At six months, 91% of patients reported continued >50% improvement of their baseline knee pain. In this report, we present the long-term clinical outcomes (18–29 months) from this cohort.

2. Methods

Ethical Institutional Review Board approval for the study was provided by the Nova Scotia Health Authority, and the study was conducted according to the Declaration of Helsinki. The time for enrollment in this study was from February 27, 2019, until January 15, 2020.11 consecutive patients, consisting of retired veterans of the Canadian Army, were treated with GNRFA as previously described in detail [13]. Prognostic blocks were not performed. To participate, each patient had to meet the following inclusion criteria: (1) Age >18 years; (2) Kellgren-Lawrence osteoarthritis score grade (KL) ≥2 or previous TKA; (3) Knee pain score >3 on the numeric rating scale (NRS); (4) Knee pain present >6 months. There were no specific exclusion criteria. Patients with previous TKAs were included because of continued pain, lack of treatment options, and the possibility that the novel protocol resulted in improved outcomes compared to previous studies [17,18].

Radiofrequency Iesioning

We previously reported a step-by-step description of the novel protocol used for GNRFA [13]. Briefly after appropriate positioning, sterile preparation, and subcutaneous anesthesia, a 100-mm-length 18 gauge three-tined RFA cannula with 5-mm active tips (Trident 18 gcanula, Diros Technology, Markham, ON, Canada) was advanced under fluoroscopic guidance to the known locations of the SMGN, SLGN, IMGN, NVM, NVL, and NVI. Radiofrequency lesioning was performed for 120 second at 80° celsius. A computer simulation indicates that a 2-min lesion at 75 °C would result in thermal coagulation in a lesion geometry area measuring 7.6 mm wide by 7.6 mm length in the axial plane (at the periosteal surface) and 9.1 mm in height in the sagittal plane (soft tissue lesion) [19]. Thus, the lesions produced using an 80° celsius RFA generator setting would be expected to produce tissues destruction zones of slightly larger volume.

Data collection

Patient demographic and clinical data were extracted from patient medical records (age, sex, previous TKA, pain duration, and a baseline average pain NRS). Each patient was called to assess their symptoms one, six, and ≥18 months after the GNRFA. We previously reported the one- and six-month outcomes [13]. The long-term (≥18 months) pain outcomes were collected in a cross-sectional manner meaning that each patient was contacted by telephone on August 1, 2021, regardless of the date of the GNRFA. Ten of the 11 participants reported (1) the percent pain relief post-procedure compared to pre-procedure and (2) the patient global impression of change (PGIC) on a 1–7 scale (with 1 being "no change" or "worsening condition" and 7 being "much improved") to assess long-term clinical outcomes. PGIC has not been specifically validated by phone; however, given that PGIC is a questionnaire, it was deemed appropriate by the authors to administer it by phone. Each patient was asked about the use of any co-interventions after the procedure, including physical therapy, massage, or surgery. Each was also asked about whether they were considering a TKA. One patient was not contacted at long-term follow-up because this individual experienced no improvement at one and six months; however, the data was included in the analysis as a treatment failure (worst case analysis). All outcome data was collected by one investigator (EK).

Outcomes

The primary outcome of interest was the proportion of patients reporting ≥50% knee pain NRS reduction ≥18 months post-procedure. Secondary outcomes included the proportion of patients who experienced ≥80% and 100% knee pain reduction and a minimum clinically important difference (MCID) for the PGIC of ≥6 at ≥18 months post-procedure [20].

Statistical analysis

Descriptive statistics were calculated including medians and interquartile ranges for continuous data, as well as proportions and 95% confidence intervals (CIs) for categorical data. Descriptive statistics were calculated using Microsoft Excel, version 16.33.

3. Results

Eleven consecutive patients with a median age (IQR) of 55 (6) years underwent GNRFA between January and August of 2019. Patient demographics are shown in Table 1. The median (IQR) duration of follow-up was 24.5 (9). The median baseline NRS pain score for this cohort (IQR) was 7 (1.0).

Pain reduction at ≥18 months after GNRFA is shown in Table 2. At ≥18 months postprocedure, 91% (95% CI = 59, 100%) of patients reported ≥50% knee pain relief, 73% (95% CI = 46, 99%) reported ≥80% pain relief, and 9% (95% CI = 0, 26%) reported 100% pain relief.

Patient Global Impression of Change scores at ≥18 months after GNRFA are shown in Table 3. At ≥18 months, 27% (95% CI = 1, 54%) and 64% (95% CI = 35, 92%) of individuals reported a PGIC score of 6 ("much improved") and 7 ("very much improved"), respectively. The proportion of individuals who reported the MCID for the PGIC (score of ≥6) was 91% (95% CI = 59, 100%). 91% (10/11) of the participants had both a PGIC of 6 or 7 and ≥ 50% pain relief at ≥18 months after GNRFA.

Both patients who had prior TKAs reported ≥50% knee pain relief and a PGIC score ≥6 at ≥18 month follow up.

At the time of the phone calls, one patient was considering revision surgery on the treated knee. One patient was waiting for surgery on the treated knee planned before the GNRFA but was delayed by the COVID-19 pandemic. This patient reported 60% pain relief yet endorsed continued knee instability, which began occurring prior to the procedure, with one fall occurrence 9 months following the procedure, and thus,

Table 1
Patient Demographics [13].

No.	11
Median patient age (IQR), y	55 (6)
Male, No.	10
Female, No.	1
Previous TKA	2
Duration of pain, median (IQR), y	18 (10)

IQR = interquartile range; TKA = total knee arthroplasty.

Table 2
Proportion of Patients Reporting ≥50% NRS Reduction at ≥18 months.

Duration	Proportion of Patients Reporting ≥50% NRS Reduction, % (n/N)	95% CI, %	Proportion of Patients Reporting ≥80% NRS Reduction, % (n/N)	95% CI, %	Proportion of Patients Reporting 100% NRS Reduction, % (n/N)	95% CI, %
≥18 mo	91 (10/11*)	74, 100	73 (8/11*)	46, 99	9 (1/11*)	0, 26

GNRFA = Genicular nerve radiofrequency ablation; NRS = Numerical rating scale; 95% CI = 95% confidence interval.
*1 patient was not contacted as a result of treatment failure.

Table 3
Patient Global Impression of Change at ≥18 months.

Duration	Proportion of Patients Reporting 6 on PGIC, % (n/N)	95% CI, %	Proportion of Patients Reporting 7 on PGIC, % (n/N)	95% CI, %	Proportion of Patients Reporting MCID (PGIC ≥6), % (n/N)	95% CI, %
≥18 mo	27 (3/11*)	1, 54	64 (7/11*)	39, 91	91 (10/11*)	59, 100

PGIC = Patient Global Impression of Change; MCID = Minimum Clinically Important Difference.
*1 patient was not contacted as a result of treatment failure.
PGIC 6 = much improved.
PGIC 7 = very much improved.

remained interested in surgery.

There were no co-interventions used during follow-up that could have contributed to or been responsible for any improvement. None of the patients had any physical therapy after the GNRFA treatment.

There were no adverse events reported amongst the patients in this cohort.

4. Discussion

In this long-term single-arm cohort study, we observed reductions in knee pain and patient-perceived global improvement after a comprehensive GNRFA procedure using a multi-tined canula at ≥18 months. The responder rate with a definition of "treatment success" of ≥50% knee pain NRS reduction in this study is higher than many studies of GNRFA which have targeted just the SMGN, SLGN, and IMGN, and may be attributable to more comprehensive denervation. Alternatively, the favorable findings in this series may overestimate the true treatment effect given the small size of the cohort. Notably, the lower bound of the 95% CI for the primary outcome is 59% (proportion of individuals who reported ≥50% knee pain NRS reduction). Larger studies will be needed to provide more confidence in the accuracy of the responder rate observed in the present study.

Genicular nerve RFA has most commonly been studied with regard to targeting the SMGN, SLGN, and IMGN, though two prospective studies have additionally targeted the NVI [21,22]. Chen et al. have reported favorable practice audit data including GNRFA when targeting additional nerves [12]. The present study utilized a six-nerve protocol, targeting the SMGN, SLGN, IMGN, as well as the NVM, NVL, and NVI. The three-tined, expandable radiofrequency cannula used in this study allowed for a perpendicular approach and creation of a relatively large lesion and may have resulted in increased neural capture. When examining the lesion geometry created by differing RFA cannulae, Trident utilizes a pyramidal shape which creates more of a lesion at the footprint of the tynes; whereas, cooled GNRFA, used most commonly in the published randomized-controlled trials, creates a larger volume spherical lesion. This can also be analyzed in regard to monopolar vs. bipolar RF current flow. Monopolar RF current flows between a probe electrode and a ground pad, creating an egg-shaped lesion. Bipolar RF current flows between two probe electrodes without the presence of a ground pad and with large gauge cannulae and 10 mm active tips creates the largest rounded brick-shaped lesion of all, but has not been studied much in the context of GNRFA to date [23].

Another notable finding was the durability of symptom improvement after GNRFA. While the minimum follow-up was 18 months after GNRFA, the median (IQR) duration of follow-up was 24.5 (9). To our knowledge, only one other study has reported outcomes beyond 18 months after GNRFA [24]. In that study of cooled GNRFA, 12 patients experienced ≥50% pain reduction at 18 months and 11 ≥ 50% pain reduction at 24 months with 24% of patients lost to follow-up.

Limitations

There are several limitations in the current study, including non-validated functional outcome; no prospective comparison group; and a small sample size.

The study design is a limitation of the current study. In general, the causal relationship or efficacy of an intervention (e.g., GNRFA technique) and a multiple validated outcome(s) (e.g. pain) is established when variables are tested in a specific population that is free of bias, confounders, or chance. The most effective way to establish a causal relationship or interventional efficacy is in a large, blinded, randomized controlled trial or a large, well-controlled cohort study. The present study is a consecutive small single-arm, homogenous, cohort study without a comparison group; therefore, the positive results of the novel technique should be investigated in large head-to-head trials. In addition, it should be noted that all patients were veterans and 10/11 were male, which is not representative of the general population.

Additionally, we did not include a validated functional outcome measurement specific to the knee like the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) or the Oxford Knee Score (OKS).

5. Conclusion

This novel GNRFA approach of targeting six genicular nerves utilizing a three-tined electrode resulted in significant long-term (≥18 months [mean 24 months]) improvements in pain and patient perceived global improvement. There were no adverse events. Although small, this cohort study contributes to the expanding literature on GNRFA with an important contribution to our understanding of durability and the potential effect of more comprehensive ablation. Large, head-to-head trials are needed to establish whether this GNRFA protocol is superior those used in previous clinical studies as well as those currently used more commonly in practice.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Zachary L. McCormick, MD, serves on the Board of Directors of the Spine Intervention Society.

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