Viewpoint: Genicular Nerve Hydrodissection for Knee Osteoarthritis Pain Management

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ABSTRACT

Knee pain secondary to knee osteoarthritis is one of the most common reasons for consultation in patients 50 years old and above. Due to limitations of current management options for knee osteoarthritis, studies seeking alternative treatment techniques have emerged, including procedures targeting knee innervation. The effectiveness of nerve hydrodissection for managing neuropathies such as carpal tunnel syndrome has been demonstrated but has not been applied to nerves that innervate the knee to manage osteoarthritis. This article discusses the potential application of ultrasound-guided nerve hydrodissection to the anterior innervation of the knee, known as the genicular nerves, for pain management in patients with osteoarthritis.

Keywords Knee osteoarthritis, knee pain, nerve hydrodissection, genicular nerves, genicular nerve hydrodissection

INTRODUCTION

Knee osteoarthritis (OA) is a significant cause of pain and disability in individuals 50 years old and above. The World Health Organization (WHO) predicts that the aging population will steadily increase in size and proportion, with a projected one in six people worldwide being 60 years old and above by 2030. An estimated 654 million people were known to be suffering from knee OA in 2020, and this number is expected to increase exponentially in the coming years due to a worldwide shift toward "living longer." [1]

The current management options for knee OA include conservative management in the form of medication, exercise, physical therapy, activity adjustment, and lifestyle modification. Surgical options, such as knee arthroplasty, are contemplated for severe knee OA. However, due to the dangers of prolonged medication use, limitations of conservative management, and reports of persistent pain even after surgery, [2–4] other treatment options have been sought.

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In 2011, the first randomized controlled trial that explored the effectiveness of radiofrequency neurotomy was published. This procedure targeted the articular branches of various nerves around the knee joint, known as genicular nerves, based on the theory that cutting the nerve supply to a painful structure may alleviate pain and restore function in patients with knee OA.[5] Since then, there has been a growing interest in studying sensory innervation of the knee joint and how to target these nerves effectively for pain relief.[6–11]

In this article, we discuss the potential of genicular nerve hydrodissection as an alternative management option for knee OA pain.

Innervation of the Anterior Knee Joint

The knee joint is innervated by terminal branches of the femoral and obturator nerves and articular branches of the sciatic nerve.[9] Most studies on knee denervation procedures have focused on anterior knee innervation because of the proximity of the sciatic nerve, popliteal artery, and vein to the posterior aspect of the knee. The posterior innervation is not targeted with ablation techniques due to the risk of injury to vital neurovascular structures.[9,10]

The knee is generally divided into four quadrants: the superomedial, superolateral, inferomedial, and inferolateral quadrants.[6,8,9,12] The nerves responsible for innervating the superomedial quadrant are the nerve to vastus medialis (NVM), the medial branch of the nerve to vastus intermedius (NVI), and the superior medial genicular nerve (SMGN). The nerves responsible for the innervation of the superolateral quadrant are the nerve to vastus lateralis (NVL), lateral branch of the nerve to NVI, articular branch of the common fibular nerve and the superior lateral genicular nerve (SLGN). The inferomedial quadrant is innervated by the infrapatellar branch of the saphenous nerve (IPBSN) (superiorly) and the inferior medial genicular nerve (IMGN) (inferiorly). Lastly, the inferolateral quadrant is innervated by the inferior lateral genicular nerve (ILGN) and recurrent fibular nerve (RFN).

The nerves of significance to radiofrequency ablation (RFA) and targets for radiofrequency neurotomy described in Choi and colleagues' landmark paper are the SMGN, SLGN, and IMGNs.[5] The inferolateral quadrant is often not targeted because of the proximity of the common peroneal nerve to the sensory articular branches of the knee, and ablation of this nerve may result in motor deficit.[5,10]

Current Knee Denervation Techniques

Several procedures targeting the genicular nerves have emerged in the past years. The most notable and studied among them is RFA, a process of thermal nerve degradation that uses a probe to provide radiofrequency energy.[13] The use of RFA for intractable pain is based on the premise that transmitting radiofrequency currents near nociceptive pathways will interrupt pain impulses. The thermal energy associated with RFA leads to tissue destruction, targeted at the nerves responsible for transmitting and/or modulating pain sensation.[14] Different types of RFA procedures for genicular nerves exist today and include conventional, pulsed, and cooled RFA. These types differ in the parameters and temperature of the radiofrequency impulses they apply to the nerves.

Other denervation techniques have been explored thereafter and included cryoneurolysis, which involves the application of cold temperatures to induce Wallerian degeneration and subsequent analgesia;[13,15] alcohol neurolysis, which entails injection of alcohol to cause iatrogenic neural degeneration to produce sensory denervation;[16,17] and genicular nerve block which uses local anesthesia to provide pain relief.[16] However, the effectiveness of these techniques has been less extensively studied than that of RFA.

The study of Choi et al. demonstrated the efficacy of genicular nerve RFA in improving pain and function in patients with knee OA, and subsequent studies and reviews have confirmed these findings.[5,18–20] However, due to the heterogeneity of patient characteristics, study protocols, and intervention parameters because of lack of standardization, the authors of these studies have advised caution when interpreting their results.[5,18–20] As studies on RFA have used varied methodologies with varied levels of quality, it is too early to conclude if RFA of the genicular nerves is a superior alternative to knee procedures currently available.[21–25]

Although some studies have shown the relative safety of RFA,[20] others have highlighted possible adverse effects such as local hemorrhage, hematoma formation, vascular complications,

injury to surrounding soft tissue structures, thermal injury, infection, and failure rate of over 25%[17,18,21,22,26,27] that may outweigh the benefit of its use. Aside from these potential side effects, application to local clinical practice is limited by the high procedure and equipment cost and longer procedural time posed by RFA.

The search for a safe, effective, and practical management option that provides consistent results and long-term pain relief is still underway. Considering that targeting the genicular nerves is a worthwhile strategy, nerve hydrodissection may be an alternative worth investigating.

Nerve Hydrodissection

Nerve hydrodissection is a technique used to manage peripheral nerve entrapments. It is an ultrasound-guided technique that involves the injection of fluid to relieve pressure around the entrapped nerve.[28] The fluid separates the nerve from surrounding tissues to relieve neuropathic pain symptoms. This technique has been reported to be effective in several types of focal neuropathies and is most known for its use in carpal tunnel syndrome[29–35] and has been included in the 20th edition of Harrison's Principles of Internal Medicine as a treatment option for carpal tunnel syndrome.[29]

The detailed mechanism of action of this technique is still poorly understood, but several theories have been suggested to explain its effect. The first theory is the improvement of mobility of the entrapped nerve. Peripheral nerves are said to be susceptible to compression during injury, mechanical stretching or movement against prominences, and morphologic derangement. When a nerve is impinged, free nerve endings supplying the main nerves and small blood vessels around the nerves may also be compressed. Nerve hydrodissection releases the pressure around these structures, thereby preventing further nerve damage and relieving nerve impingement symptoms such as pain.

Aside from mechanical dissection of the area around the nerve, it is believed that the injectate is also crucial to the mechanism of action of nerve hydrodissection, which leads to the second theory, which is the correction of perineural/intraneural glycopenia. Peripheral nerves, like the brain, are known to have a high requirement for glucose. Neuropathic pain, especially when prolonged, may signify perineural or intraneural glycopenia. The commonly used injectates for nerve hydrodissection are 5% dextrose water (D5W), saline, anesthetic, steroid, and combinations of these fluids.[36] The injection of D5W around the entrapped nerve corrects this low glucose state, decreasing or relieving pain.[37]

The third theory involves the transient receptor potential vanilloid receptor-1 (TRPV1). The precise regulation of TRPV1 is still poorly understood, but studies have shown that chronic neuropathic pain is strongly associated with persistent opening of the TRPV1 ion channel.[38] This ion channel is known as the capsaicin receptor and is said to be responsible for the "burning sensation" that patients with neuropathic pain report. Glucose indirectly inhibits the capsaicin-sensitive receptor, TRPV-1, and blocks the secretion of substance P and calcitonin gene-related peptide (CGRP), which are pro-nociceptive substances involved in neurogenic inflammation.[39] Interestingly, mannitol, which has the same structure as glucose, has been shown to decrease burning sensation when applied as a cream in patients with capsaicin-induced lip pain, implying indirect inhibition of the TRPV-1 receptor.[37,39] A direct effect has not been postulated since no glucose or mannitol binding points to the TRPV-1 receptor have been found.[39,40]

Further indirect evidence to support nerve hydrodissection is what is known as perineural injection therapy (PIT). This injection technique refined by Lyftogt is used for the management of persistent and recurrent pain. In this treatment, 5% buffered dextrose is injected subcutaneously near peripheral nerve tracts to restore nerve function. Like nerve hydrodissection, PIT targets peptidergic small fibers with TRPV1 expression in the skin and fascial tissues.[41] This procedure, however, is done blindly and is only guided by theoretical surface anatomy maps of nerves. This technique is being used for trigger point injection, radial nerve palsy, carpal tunnel syndrome, chronic low back pain and chronic postsurgical pain after total knee arthroplasty. To our knowledge, PIT has not been used for knee OA either. Still, compared to nerve hydrodissection, the latter may be a better technique to translate to knee OA management, as nerve localization will be guided by ultrasound and not done blindly.

There is currently a lack of knowledge on the mechanisms underlying nerve hydrodissection, but

its effectiveness in neuropathic pain validates further investigation into its possible application to other pain syndromes.

Nerve hydrodissection is a relatively simple and cost-effective procedure that only requires a diagnostic ultrasound machine for guidance and simple, readily available materials to be performed. Its accessibility and decreased procedural cost would make this easily adaptable to local clinical practice. Since heat, cryotherapy, or chemicals such as alcohol are not involved, it is predicted that nerve hydrodissection would have fewer adverse events than those found in denervation procedures. As it has been proven effective for neuropathic pain, it is a promising technique to be explored for managing knee OA pain.

CONCLUSION

Knee OA is a complex disease that causes significant pain and disability worldwide. The limitations of currently available management options in patients with knee OA underscore the need to investigate alternatives that may provide better symptom control. Nerve hydrodissection targeting the genicular nerves, a potentially cheaper and safer alternative to current techniques, is a promising option that warrants further research and exploration.

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Conflict of Interest:

The authors have no conflicts of interest to declare.

Authors' Contributions:

1. Research Project: A. Conception, B. Organization, C. Execution
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique
3. Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique

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REFERENCES

1. World Health Organisation. WHO Factsheet. 2021 [cited 2022 Sep 19]. Ageing and health. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
2. Hasegawa M, Tone S, Naito Y, Wakabayashi H, Sudo A. Prevalence of persistent pain after total knee arthroplasty and the impact of neuropathic pain. *J Knee Surg* [Internet]. 2019 [cited 2022 Sep 6];32(10):1020–3. Available from: http://www.thieme-connect.com/products/ejournals/html/10.1055/s-0038-1675415
3. Rice DA, Kluger MT, McNair PJ, Lewis GN, Somogyi AA, Borotkanics R, et al. Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. *Br J Anaesth*. 2018 Oct 1;121(4):804–12.
4. Wylde V, Beswick A, Bruce J, Blom A, Howells N, Gooberman-Hill R. Chronic pain after total knee arthroplasty. EFORT open Rev [Internet]. 2018 Aug 1 [cited 2022 Aug 5];3(8):461–70. Available from: https://pubmed.ncbi.nlm.nih.gov/30237904/
5. Choi WJ, Hwang SJ, Song JG, Leem JG, Kang YU, Park PH, et al. Radiofrequency treatment relieves chronic knee osteoarthritis pain: A double-blind randomized controlled trial. *Pain*. 2011 Mar;152(3):481–7.
6. Tran J, Peng PWH, Lam K, Baig E, Agur AMR, Gofeld M. Anatomical study of the innervation of anterior knee joint capsule: Implication for image-guided intervention. *Reg Anesth Pain Med*. 2018 May 1;43(4):407–14.
7. Fonkoue L, Stoenoiu MS, Behets CW, Steyaert A, Kouassi JEK, Detrembleur C, et al. Validation of a new protocol for ultrasound-guided genicular nerve radiofrequency ablation with accurate anatomical targets: Cadaveric study. *Reg Anesth Pain Med*. 2021 Mar 1;46(3):210–6.
8. Fonkoué L, Behets C, Kouassi JÉK, Coyette M, Detrembleur C, Thienpont E, et al. Distribution of sensory nerves supplying the knee joint capsule and implications for genicular blockade and radiofrequency ablation: an anatomical study. *Surg Radiol Anat*. 2019 Dec 1;41(12):1461–71.
9. Roberts SL, Stout A, Dreyfuss P. Review of knee joint innervation: Implications for diagnostic blocks and radiofrequency ablation. Vol. 21, Pain Medicine (United States). Oxford University Press; 2020. p. 922–38.
10. Alomari A, Bhatia A. An update on radiofrequency denervation for arthritis-related knee joint pain: a synthesis of the current evidence. *BJA Educ*. 2024 May 1;24(5):164–72.
11. Kim JH, Shustorovich A, Arel AT, Downie SA, Cohen SP, Kim SY. Genicular nerve anatomy and its implication for new procedural approaches for knee joint denervation: A cadaveric study. *Pain Med*. 2022;23(1):144–51.
12. Gardner E. The innervation of the knee joint. *Anat Rec* [Internet]. 1948 May 1 [cited 2022 Jul 29];101(1):109–30. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/ar.1091010111
13. Panagopoulos A, Tsiplakos P, Katsanos K, Antzoulas P, Lakoumentas J. Cooled radiofrequency ablation versus cryoneurolysis of the genicular nerves for the symptomatic pain management in knee osteoarthritis: a study protocol of a prospective, randomized, single-blinded clinical trial. *J Orthop Surg Res* [Internet]. 2023;18(1):295. Available from: https://doi.org/10.1186/s13018-023-03737-1
14. Wray JK, Dixon B, Przkora R. Radiofrequency Ablation. Innov Gastrointest Endosc [Internet]. 2023 Jun 12 [cited 2024 Sep 5];207–15. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482387/
15. Radnovich R, Scott D, Patel AT, Olson R, Dasa V, Segal N, et al. Cryoneurolysis to treat the pain and symptoms of knee osteoarthritis: a multicenter, randomized, double-blind, sham-controlled trial. *Osteoarthritis Cartilage* [Internet]. 2017;25(8):1247–56. Available from: https://doi.org/10.1016/j.joca.2017.03.006
16. Elashmawy MM, Shabana AAH, Elsaid TO, Elhawary GM. Ultrasound-guided genicular nerve block versus alcoholic neurolysis for treatment of advanced knee osteoarthritis patients. *Egypt Rheumatol*. 2022 Oct 1;44(4):307–11.
17. Dass RM, Kim E, Kim H Kyu, Lee JY, Lee HJ, Rhee SJ. Alcohol neurolysis of genicular nerve for chronic knee pain. *Korean J Pain* [Internet]. 2019 [cited 2022 Sep 25];32(3):223. Available from: /pmc/articles/PMC6615444/
18. Zhang H, Wang B, He J, Du Z. Efficacy and safety of radiofrequency ablation for treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. *J Int Med Res* [Internet]. 2021;49(4):3000605211006647. Available from: https://doi.org/10.1177/03000605211006647
19. Li G, Zhang Y, Tian L, Pan J. Radiofrequency ablation reduces pain for knee osteoarthritis: A meta-analysis of randomized controlled trials. *Int J Surg*. 2021 Jul 1;91:105951.
20. Liu J, Wang T, Zhu ZH. Efficacy and safety of radiofrequency treatment for improving knee pain and function in knee osteoarthritis: a meta-analysis of randomized controlled trials. *J Orthop Surg Res* [Internet]. 2022 Dec 1 [cited 2022 Sep 25];17(1):1–14. Available from: https://josr-online.biomedcentral.com/articles/10.1186/s13018-021-02906-4
21. Tate Q, Conger A, Burnham T, Cushman DM, Kendall R, Schneider B, et al. The Effectiveness and Safety of Genicular Nerve Radiofrequency Ablation for the Treatment of Recalcitrant Knee Pain Due to Osteoarthritis: a Comprehensive Literature Review. Curr Phys Med Rehabil Reports 2019 74 [Internet]. 2019 Sep 14 [cited 2022 Sep 25];7(4):404–13. Available from: https://link.springer.com/article/10.1007/s40141-019-00246-3
22. Le PU, Kim SY, Kosharskyy B, Kaye AD, Shaparin N, Downie SA. Comprehensive review is genicular nerve radiofrequency ablation safe? A literature review and anatomical study. *Pain Physician* [Internet]. 2016 [cited 2022 Jul 6];19:697–705. Available from: www.painphysicianjournal.com
23. Jamison DE, Cohen SP. Radiofrequency techniques to treat chronic knee pain: A comprehensive review of anatomy, effectiveness, treatment parameters, and patient selection. Vol. 11, *Journal of Pain Research*. Dove Medical Press Ltd.; 2018. p.1879–88.
24. Kim PY, Cohen SP. Genicular Nerve Blocks and Radiofrequency Ablation for Knee Osteoarthritis: More Nerves, More Questions. Pain Med [Internet]. 2021 May 21 [cited 2022 Sep 25];22(5):1019–21. Available from: https://academic.oup.com/painmedicine/article/22/5/1019/6128518
25. Abd-Elsayed A, Strand N, Gritsenko K, Martens J, Chakravarthy K, Sayed D, et al. Radiofrequency ablation for the knee joint: A survey by the American Society of pain and Neuroscience. *J Pain Res* [Internet]. 2022;15:1247–55. Available from: https://doi.org/10.2147/JPR.S342653
26. Conger A, Gililland J, Anderson L, Pelt CE, Peters C, McCormick ZL. Genicular Nerve Radiofrequency Ablation for the

Treatment of Painful Knee Osteoarthritis: Current Evidence and Future Directions. Pain Med. 2021 Jul 25;22:S20–23.
27. McCormick ZL, Patel J, Conger A, Smith CC. The Safety of Genicular Nerve Radiofrequency Ablation. Pain Med [Internet]. 2021 Feb 23 [cited 2024 Sep 5];22(2):518–9. Available from: https://dx.doi.org/10.1093/pm/pnaa355
28. Cass SP. Ultrasound-guided nerve hydrodissection: what is it? A review of the literature. *Curr Sports Med Rep* [Internet]. 2015;15(1):20–2. Available from: www.acsm-csmr.org
29. Lam S, Hung CY, Chiang YP, Onishi K, Su DCJ, Clark TB, et al. Ultrasound-guided nerve hydrodissection for pain management: rationale, methods, current literature, and theoretical mechanisms. *J Pain Res*. 2020;13:1957–68.
30. Buntragulpoontawee M, Chang K-V, Vitoonpong T, Pornjaksawan S, Kitisak K, Saokaew S, et al. The effectiveness and safety of commonly used injectates for ultrasound-guided hydrodissection treatment of peripheral nerve entrapment syndromes: A systematic review. *Front Pharmacol* [Internet]. 2020;11:621150. Available from: https://doi.org/10.3389/fphar.2020.621150
31. Chao TC, Reeves KD, Lam KHS, Li TY, Wu YT. The effectiveness of hydrodissection with 5% dextrose for persistent and recurrent carpal tunnel syndrome: a retrospective study. *J Clin Med* [Internet]. 2022;11(13):1–10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35806998%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC9267718
32. Mathieu T, Lemmens E, Stassijns G. A safe and easy-to-use ultrasound-guided hydrodissection technique for the carpal tunnel syndrome: a minimally invasive approach. *J Ultrasound* [Internet]. 2022;25(3):451–5. Available from: https://doi.org/10.1007/s40477-021-00597-5
33. Song B, Marathe A, Chi B, Jayaram P. Hydrodissection as a therapeutic and diagnostic modality in treating peroneal nerve compression. *Baylor Univ Med Cent Proc*. 2020 Jul 2;33(3):465–6.
34. Wu Y-T, Lam KHS, Lai C-Y, Chen S-R, Shen Y-P, Su Y-C, et al. Novel motor-sparing ultrasound-guided neural injection in severe carpal tunnel syndrome: A comparison of four injectates. *Biomed Res Int* [Internet]. 2022;2022:9745322. Available from: https://doi.org/10.1155/2022/9745322.
35. Wu YT, Wu CH, Lin JA, Su DCJ, Hung CY, Lam SKH. Efficacy of 5% dextrose water injection for peripheral entrapment neuropathy: A narrative review. Vol. 22, *International Journal of Molecular Sciences*. MDPI; 2021.
36. Bernardo-Bueno MM, Gonzalez-Suarez C, Milanese S, Gambito ED. Nerve hydrodissection for pain management: A scoping review. *Asia Pacific J Pain* [Internet]. 2023 Nov 2 [cited 2023 Dec 27]; Available from: https://www.airitilibrary.com/Article/Detail/P20220207001-PP202202070001-PP2023110002-00001
37. Lam KHS, Hung CY, Chiang YP, Onishi K, Su DCJ, Clark TB, et al. Ultrasound-guided nerve hydrodissection for pain management: Rationale, methods, current literature, and theoretical mechanisms. *J Pain Res*. 2020;13:1957–68.
38. Malek N, Pajak A, Kolosowska N, Kucharczyk M, Starowicz K. The importance of TRPV1-sensitisation factors for the development of neuropathic pain. *Mol Cell Neurosci*. 2015 Mar 1;65:1–10.
39. Wu YT, Chen YP, Lam KHS, Reeves KD, Lin JA, Kuo CY. Mechanism of glucose water as a neural injection: A perspective on neuroinflammation. *Life*. 2022;12(6):1–13.
40. Cui M, Gosu V, Basith S, Hong S, Choi S. Polymodal Transient Receptor Potential Vanilloid Type 1 Nocisensor: Structure, Modulators, and Therapeutic Applications. Adv Protein Chem Struct Biol. 2016 Jan 1;104:81–125.
41. Güzel İ, Gül D, Akpancar S, Lyftogt J. Effectiveness of perineural injections combined with standard postoperative total knee arthroplasty protocols in the management of chronic postsurgical pain after total knee arthroplasty. *Med Sci Monit* [Internet]. 2021;27:e928759. Available from: https://doi.org/10.12659/MSM.928759.