Scientific Foundation SPIROSKI, Skopje, Republic of North Macedonia
Open Access Macedonian Journal of Medical Sciences. 2025 Mar 15; 13(1):7-13.
https://doi.org/10.3889/oamjms.2025.12030
eISSN: 1857-9655
Category: *F - Review Articles*
Section: *Systematic Review*

Efficacy of Pre-operative Cryoneurolysis for Reducing Pain and Opioid Use in Patients Undergoing Knee Arthroplasty: A Systematic Review

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Edited by: Eli Djulejic
Citation: Mirt PK. Efficacy of Pre-operative Cryoneurolysis for Reducing Pain and Opioid Use in Patients Undergoing Knee Arthroplasty: A Systematic Review. Open Access Maced J Med Sci. 2025 Mar 15; 13(1):7-13. https://doi.org/10.3889/oamjms.2025.12030
Keywords: Cryoneurolysis; Pain management; Total knee arthroplasty; Multimodal analgesia; Opioid reduction
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Received: 07-Jan-2025
Revised: 24-Feb-2025
Accepted: 27-Feb-2025

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Pre-operative cryoneurolysis is an emerging analgesic technique that shows promise in managing post-operative pain and reducing opioid use in patients undergoing total knee arthroplasty (TKA). By inducing targeted Wallerian degeneration of sensory nerves, cryoneurolysis provides prolonged analgesia while preserving motor function, making it a valuable addition to multimodal pain management strategies.

METHODS: This systematic review evaluates the efficacy, safety, and clinical utility of cryoneurolysis, synthesizing findings from eight studies, including randomized controlled trials and observational analyses, in adherence to Preferred Reporting Items for Systematic Review and Meta-Analysis 2020 guidelines. Data on pain scores, opioid consumption, functional recovery, and adverse effects were extracted and analyzed to assess clinical outcomes.

RESULTS: Cryoneurolysis consistently reduced post-operative pain scores and opioid consumption, with opioid use reductions up to 72%. Enhanced functional recovery, including improved range of motion and quicker rehabilitation milestones, was also observed. The intervention's safety profile was favorable, with only minimal transient side effects reported and no long-term complications.

CONCLUSION: Cryoneurolysis offers significant potential as a cornerstone in multimodal pain management strategies for TKA, particularly in addressing opioid-related public health challenges. While current evidence supports its efficacy, variations in study design and sample sizes necessitate further multicenter trials to establish standardized protocols and optimize its clinical application.

Introduction

Total knee arthroplasty (TKA) is one of the most commonly performed orthopedic surgeries worldwide, with a demand expected to rise exponentially as populations age and the prevalence of osteoarthritis increases [1], [2]. This procedure, although highly effective in improving mobility and quality of life, is often associated with significant post-operative pain, which can impede recovery and rehabilitation [3], [4]. Pain management in the perioperative period is critical not only for enhancing patient comfort but also for optimizing surgical outcomes, reducing the length of hospital stays, and minimizing healthcare costs [4], [5], [6], [7].

Conventionally, opioid-based analgesics have been the cornerstone of post-operative pain management in TKA. However, the growing opioid epidemic has underscored the need for alternative pain control strategies that reduce reliance on these drugs [4], [5], [6]. Opioids are associated with numerous side effects, including nausea, sedation, constipation, and the risk of dependency or addiction.

Furthermore, excessive use of opioids can delay functional recovery by impairing cognitive and physical abilities [5]. In this context, innovative approaches such as cryoneurolysis have emerged as promising modalities to improve post-operative pain management and reduce opioid consumption [7], [8], [9], [10].

Cryoneurolysis involves the application of extremely cold temperatures to targeted sensory nerves, inducing Wallerian degeneration and disrupting pain signal transmission [11]. Unlike other neuroablative techniques, cryoneurolysis is designed to be temporary, allowing nerve function to recover over weeks to months [8], [9], [11]. This makes it particularly suitable for perioperative pain management, where prolonged but reversible analgesia is desired. By targeting the infrapatellar branch of the saphenous nerve and other relevant

sensory nerves, cryoneurolysis provides localized pain relief without affecting motor function [8], [9]. This capability is especially valuable in TKA patients, where early mobilization and rehabilitation are key to successful recovery [7], [9].

Some studies, primarily from the United States, have demonstrated the effectiveness of cryoneurolysis in reducing post-operative pain and opioid consumption following surgery [2], [7], [8], [9], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24]. However, these findings are based on a limited number of clinical trials, and no published studies from Europe have yet explored its efficacy. The incorporation of pre-operative cryoneurolysis into multimodal pain management strategies aligns with modern perioperative care principles, which emphasize personalized, opioid-sparing regimens aimed at optimizing patient outcomes [17], [23].

Furthermore, cryoneurolysis has demonstrated a favorable safety profile, with minimal side effects reported in clinical studies [2], [9], [15], [16], [18], [19], [20], [24], [25]. Despite these promising results, important questions remain regarding its long-term effectiveness, optimal application techniques, and its cost-efficiency in broader clinical practice. Thus, although pre- operative cryoneurolysis has shown promise as an analgesic technique for managing post-operative pain and reducing opioid consumption in patients undergoing TKA, there is a lack of a comprehensive systematic review synthesizing current evidence on its efficacy, safety, and clinical application. This systematic review aims to synthesize the existing evidence on cryoneurolysis, focusing on its clinical efficacy, safety, and potential role in TKA pain management.

Methods

Protocol

This systematic review adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines [26] and was conducted according to a predefined protocol. The analysis aimed to collate and assess existing evidence on the clinical efficacy of cryoneurolysis in reducing post-operative pain and opioid use following TKA.

Eligibility criteria

Studies were included based on the following criteria:

• Evaluated cryoneurolysis as a pre-operative intervention in TKA patients

• Reported outcomes related to pain management, opioid consumption, or functional recovery

• Were randomized controlled trials (RCTs), cohort studies, or observational studies

• Published in peer-reviewed journals.

Information sources

A systematic search was conducted using PubMed and MEDLINE databases to identify relevant studies, from 15th to December 31st, 2024. The keywords used for the search were as follows: Cryoneurolysis, knee, and arthroplasty. In addition, reference lists of included articles were manually reviewed to ensure comprehensive coverage. Data from 40 studies, checked by the reviewers, were analyzed.

Data extraction

Initially, the titles of the studies in the search results were screened against the inclusion and exclusion criteria, removing studies that were not relevant to the review. The remaining studies were reviewed by a researcher who read the abstracts of each study to determine whether they should be included in the review. For the included studies, data extraction focused on study design, sample size, cryoneurolysis protocols, and primary outcomes, including pain scores, opioid use, and range of motion (ROM). Independent reviewers ensured accuracy and resolved discrepancies through consensus.

According to PRISMA's guidelines, a total of 40 articles (PubMed-40, MEDLINE-0) were found. After initial screening, 24 articles were excluded as they did not address our topic (the article did not address the population of patients with knee problems). Subsequently, the remaining 16 studies were screened according to our inclusion and exclusion criteria. The remaining eight articles were critically appraised and included in our systematic review (Figure 1).

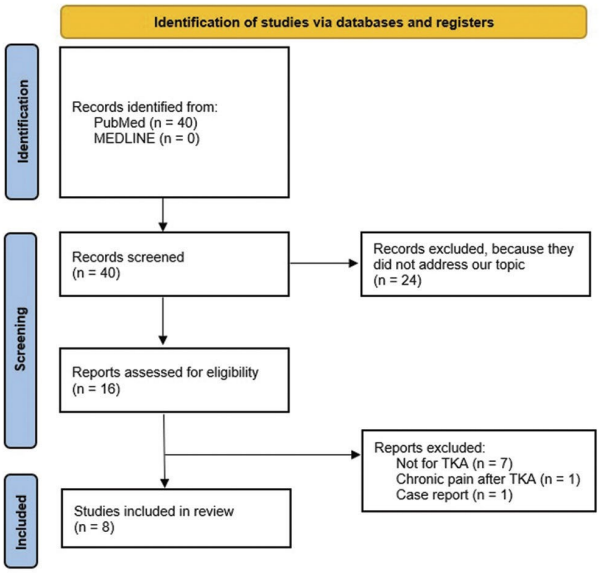

Figure 1: Flow diagram of the search process

Results

Study characteristics

A systematic review of the literature shows that the studies used different methodological approaches to measure efficacy of pre-operative cryoneurolysis in patient with TKA. As indicated in Table 1, the systematic review incorporated eight studies, comprising two RCTs, three retrospective cohort studies, one case series and one observational study. Sample sizes ranged from 10 to 267 participants, with varied follow-up durations. Intervention protocols involved targeting peripheral sensory nerves, primarily the infrapatellar branch of the saphenous nerve, secondary anterior femoral cutaneous nerve. Cryoneurolysis was performed using the Iovera device in most studies.

Pain reduction

Significant reductions in post-operative pain scores were reported in multiple studies. Dasa et al. observed a reduction in pain intensity at 2 and 6 weeks postoperatively [9]. Lung et al. reported statistically significant lower pain scores at 6 weeks and 1 year follow-up [19]. Jennewine et al. highlighted a statistically significant reduction in the early post-operative pain compared to control groups [15]. Swisher et al. reported lower pain intensity during the first 3 post-operative weeks with active cryoneurolysis compared to sham treatment [18]. Urban et al. found a 22% reduction in mean pain scores during hospital stay for the cryoneurolysis group [16]. Roth et al. reported post-anesthesia care unit pain scores of zero in 90% of patients treated with cryoneurolysis [20].

Further, Mont et al. (2024) highlighted a continued reduction in pain scores even at 6 months postoperatively [24]. Several studies also observed improvements in pain control during physical therapy sessions, contributing to enhanced rehabilitation experiences [2], [20].

Opioid reduction

Pre-operative cryoneurolysis significantly reduced opioid consumption across multiple studies. Urban et al. reported a 51% reduction in daily morphine milligram equivalents during hospitalization [16]. Mont et al. showed a 72% lower likelihood of opioid use in the cryoneurolysis group compared to controls [24]. Mihalko et al. observed a significant reduction in cumulative opioid consumption through 6 weeks postoperatively [2]. Lung et al. showed reduced opioid requirements both in the immediate post-operative period and at long-term follow-up [19]. Swisher et al. reported lower average opioid consumption throughout the 1st 3 weeks postoperatively [18]. Roth et al. reported lower post-operative opioid use compared to a historical control group [20]. In addition, Mont et al. noted that patients receiving cryoneurolysis required fewer opioid refills during the recovery phase [24].

Functional outcomes and length of stay (LOS)

Cryoneurolysis significantly improved functional recovery, as evidenced by better scores on the

Table 1: Characteristics of included studies

Study	Design	Sample size	Intervention	Comparator	Nerve localization	Outcome Measures
Dasa et al., 2016	Retrospective cohort study	100 total; 50 intervention, 50 control, USA	6 cycles of 50 s per cycle, -125°F	Standard therapy (preop, intraop, postop multimodal pain regimen)	IPBSN and AFCN; anatomic landmarks, diagnostic block unknown	TMEs, LOS, WOMAC, KOOS, OKS, SF-12, PROMIS, AEs
Mihalko et al., 2021	Parallel-group RCT	124 total; 62 intervention, 62 control, USA	Unknown number of cycles, duration and temperature	Standard therapy (preop, intraop, postop multimodal pain regimen)	IPBSN and AFCN; anatomic landmarks, diagnostic block unknown	TME, NRS, KOOS JR, TUG, ROM, AEs
Urban et al., 2021	Retrospective cohort study	267 total; 169 intervention, 98 control, USA	1 cycles of 105 s per cycle, unknown temperature	Standard therapy (preop, intraop, postop multimodal pain regimen)	IPBSN and AFCN; US guidance, pre-procedure diagnostic block	TME, NRS, LOS, ROM, AEs
Lung et al., 2022	Retrospective cohort study	57 total; 29 intervention, 28 control, USA	6 cycles of 1 min, unknown temperature	Standard therapy (preop, intraop, postop multimodal pain regimen)	IPBSN and AFCN; anatomic landmarks, diagnostic block unknown	TMEs, AEs, ROM, PAC, KOOS JR, SF-12, VAS
Roth et al., 2022	Case series	10 total, USA	Unknown number of cycles of 60 s per cycle, -88°C	N/A	IPBSN, US guidance, pre-procedure diagnostic block	NRS, TME, ROM
Swisher et al., 2022	Parallel-group RCT	16 total; 8 intervention, 8 control, USA	3 cycles of 120 s per cycle, -70°C	Sham cryoneurolysis	IPBSN, US guidance, diagnostic block unknown	TME, NRS, difficulty sleeping, number of awakenings due to pain, nausea
Jennewine et al., 2023	Retrospective chart review	114 total; 56 intervention (divided in 3 groups), 58 control, USA	Unknown number of cycles, duration and temperature	Standard therapy (preop, intraop, postop multimodal pain regimen)	ISN and AFCN; anatomic landmarks, diagnostic block unknown	TME, NRS, ROM, KOOS JR, use of assistive device
Mont et al., 2024	Multicentre, prospective observational study	140 total; 80 intervention, 60 control, USA	Unknown number of cycles, duration and temperature	Standard therapy (preop, intraop, postop multimodal pain regimen)	IPBSN, AFCN, anatomic landmarks or US guidance, diagnostic block unknown	BPI-SF, KOOS JR, sleep disturbance

VAS, Visual Analogue Scale; AE, adverse event; IPBSN, infrapatellar branch of the saphenous nerve; AFCN, anterior femoral cutaneous nerve; TME, total morphine equivalent; LOS, length of stay; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; PAC, Post Acute Care; SF-12, Short Form-12; PROMIS, Patient Reported Outcomes Measurement Information System; NRS, Numeric Rating Scale; ROM, range of motion; RCT, randomized controlled trial; KOOS JR, Knee Injury and Osteoarthritis Outcome Score for Joint Replacements; TUG, Timed-Up-and-Go test; SF-36, Short Form-36; N/A: not applicable.

knee injury and osteoarthritis outcome score (KOOS) and enhanced ROM. These improvements were noted as early as 6 weeks postoperatively and sustained up to 12 weeks [19]. Functional outcomes and length of stay (LOS) were consistently improved with cryoneurolysis. Dasa et al. reported a shorter LOS (0.8 days) compared to the control group (1.7 days) [9]. Urban et al. observed greater knee flexion at discharge in the cryoneurolysis group [16]. Lung et al. reported improved ROM and faster recovery milestones [19]. Mont et al. noted earlier discharge and better early functional recovery compared to controls [24]. Swisher et al. found improved knee extension and ROM by the 3rd post-operative week [18]. Mihalko et al. reported better functional scores in 12 weeks compared to controls [2].

Safety profile and adverse events

Cryoneurolysis was generally well tolerated. Minor complications included localized numbness and tingling sensations but resolved without intervention. No severe adverse events were reported across the included studies. Urban et al. specifically noted no increased risk of infection or delayed wound healing [16]. Roth et al. also reported no significant adverse effects, with most discomfort resolving within days [20].

In addition, no long-term complications, such as persistent neuropathy or sensory deficits, were reported across studies, further supporting the safety profile of cryoneurolysis as a pre-operative intervention.

Discussion

Clinical implications

Cryoneurolysis has become an important addition to multimodal pain management strategies for TKA, offering prolonged analgesia without causing motor blockade. This technique effectively addresses key post-operative concerns, such as pain control and opioid reduction. Its mechanism involves targeted cold-induced axonal degeneration, creating an extended sensory block while preserving motor function, which is crucial for the early mobilization and recovery [11].

The findings from this systematic review highlight the significant benefits of pre-operative cryoneurolysis, including reduced post-operative pain, lower opioid consumption, and improved functional recovery in patients undergoing TKA. Multiple studies emphasized the rapid onset of pain relief with cryoneurolysis, often within the first 24 h hour postoperatively, a critical period when pain is typically most severe. This early and sustained reduction in pain intensity aligns with its proposed mechanism of action, where cryoneurolysis temporarily disrupts sensory nerve transmission, diminishing pain perception during the early post-operative phase when discomfort tends to peak [9], [24].

Notably, cryoneurolysis has demonstrated consistent pain relief across diverse patient populations, including those with varying degrees of pre-operative pain sensitivity [8]. This adaptability makes it particularly suitable for patients at higher risk for opioid-related complications, such as individuals with obesity, diabetes, or chronic pain syndromes. Such populations often experience heightened post-operative pain and require higher opioid doses, making non-opioid alternatives like cryoneurolysis highly valuable. Furthermore, its non-invasive nature and ease of application make it a practical pain management strategy suitable for various healthcare settings, including outpatient surgical centers.

Patientstreated with cryoneurolysis consis-tently reported lower opioid consumption compared to control groups, with several studies noting that up to 40% of patients could avoid opioids entirely during the 1st post- operative week. This underscores cryoneurolysis' effectiveness in minimizing opioid reliance and mitigating associated risks such as dependency, nausea, and respiratory depression. The reduction in opioid use aligns with enhanced recovery after surgery protocols, which emphasize opioid-sparing strategies to accelerate recovery. Patients receiving cryoneurolysis often achieved faster rehabilitation milestones, such as unassisted ambulation and resumption of daily activities. These functional improvements likely result from both effective pain control and reduced sedative effects commonly associated with opioid use, which can impair cognitive and physical performance [16], [19].

The benefits of cryoneurolysis extend beyond the immediate post-operative period. By controlling pain effectively during the critical early recovery phase, cryoneurolysis may reduce pain-related rehabilitation delays and prevent the development of chronic pain syndromes. Consistent early pain management is known to play a pivotal role in minimizing maladaptive pain pathways that can contribute to long-term complications [27]. In addition, faster rehabilitation and reduced pain levels may lead to long-term functional benefits, such as enhanced joint mobility and reduced stiffness, ultimately improving overall surgical outcomes.

From a public health standpoint, the reduction in opioid consumption observed with cryoneurolysis is particularly significant given the ongoing opioid crisis. Lower post-operative opioid use not only reduces the risk of dependency but also minimizes side effects such as respiratory depression, nausea, constipation, and cognitive impairment. These results reinforce the importance of adopting opioid-sparing techniques within multimodal pain management frameworks [24].

Cryoneurolysis also offers potential economic advantages. While the initial costs associated with the device and training may be higher than standard pain management approaches, these expenses could be offset by the reduction in opioid use, shorter hospital stays, and fewer post-operative complications. Faster recovery times and lower rates of readmission may also contribute to overall cost savings in healthcare systems. Further cost-effectiveness analyses will be critical in confirming these economic benefits and guiding broader implementation in clinical practice.

Importantly, cryoneurolysis has consistently demonstrated a favorable safety profile across all reviewed studies, as well as in other published literature [12], [14], [17], [21], [22], [23], [25], [27], [28].

The most commonly reported side effects were minor, including localized numbness and tingling sensations, both of which were resolved without the need for intervention. No long-term complications, such as persistent neuropathy or sensory deficits, were observed in any of the included trials, further supporting cryoneurolysis as a safe and effective pre-operative intervention for TKA patients.

Limitations

While the findings were positive across multiple studies, some limitations exist. Variability in cryoneurolysis techniques, patient populations, and sample sizes could impact the consistency of results. Standardizing the procedure and ensuring uniform outcome measures in future trials would provide a clearer understanding of its efficacy [2].

Despite promising outcomes, several limitations must be acknowledged:

1. Study design variability: Included studies exhibited heterogeneity in protocols, follow-up durations, and outcome measures

2. Sample size: Many studies had small sample sizes, limiting the generalizability of findings

3. Long-term outcomes: Data beyond 12 weeks post-surgery remain scarce, necessitating further research to evaluate the sustained benefits of cryoneurolysis

4. Cost considerations: Limited data exists on the cost-effectiveness of cryoneurolysis, which is a critical factor for its widespread adoption.

Future directions

Cryoneurolysis presents a promising avenue for innovation in perioperative care, particularly in the management of post-operative pain. Advances in imaging technologies, such as ultrasound guidance, offer the potential to further refine the precision of cryoneurolysis by improving nerve targeting accuracy. Enhanced precision could lead to more consistent clinical outcomes, reduced procedural variability, and improved patient satisfaction. In addition, integrating cryoneurolysis with other non-opioid analgesic strategies, such as local infiltration analgesia in knee arthroplasty, may create synergistic effects. This combination could enhance pain relief while minimizing adverse effects, aligning with the principles of multimodal and personalized pain management protocols.

To fully establish the role of cryoneurolysis in perioperative care, future research should prioritize multicenter RCTs with larger patient populations and standardized methodologies. Such studies would provide a more robust evaluation of its efficacy and safety across diverse patient demographics. Long-term follow-up studies are also essential to assess the sustained impact of cryoneurolysis on post-operative pain control, opioid consumption, and functional recovery. Furthermore, cost-effectiveness analyses could help determine whether the benefits of reduced opioid use and faster recovery offset the initial costs associated with cryoneurolysis technology and training.

Continued research should also aim to refine the technical aspects of cryoneurolysis. Optimizing probe designs and improving targeting precision through advanced imaging innovations could enhance both the efficiency and safety of the procedure. These advancements may help ensure more uniform clinical results and expand the applicability of cryoneurolysis to a broader range of surgical procedures.

Moreover, the potential role of cryoneurolysis in outpatient surgical pathways warrants further exploration. As healthcare systems increasingly shift toward same-day discharge protocols for TKA, ensuring effective pain control without complex catheter-based techniques becomes critical. Cryoneurolysis, with its capacity to provide prolonged analgesia without requiring continuous monitoring, could be an ideal solution for outpatient TKA. Future studies should explore how best to integrate cryoneurolysis into these evolving care models, ensuring optimal pain control while supporting faster discharge and improved patient outcomes across diverse healthcare settings.

Conclusion

Pre-operative cryoneurolysis appears to be a highly effective intervention for reducing post- operative pain and opioid use in TKA patients. The consistent findings across multiple trials indicate a significant clinical benefit in terms of pain management, reduced opioid reliance, and faster functional recovery. However, further large-scale, standardized trials are recommended to confirm these findings and establish comprehensive guidelines for their implementation in clinical practice.

Availability of Data and Material

The data supporting the findings of this systematic review are available within the included articles cited throughout the manuscript. No new datasets were generated or analyzed during this study. All data used in this review were obtained from publicly available sources and peer-reviewed publications referenced in the text.

Acknowledgments

The author acknowledges the contributions of the studies reviewed and the guidance provided by the PRISMA 2020 framework in structuring this systematic review.

References

1. Shichman I, Roof M, Askew N, Nherera L, Rozell JC, Seyler TM, et al. Projections and epidemiology of primary hip and knee arthroplasty in medicare patients to 2040-2060. JB JS Open Access. 2023;8(1):e22.00112. https://doi.org/10.2106/JBJS.OA.22.00112 PMid:36864906

2. Mihalko WM, Kerkhof AL, Ford MC, Crockarell JR Jr., Harkess JW, Guyton JL. Cryoneurolysis before total knee arthroplasty in patients with severe osteoarthritis for reduction of postoperative pain and opioid use in a single-center randomized controlled trial. J Arthroplasty. 2021;36(5):1590-8. https://doi.org/10.1016/j.arth.2020.11.013 PMid:33279353

3. Li JW, Ma YS, Xiao LK. Postoperative pain management in total knee arthroplasty. Orthop Surg. 2019;11(5):755-61. https://doi.org/10.1111/os.12535 PMid:31663286

4. Ashoorion V, Sadeghirad B, Wang L, Noori A, Abdar M, Kim Y, et al. Predictors of persistent post-surgical pain following total knee arthroplasty: A systematic review and meta-analysis of observational studies. Pain Med. 2023;24(4):369-381. https://doi.org/10.1093/PM/PNAC154 PMid:36255268

5. Lamplot JD, Wagner ER, Manning DW. Multimodal pain management in total knee arthroplasty: A prospective randomized controlled trial. J Arthroplasty. 2014;29(2):329-34. https://doi.org/10.1016/j.arth.2013.06.005 PMid:23850410

6. Lavand'homme P, Thienpont E. Pain after total knee arthroplasty: A narrative review focusing on the stratification of patients at risk for persistent pain. Bone Joint J. 2015;97-B(10 Suppl A):45-8. https://doi.org/10.1302/0301-620X.97B10.36524 PMid:26430086

7. Lavie LG, Fox MP, Dasa V. Overview of total knee arthroplasty and modern pain control strategies. Curr Pain Headache Rep. 2016;20(11):59. https://doi.org/10.1007/s11916-016-0592-6 PMid:27655139

8. Dasa V, Lensing G, Bliss R, Preciado J, Guirguis M. An ancient treatment for present-day surgery: Percutaneously freezing sensory nerves for treatment of postsurgical knee pain. Tech Reg Anesth Pain Manag. 2014;18(4):145-9.

9. Dasa V, Lensing G, Parsons M, Harris J, Volaufova J, Bliss R. Percutaneous freezing of sensory nerves prior to total knee arthroplasty. Knee. 2016;23(3):523-8. https://doi.org/10.1016/j.knee.2016.01.011 PMid:26875052

10. Langworthy M, Dasa V, Spitzer AI. Knee osteoarthritis: disease burden, available treatments, and emerging options. Ther Adv Musculoskelet Dis. 2024;16. doi:10.1177/1759720X241273009 https://doi.org/10.1177/1759720X241273009 PMid:39290780

11. Trescot AM. Cryoanalgesia in interventional pain management. Pain Physician. 2003;6(3):345-60. PMid:16880882

12. Ilfeld BM, Gabriel RA, Trescot AM. Ultrasound-guided percutaneous cryoneurolysis providing postoperative analgesia lasting many weeks following a single administration: A replacement for continuous peripheral nerve blocks?: A case report. Korean J Anesthesiol. 2017;70(5):567-70. https://doi.org/10.4097/kjae.2017.70.5.567 PMid:29046778

13. Elmallah RK, Chughtai M, Khlopas A, Newman JM, Stearns KL, Roche M, et al. Pain control in total knee arthroplasty. J Knee Surg. 2018;31(6):504-13. https://doi.org/10.1055/s-0037-1604152 PMid:28719941

14. Gabriel RA, Ilfeld BM. Novel methodologies in regional anesthesia for knee arthroplasty. Anesthesiol Clin. 2018;36(3):387-401. https://doi.org/10.1016/j.anclin.2018.05.002 PMid:30092936

15. Jennewine BR, Wing CW, Mihalko WM. Body habitus impact on success of cryoneurolysis for postoperative total knee arthroplasty pain control: A retrospective cohort study. Arthroplast Today. 2023;22:101164. https://doi.org/10.1016/j.artd.2023.101164 PMid:37521741

16. Urban JA, Dolesh K, Martin E. A multimodal pain management protocol including preoperative cryoneurolysis for total knee arthroplasty to reduce pain, opioid consumption, and length of stay. Arthroplast Today. 2021;10:87-92. https://doi.org/10.1016/j.artd.2021.06.008 PMid:34286056

17. Juncker RB, Mirza FM, Gagnier JJ. Reduction in opioid use with perioperative non-pharmacologic analgesia in total knee arthroplasty and ACL reconstruction: A systematic review. SICOT J. 2021;7:63. https://doi.org/10.1051/sicotj/2021063 PMid:34928208

18. Swisher MW, Ball ST, Gonzales FB, Cidambi KR, Trescot AM, Ilfeld BM. A Randomized controlled pilot study using ultrasound-guided percutaneous cryoneurolysis of the infrapatellar branch of the saphenous nerve for analgesia following total knee arthroplasty. Pain Ther. 2022;11(4):1299-307. https://doi.org/10.1007/s40122-022-00427-4 PMid:36018541

19. Lung BE, Karasavvidis T, Sharma AK, Amirhekmat A, Stepanyan H, McMaster W, et al. Cryoneurolysis is a safe, effective modality to improve rehabilitation after total knee arthroplasty. Life (Basel). 2022;12(9):1344. httsp://doi.org/10.3390/life12091344 PMid:36143381

20. Roth ZA, Sutton K, Wenende J, Pecka S. Preoperative cryoneurolysis for total knee arthroplasty: A case series. J Perianesth Nurs. 2023;38(1):33-38. https://doi.org/10.1016/j.jopan.2022.03.006 PMid:35753934

21. Biel E, Aroke EN, Maye J, Zhang SJ. The applications of cryoneurolysis for acute and chronic pain management. Pain Pract. 2023;23(2):204-15. https://doi.org/10.1111/papr.13182 PMid:36370129

22. Diep D, Mittal N, Sangha H, Farag J. Cryoneurolysis for non-cancer knee pain: A scoping review. Interv Pain Med. 2023;2(2):100247. https://doi.org/10.1016/j.inpm.2023.100247 PMid:39238668

23. Hansen CW, Carlino EK, Saunee LA, Dasa V, Bhandutia AK. Modern perioperative pain management strategies to minimize opioids after total knee arthroplasty. Orthop Clin North Am. 2023;54(4):359-68. https://doi.org/10.1016/j.ocl.2023.05.002 PMid:37718075

24. Mont MA, Lin JH, Spitzer AI, Dasa V, Rivadeneyra A, Rogenmoser D, et al. Cryoneurolysis associated with improved pain, function, and sleep in patients following total knee arthroplasty: Use of a new real-world registry. J Arthroplasty. 2025;40(1):92-101.e3. https://doi.org/10.1016/j.arth.2024.06.054 PMid:38942249

25. 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. 2017;25(8):1247-56. https://doi.org/10.1016/j.joca.2017.03.006 PMid:28336454

26. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated

guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71 PMid:33782057

27. Finneran Iv JJ, Ilfeld BM. Percutaneous cryoneurolysis for acute pain management: Current status and future prospects. Expert Rev Med Devices. 2021;18(6):533-43. https://doi.org/10.1080/17434440.2021.1927705 PMid:33961531

28. McMillan S, Zangrilli J, Amedee A, Dasa V. Safety of cryoneurolysis as a preoperative treatment for total knee arthroplasty (TKA). Surg Technol Int. 2023;42:350-2. https://doi.org/10.52198/23.STI.42.OS1694 PMid:37311570