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Does genicular nerve radiofrequency ablation continue to reduce knee pain in adult patients with chronic knee osteoarthritis at six months after treatment?

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ABSTRACT

OBJECTIVE: The objective of this systematic EBM review is to determine whether or not "Does genicular nerve radiofrequency ablation continue to reduce knee pain in adult patients with chronic knee osteoarthritis at six months after treatment?"

STUDY DESIGN: A review of three randomized controlled trials (RCTs) published between 2018 and 2021.

DATA SOURCES: All three RCTs were published in peer-reviewed journals and researched using PubMed. Studies were selected based on relevance to the clinical question.

OUTCOMES: All three RCTs measured knee pain as the primary outcome via the 10-point VAS pain scale or the 11-point NRS pain scale. Chen et al. and Davis et al. studies dichotomized data by further defining their outcomes as ≥50% pain reduction from baseline.

RESULTS: Elawamy et al. report difference of medians from baseline of -1 for both GNRFA and PRP on the VAS pain scale, with significant difference ($p = 0.01$) between the groups favoring GNRFA. Chen et al. data yield mean change from baseline of -4.2 and -2.0 for GNRFA and HA groups, respectively, on NRS pain scale. Chen et al. also report proportions with ≥50% pain reduction from baseline of 0.71 and 0.29 for GNRFA and HA, respectively, yielding NNT = 3. Davis et al. report mean change from baseline of -4.9±2.4 and -1.3±2.2 for GNRFA and IAS groups, respectively, on NRS pain scale ($p < 0.0001$). Davis et al. also report proportions with ≥50% pain reduction from baseline of 0.74 and 0.16, yielding NNT = 2.

CONCLUSIONS: The results are inconclusive. The results of Chen et al. and Davis et al. show that GNRFA greatly reduces knee pain and offers superior pain reduction compared to HA and IAS injections at six months after treatment, but conflict of interest cannot be ruled out. The Elawamy et al. study similarly favors GNRFA compared to PRP, but data interpretation is limited. Future research with larger sample size and consistent data reporting may lend clearer insight into GNRFA efficacy for OA-related knee pain.

KEYWORDS: genicular nerve radiofrequency ablation, knee pain, knee osteoarthritis

INTRODUCTION:

Osteoarthritis (OA) is a chronic progressive joint disease that develops from long-term mechanical stress on the joints. OA is the most common joint disease,[1] and it most commonly affects the knee, with symptomatic knee OA afflicting an estimated 14 million in the US.[1] Along with increasing life expectancy and BMI, the incidence of knee OA is also increasing. It has the third highest incidence rate of all disabling diseases in the US, just behind diabetes and dementia,[2] and it ranks as the second most common reason for visit in primary care settings, behind skin disorders.[3] OA requires life-long pain management, and lifetime costs related to knee OA average $140,300 per person.[4] In addition to direct medical costs, indirect costs such as missed work days from 2008-2014 amounted to $6,783 of economic loss per person.[4] OA-related pain also interferes with many other aspects of quality of life, such as sleep, mood, functional capacity, and ability to participate in social activities.

First-line options for painful knee OA typically include over-the-counter oral or topical anti-inflammatory agents (acetaminophen, NSAIDs), physical therapy, and weight management. Second-line options include duloxetine, tricyclic antidepressants, opioid pain medications, transcutaneous electrical nerve stimulation (TENS), intra-articular steroid (IAS) injection, lubrication injection such as hyaluronic acid (HA), platelet-rich plasma (PRP) injection, and total knee replacement (TKR). Although oral analgesics must be taken daily for chronic OA-related pain, the long-term efficacy of these agents for OA-related pain remains uncertain in the literature.[5] It is known, however, that oral analgesics commonly used for chronic OA-related pain, such as NSAIDs and opioids, carry pill burden as well as long-term risks ranging from gastritis to opioid use disorders and death. According to the CDC, opioids have not demonstrated long-term efficacy for chronic conditions such as arthritis.[6] However, 40% of patients with knee

OA in the US are prescribed opioid medications,[7] and 43% of those who use opioids for 30 days will continue to use them for at least one year.[8]

Genicular nerve radiofrequency ablation (GNRFA) is an outpatient procedure that involves targeted heat deactivation of the three genicular nerves responsible for sensing osteoarthritic knee pain.[9] GNRFA offers pain relief for a longer period of time compared to oral analgesics, which must be taken daily and contribute to pill burden and health risks. In contrast to conventional GNRFA, newer pulsed and cooled techniques maintain tissue temperatures below 42°C, thereby deactivating genicular nerve pain signaling without destroying nerve tissue. GNRFA provides sustained pain relief until the genicular nerves restore function, at which point GNRFA can be safely repeated. Conversely, intra-articular injection therapies are repeated with caution as not to further damage intra-articular structures and tendons. Although earlier studies had estimated a 3-month duration of effect, newer studies have suggested pain relief may last up to 6 to 12 months.[10] This paper evaluates three randomized controlled trials (RCTs), which each compare the reduction in OA-related knee pain at six months after treatment with GNRFA versus another outpatient procedure for OA-related knee pain.

OBJECTIVE:

The objective of this systematic EBM review is to determine whether or not genicular nerve radiofrequency ablation continues to reduce knee pain in adult patients with chronic knee osteoarthritis at six months after treatment.

METHODS:

Studies were selected by the author of this paper based on credibility, relevance to the clinical question, and inclusion and exclusion criteria. All three articles were published in peer-reviewed journals in the years 2018, 2020, and 2021 and found using the MeSH terms

"Osteoarthritis, Knee" AND "Radiofrequency Ablation" on PubMed. Inclusion criteria for article selection were publication date 2016-present, English language, RCTs, and adult patients with chronic OA-related knee pain refractory to conservative therapies. Exclusion criteria were publication date prior to 2016, patients under 18 years of age, and secondary research studies. Each study compared reduction in knee pain at six months after treatment with GNRFA versus another outpatient procedure for OA-related knee pain. In the selected studies, comparison groups were PRP injection, HA injection, and IAS injection of the knee joint. Reported statistics include difference of medians from baseline, mean change from baseline, NNT, and p-values.

OUTCOMES MEASURED:

All three studies in this review evaluated reduction in knee pain as the primary outcome, measured via the 11-point Numeric Rating Scale (NRS) or the 10-point Visual Analog Scale (VAS). Given that chronic pain directly influences functional capacity and quality of life, self-reported rating of knee pain by patients is patient-oriented evidence that matters (POEM).

- Elawamy et al.[11]: "...pain relief of the involved joint as evaluated by the visual analog scale (VAS)".
- Chen et al.[12]: "...'response' defined as >50% reduction in pain on the NRS from baseline".
- Davis et al.[13]: "...primary efficacy endpoint was the proportion of subjects whose knee pain was reduced by 50% or greater from baseline at 6 months after treatment. The 11-point NRS captured the amount of index knee pain at all study time points".

RESULTS:

Each of the three studies in this review compare the efficacy of GNRFA to another outpatient procedure in providing sustained reduction of OA-related knee pain at six months

Table 1. Demographics & Characteristics of Included Studies

Study	Type	#pt's	Age (avg)	Inclusion Criteria	Exclusion Criteria	W/D	Intervention
Elawamy (2021)[11]	RCT	200	45.12	Chronic KOA pain > 3months refractory to conservative management, radiologic evidence of Grade III-IV according to Kellgren-Lawrence Grading Scale	Sciatic pain, any connective tissue disorder affecting the knee, recent intraarticular injection within past 3 months, any prior knee surgery, current use of anticoagulants	0	Pulsed GNRFA vs PRP
Chen (2020)[12]	RCT	158	63	Chronic knee pain > 6months interfering with ADLs and > 3months despite conservative management, NRS > 6 in index knee, radiologic evidence of Grade II-IV according to Kellgren-Lawrence Grading Scale, age > 21, positive response to singular genicular nerve block in index knee.	Serious neurological or psychiatric disorders	19	Cooled GNRFA vs HA
Davis (2018)[13]	RCT	151	64	Chronic knee pain > 6 months despite conservative management, NRS > 6 in index knee, radiologic evidence of Grade II-IV according to Kellgren-Lawrence Grading Scale, Oxford Knee Score < 35, positive response to singular genicular nerve block in index knee.	BMI > 40, prior TKR, prior GNFRA, any systemic inflammatory condition (RA, DM, cancer, etc), any coagulopathy	23	Cooled GNRFA vs IAS

after treatment. Elawamy et al.[11] conducted a single-blind RCT comparing GNRFA to PRP. Prior to treatment, baseline VAS pain scores were collected and reported as median values 6±2 and 6±3 for GNRFA and PRP groups, respectively, which were statistically similar with $p > 0.05$. Six months after treatment, VAS pain scores were reported as median values 5±4 and 5±2 for GNRFA and PRP groups, respectively. The authors report a statistically significant reduction of OA-related knee pain in each group after six months compared to baseline, with a difference of medians from baseline of -1 on the VAS pain scale in each group and $p < 0.05$. Furthermore, the authors report a statistically significant difference ($p = 0.01$) between the groups' median VAS scores at six months, demonstrating superior efficacy of GNRFA compared to PRP. Results are summarized in Table 2 below.

Table 2. GNRFA versus PRP; Knee Pain on VAS Scale[11]

	Baseline VAS (median±SD)	6-month VAS (median±SD)	Change from Baseline (calculated)	p-value (compared to baseline)
GNRFA group	6±2	5±4	-1	$p < 0.05$
PRP group	6±3	5±2	-1	$p < 0.05$
p-values of GNRFA vs PRP	$p > 0.05$	$p = 0.01$		

Chen et al.[12] conducted an RCT comparing GNRFA to HA. Prior to treatment, baseline NRS scores in the index knee were collected and reported as mean values 6.9 and 7.0 for GNRFA and HA groups, respectively, which were statistically similar with $p > 0.05$. Six months after treatment, NRS scores in the index knee were reported as mean values 2.7 and 5.0 for GNRFA and HA groups, respectively. The authors report a statistically significant reduction of OA-related knee pain on the NRS pain scale in each group after six months compared to baseline ($p < 0.05$), with a mean change from baseline of -4.2 and -2.0 for GNRFA and HA groups,

respectively. Furthermore, the authors report a statistically significant difference between the mean NRS pain scores of the groups at six months, demonstrating superior efficacy of GNRFA compared to HA with $p < 0.05$. The authors defined treatment response as "≥50% reduction in pain on the NRS from baseline" and recorded the proportion of patients still exhibiting treatment response at each time interval. Six months after treatment, 71% and 29% were exhibiting treatment response in the GNRFA and HA groups, respectively. Using this data, NNT = 3 was calculated. Results are summarized in Table 3 below.

Table 3. GNRFA vs HA; Knee Pain on NRS Scale[12]

	Baseline NRS (mean)	6-month NRS (mean)	Mean change from baseline (calculated)	Proportion with ≥50% pain reduction	NNT (calculated†): GNRFA vs HA
GNRFA group	6.9	2.7*	-4.2	0.71	3
HA group	7.0	5.0*	-2.0	0.29	
p-values of GNRFA vs HA	$p > 0.05$	$p < 0.05$			

*p-values < 0.05 at six months compared to baseline for each group
†NNT calculated using proportions with ≥50% pain reduction after six months

Davis et al.[13] conducted an RCT comparing GNRFA to IAS. Prior to treatment, baseline NRS scores in the index knee were collected and reported as mean values 7.3±1.2 and 7.2±1.0 for GNRFA and IAS groups, respectively, which were statistically similar with $p = 0.37$. Six months after treatment, NRS scores in the index knee were reported as mean values 2.5±2.3 and 5.9±2.2 for GNRFA and IAS groups, respectively. The authors report a statistically significant reduction of OA-related knee pain on the NRS pain scale in each group after six months compared to baseline ($p < 0.0001$), with a mean change from baseline of -4.9±2.4 and -1.3±2.2 for GNRFA and IAS groups, respectively. Furthermore, the authors report a statistically significant difference between the mean NRS pain scores of the groups at six months,

demonstrating superior efficacy of GNRFA compared to IAS with $p < 0.0001$. The authors defined treatment response as "≥50% NRS score reduction" from baseline and recorded the proportion of patients still exhibiting treatment response at each time interval. Six months after treatment, 74% and 16% were exhibiting treatment response in the GNRFA and IAS groups, respectively. Using this data, NNT = 2 was calculated. Results are summarized in Table 4 below.

Table 4. GNRFA vs IAS; Knee Pain on NRS Scale[13]

	Baseline NRS (mean±SD)	6-month NRS (mean±SD)	Mean change from baseline ±SD	Proportion with ≥50% pain reduction	NNT (calculated†): GNRFA vs IAS
GNRFA group	7.3±1.2	2.5±2.3*	-4.9±2.4	0.74	2
IAS group	7.2±1.0	5.9±2.2*	-1.3±2.2	0.16	
p-values of GNRFA vs IAS	p = 0.37	p < 0.0001	p < 0.0001	p < 0.0001	

*p-values < 0.0001 at six months compared to baseline for each group
†NNT calculated using proportions with ≥50% pain reduction after six months

DISCUSSION:

This review evaluates three RCTs that assess adult patients with chronic OA-related knee pain and reassess their pain at six months after receiving GNRFA versus PRP, HA, or IAS. All three studies conclude that GNRFA continues to reduce knee pain in adult patients with chronic knee OA and also offers superior pain reduction to their comparison groups at six months after treatment. Compared to the Elawamy et al. study, the Chen et al. and Davis et al. studies show more dramatic evidence favoring GNRFA. These studies report large mean changes from baseline and large statistically-significant differences from their comparison groups at six months after GNRFA, demonstrating superior pain reduction by GNRFA at six months compared to HA and IAS. It is important to note, however, that these study teams received funding from medical technology companies that produce GNRFA equipment.[12,13] Furthermore,

HA injections have been associated with little benefit in other studies,[14] and IAS injections are expected to last up to three months[15]. Thus, using these treatments as comparison may favorably skew the perceived efficacy of GNRFA at six months. It is unclear, however, how the pain reduction from baseline at six months after receiving GNRFA was apparently greater for these studies than for Elawamy et al. Current evidence supports that the difference in GNRFA technique, pulsed versus cooled, would not significantly affect efficacy.[16]

The Elawamy et al.[11] study, conversely, did not receive external funding and denies conflict of interest. Elawamy et al. report a relatively modest change from baseline for both GNRFA and PRP groups at six months. Notably, at three months after treatment, the change from baseline for both groups was -3 points on the VAS pain scale using median values.[11] Although the authors report a statistically significant difference between GNRFA and PRP at six months, favoring GNRFA, the median VAS scores were equivalent at 5 and mean values were not reported. Unfortunately, the primary outcome defined in this study was not dichotomous, and the authors did not report mean values, which limits data interpretation compared to the other studies in this review. Current research on the efficacy of PRP injections for OA-related knee pain is incomplete, but existing evidence seems to favor PRP over other intra-articular injection treatments.[17] PRP-related pain reduction is expected to last six to nine months,[17] similarly to the expected duration of GNRFA pain reduction, and thus may offer better comparison to GNRFA at six months after treatment than would HA and IAS.

In all three studies, patient allocation was randomized and each treatment group was statistically similar regarding age, radiologic grade of OA, and analgesic use.[11,12,13] Patient blinding was impossible due to the nature of the procedures, and only the Elawamy et al.[11] study incorporated blind physicians to assess patients at follow-up. Davis et al.[13] excluded patients

with BMI > 40, which limits its generalizability from 9.2% of the US population.[18] Elawamy et al.[11] and Davis et al.[13] explicitly excluded patients with history of TKR. The Chen et al.[12] study did not explicitly list its exclusion criteria nor mention participants with knee replacements in their samples. Though not pertinent to these three trials, GNRFA has been increasingly studied as a safer noninvasive approach to managing knee pain in the 20% of post-op TKR patients reporting dissatisfaction and persistent knee discomfort.[19] As GNRFA is relatively new, more evidence is still needed to establish its safety and efficacy for this application.

Although the Elawamy et al.[11] article mentions instructing patients to use only paracetamol within the first month and full-dose ibuprofen thereafter, the authors did not report actual analgesic use by their participants during the trial period and acknowledge this as a limitation. The Chen et al.[12] and Davis et al.[13] studies recorded and monitored use of nonopioid and opioid analgesics at each timepoint, finding that patients did not significantly change their dosage over time. Thus, analgesic use remained constant and did not interfere with outcomes in these studies. Oral analgesics remain as common therapies for alleviating chronic OA-related knee pain, with regimens varying from patient to patient, and continuation of these patient-specific regimens throughout the trial period enhances the real-life applicability of their results. In theory, however, pain reduction achieved with GNRFA should reduce the need for oral analgesics. Future studies specifically assessing GNRFA and changes in analgesic use would be useful in exploring this relationship.

Aside from pain reduction, two other patient-oriented outcomes of importance are tolerability and safety. GNRFA is well-tolerated under local anesthesia, and patients can expect mild swelling and soreness at the injection sites lasting a few days after the procedure.[20] Serious complications such as hemarthrosis and septic arthritis are rare but have been noted in case

reports.[21] Thus, current literature suggests that GNRFA is a well-tolerated and safe procedure, with rare serious complications, but future research with larger population sizes will be required to determine the true incidence of these complications.

In addition to tolerability and safety, cost-effectiveness is another attractive feature of GNRFA. The procedure is generally regarded as a cost-effective option for chronic knee OA-related pain, and most insurance policies cover GNRFA when the procedure is deemed necessary by a medical professional. One economic analysis[22] found GNRFA to be more cost-effective and improve quality of life better than HA and IAS. Another economic analysis[23] found PRP not to be cost-effective, with total healthcare costs similar to TKR. Cost-effectiveness factors are varied but may include the cost per procedure, efficacy of pain reduction, functional improvement, and insurance coverage.

CONCLUSION:

According to the studies evaluated in this systematic review, it is inconclusive whether GNRFA continues to reduce knee pain in adult patients with chronic knee OA at six months after treatment. The two main factors interfering with the ability of these articles to answer the clinical question were study bias and data reporting. The Chen et al. and Davis et al. studies conclude that GNRFA offers sustained reduction of knee pain and superior pain reduction compared to HA and IAS at six months after treatment. Although GNRFA performed impressively and data were presented clearly, these studies received funding from medical technology corporations, and conflict of interest cannot be ruled out. The Elawamy et al. study, independently funded and denying any conflict of interest, reports a similar conclusion to the Chen et al. and Davis et al. studies, but data interpretation is limited. With growing literature, GNRFA continues to build its rapport in the medical community as a non-invasive, cost-effective treatment option for

persistently painful knee OA. Future studies with larger sample sizes and dichotomous outcomes with mean value reporting may lend clearer insight into GNRFA efficacy for adult patients with chronic OA-related knee pain.

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