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Systematic Review and Meta-Analysis

The Role of Cryotherapy After Total Knee Arthroplasty: A Systematic Review

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ABSTRACT

Background: Previous research shows conflicting evidence regarding the postoperative role of cryotherapy after total knee arthroplasty (TKA). This systematic review aims to further investigate the effect of various methods of cryotherapy on the following: (1) pain; (2) swelling; (3) postoperative opioid use; and (4) range of motion (ROM).

Methods: A strategic keyword search of Medline, Cochrane, Embase, and CINAHL retrieved randomized controlled trials examining cryotherapy following TKA published between February 1, 2017, and February 24, 2022. The studied outcomes included pain ratings, knee/limb swelling, opioid use, and ROM. Six studies were selected for inclusion in this review.

Results: Opioid use was significantly decreased in cryotherapy groups compared to noncryotherapy groups within the first postoperative week only ($P < .05$). This effect may be augmented by the use of computer-assisted (temperature regulated) cryotherapy devices, compared to other modalities including ice packs. Pain ratings also decrease, but this decrease may not be clinically relevant. Cryotherapy appears to confer no consistent benefit to ROM and swelling at any time point. Computer-assisted cryotherapy may be associated with decreased opioid consumption after TKA compared to traditional ice packs.

Conclusion: Cryotherapy's role after TKA appears to be in decreasing opioid consumption primarily in the first postoperative week. Pain ratings also decrease consistently with cryotherapy use, but this decrease may not be clinically relevant. Study heterogeneity requires further research focusing on optimizing cryotherapy modalities within the first postoperative week, and analyzing cost associated with modern outpatient postoperative TKA protocols.

Cryotherapy is a well-studied intervention for the management of perioperative pain in total knee arthroplasty (TKA) patients. For decades, researchers have investigated the use of such cooling devices to lower the temperature of body tissues to manage pain, inflammation, and provide early rehabilitation following TKA surgery [1]. Cryotherapy is a safe, non-narcotic intervention for

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postoperative pain control as part of a multimodal pain management approach. Some of the more popular methods of cryotherapy include traditional crushed ice packs, salt-ice packs, continuous circulating cold water cuffs, combined compression-circulating cold-water cuffs, and computer-assisted cryotherapy (CAC). CAC has become more popular in the last decade due to its ability to maintain a constant temperature (set by the operator) of the circulating water in the cuff.

TKA is a widely successful procedure, but it is often accompanied with high postoperative pain ratings [2–4]. The efficacy of cryotherapy as a pain management modality for TKA is still debated. Some studies have shown that CAC improves patient satisfaction and pain ratings after TKA [3,5–7]. Other studies have shown that traditional ice packs or salt ice packs are equally or more effective than CAC in improving pain, swelling, range of motion (ROM), and opioid consumption [8–12]. This contradictory evidence makes it difficult to conclude which outcome measures are improved the most from cryotherapy use.

Two previous systematic reviews have attempted to answer the question of whether cryotherapy is helpful for improving postoperative pain, swelling, ROM, and opioid consumption [3,13]. One was able to conclude that pain and postoperative opioid consumption likely benefit from cryotherapy, but did not reach any conclusions regarding its effect on ROM and swelling [3]. They also concluded that CAC might be superior to ice packs for improving the above outcomes, but cited multiple studies disagreeing with this conclusion [8–12]. Another systematic review was unable to draw any conclusions regarding whether cryotherapy was indeed helpful in TKA recovery at all [13]. Since the publication of these reviews, 6 randomized trials investigating various forms of cryotherapy in TKA recovery have been published.

This review aimed to clarify the role of cryotherapy regarding several important outcome measures in the setting of TKA recovery by synthesizing new information from recent studies. More specifically, this paper aims to provide clarity to the effect of various methods of cryotherapy on: (1) pain; (2) swelling; (3) postoperative opioid use; and (4) ROM.

Methods

This is a systematic review of studies on the use of cryotherapy after TKA published between February 1, 2017 and February 24, 2022. Our study used the design by Joanna Briggs Institute (JBI) on randomized control trials and Preferred Reporting Items for Systematic Reviews and Meta-analyses 2020 guidelines for reporting systematic reviews [14,15].

Search Strategy

One author (P.W.) searched the Pubmed/Medline, Cochrane, CINAHL, and Embase (OVID) databases on February 24, 2022, using the keywords “knee” and “cryotherapy”. Despite using broad search terms, the authors determined that the number of results (512) was reasonable for screening. These terms also ensured a comprehensive review of current literature on the subject.

Screening, Inclusion/Exclusion Criteria

Only studies between February 1, 2017 and the search date (February 24, 2022) were included in the current review to limit redundant findings. No studies from prior systematic reviews [3,13] were included in the present study. Duplicates and papers written in languages other than English were excluded. Two authors (P.W. and C.N.) independently screened all the articles using our inclusion and exclusion criteria. Each study was reviewed first by title and abstract, then by full text if more detail was required to make the decision of inclusion or exclusion. Inclusion criteria for this study were as follows: randomized control trial design and title or abstract including the use of cryotherapy as part of recovery from primary TKA. Exclusion criteria were as follows: studies that did not discuss a primary or secondary outcome for the postprimary TKA population, study designs other than randomized control trials, revision TKA, and knee surgeries other than primary TKA.

Data Extraction

Data were extracted by one author (P.W.). The following data was systematically extracted were as follows: (1) type of study; (2) number of total control group, and experimental group participants; (3) parameters assessed by the study; (4) timing of evaluation of these parameters; (5) the protocol of administration of the cryotherapy; (6) concomitant analgesia used by participants in the study; (7) salient findings for each parameter assessed; and (8) the favored cohort in the study. For the purposes of this article, the term “CAC” will be used to refer to any device that utilizes continuous circulating cold flow through a fitted cuff and/or constant, regulated temperature settings.

The initial search results identified 512 articles. After duplicates were removed, 301 articles were excluded during title and abstract screening. There were 19 remaining articles. Full-text versions of these articles were then assessed for eligibility. Ten of these studies were excluded because of inclusion of subjects who did not undergo a TKA. Two were excluded due to not having a randomized design. One study was excluded due to being written in a non-English language. Six studies were included in this systematic review (See Fig. 1).

Outcomes of Interest

All outcomes measured in the included studies were considered “of interest” and were therefore, reported in this paper. These outcomes included pain, patient satisfaction, opioid use, knee joint swelling/girth, ROM, strength, functional outcome measures, and patient-reported outcome measures.

Characteristics of Included Studies

The included studies were all randomized control trials published between February 1, 2017, and February, 24, 2022. In total, there were 499 subjects among these 6 studies. A more detailed summary of the study characteristics and salient findings can be found in Table 1.

Methodological Quality Assessment

The methodological quality of these studies was assessed using the JBI protocol for appraising randomized controlled trials. This criterion consists of 13 vetting questions that evaluate the validity of the methods for randomization, blindness, completeness of follow-up, and appropriateness of analysis [16]. One study [17] met all 13 criteria, one study [18] met 12/13 criteria, 3 studies [19–21] met 11/13 criteria due to the ambiguity regarding whether the deliverers of treatment and statisticians were blinded to assignment, and one study [22] met 10/13 criteria as it was non-blinded, therefore the blindness questions were not applicable. Although there are no published guidelines for JBI score interpretation for randomized control trials, the authors used the JBI protocol to collectively determine that all 6 of the included studies demonstrated adequate methodology and the overall risk of bias was low.

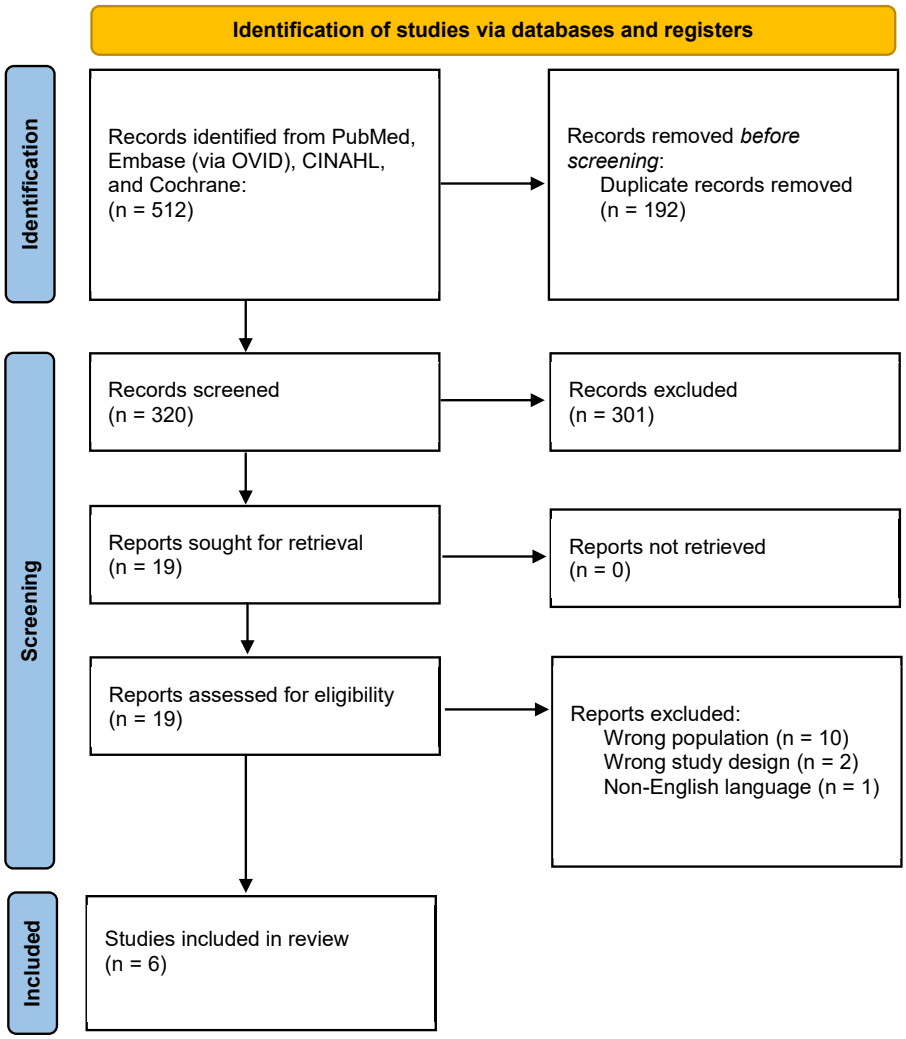

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta Analyses) flow diagram. Keywords: Knee, cryotherapy.

Results

Pain

Among the 3 studies that compared cryotherapy groups to noncryotherapy groups, 2 demonstrated that cryotherapy was superior in decreasing pain ratings during the first postoperative week ($P < .05$) [19,22]. In one study, this means decrease was 1.08 points on the numerical pain rating scale (NPRS) at discharge compared to control [19]. This is less than the minimal clinically important difference (MCID) of 1.39 ± 1.05 as defined by Kendrick et al [23]. The other study did not quantify the difference found between groups other than stating that it was significant, favoring the cryotherapy group ($P < .05$) [22]. The third study comparing cryotherapy to noncryotherapy showed no difference in pain ratings during the first week [18]. No significant difference in pain ratings was observed between cryotherapy and noncryotherapy groups at 2 weeks, 6 weeks [22], or 3 months [19].

CAC appeared to be more effective than traditional ice packs for reducing NPRS-rated "pain in motion", but not "pain at rest" within the first postoperative week ($P < .05$) [20]. The difference between CAC and control groups was 0.9 points on NPRS on average, favoring the CAC group. Furthermore, lower temperature settings (10-12 °C) better reduced NPRS pain ratings immediately after application (0.9-point reduction on average, compared to 0.7 in the warm group) within the first postoperative week compared to warmer temperature settings (21 °C) ($P < .05$) [17]. Lastly, mirabilite salt-packs were shown to be more effective than traditional ice packs for reducing pain at 72 hours postoperatively ($P < .05$), but no significant difference was found between groups at 24 hours or 48 hours postoperatively [21]. No significant differences in pain ratings were found between the studied methods of application at any time beyond the first postoperative week. It is also worth noting that none of the significant differences in pain ratings observed with CAC meet proposed MCID levels for Visual Analogue Scale ratings (15 mm) [24] or NPRS ratings (1.39 ± 1.05) [23] compared to other cryotherapy application methods.

Swelling

Each of the 6 studies used infrapatellar, midpatellar, and suprapatellar circumferential measurements to assess joint swelling/edema. Cryotherapy appeared to have a minimal effect on operative leg swelling. Only one study demonstrated a significant difference in operative leg edema in a cryotherapy group compared to a noncryotherapy group within the first postoperative week ($P < .05$) [19]. No study demonstrated a significant

difference between cryotherapy and noncryotherapy groups beyond the first postoperative week. Within the first postoperative week, mirabilite salt packs and CAC were found to be more effective than traditional ice packs in reducing swelling [20,21]. These studies did not assess outcomes beyond one week. Lastly, colder CAC temperatures (10-12 °C) appeared to be no more beneficial for reducing swelling than slightly warmer CAC temperature settings (21 °C) at any time point of evaluation, including the first postoperative week [17].

Opioid Use

Cryotherapy appeared to have both a statistically and clinically significant effect on opioid consumption. Opioid use was assessed in 3 studies, all of which evaluated it within the first postoperative week [17,20,22]. In one study, CAC appeared to be superior to noncryotherapy at reducing opioid consumption [22]. The noncryotherapy group consumed 15.6 mg of oxycodone (23.4 morphine milligram equivalents [MME]) per patient over the course of the first postoperative week compared to 7.5 mg (11.2 MME) in the CAC group, demonstrating a 52% reduction in consumption in the CAC group. At 24 hours postoperatively, the difference in total opioid consumption between groups was 40% (75 MME compared to 187 MME), exactly equal to the MCID defined by Laigaard et al for this time frame [24]. Another study showed ice packs had a similar effect to that of CAC in reducing opioid consumption, and no significant difference was found in opioid consumption between CAC and ice pack groups [20]. Additionally, colder CAC temperature settings (10-12 °C) reduced tramadol consumption by 56% ($P = .034$) (more than warmer temperature settings [21 °C] [$P < .05$]) [17]. This difference favoring the colder group also met MCID (>40%) at 24 hours postoperatively, according to Laigaard et al [24].

Range of Motion

ROM was largely unaffected by cryotherapy. Of the 3 studies that compared cryotherapy groups to noncryotherapy groups, only one demonstrated the superiority of cryotherapy (98 degrees flexion versus 91 degrees flexion [$P = .007$]) at postoperative day 4, but not at postoperative day one [18]. ROM was similar at all other time points assessed between the cryotherapy and noncryotherapy groups. Mirabilite salt ice packs were found to be superior to traditional ice packs at 72 hours postoperatively (74.5 degrees flexion versus 72.0 degrees flexion ($P = .024$)) [21]. Although there is no widely accepted MCID for knee flexion currently, this small difference in ROM is likely too small to be clinically relevant. In the single included study that compared CAC to ice packs, authors found a statistically significant difference favoring the CAC group in flexion ROM at postoperative day 6 ($P < .05$), but not on postoperative day 2 or four [20]. The inconsistent effect of cryotherapy on ROM between studies is isolated to the first postoperative week only.

Surgical Techniques

Description of surgical techniques varied among the studies. The use of a tourniquet was reported in 2 studies [18,21] and one [17] of the other 4 studies explicitly stated that a tourniquet was not used. One study included both patients that had spinal and general anesthesia, while the rest did not report on the method of anesthesia used [17]. None of the studies reported on prior opioid use or naivety. Also, none of the studies explicitly stated the use of a preoperative adductor canal nerve block.

Discussion

The growing body of literature on this topic indicates that cryotherapy is a safe and useful intervention for patients recovering from TKA. However, the heterogeneity of studies makes it difficult to determine or quantify the benefit of cryotherapy in this setting. Two previous systematic reviews in the last decade have attempted to answer the questions of whether cryotherapy is a worthwhile postoperative intervention for TKA and if so, which method of cryotherapy is superior [3,13]. Both illustrated the conflicting evidence regarding cryotherapy's use. This review suggests that the benefit of cryotherapy in postoperative TKA management is likely restricted to the first postoperative week only (regardless of the chosen modality) and its primary benefit is in decreasing postoperative opioid use.

This systematic review is limited by the heterogeneity of the studies included. Sources of heterogeneity include the use of various surgical techniques (including computer-assisted TKA), differences in postoperative care protocols, and nonstandardized evaluation timing. Multiple studies did not define "regular" postoperative care in control groups, which may introduce confounding variables. However, using broad "regular" postoperative care may provide more generalizability to the studies by comparing interventional cryotherapy groups to typical current practices. The finding that pain and opioid consumption decreases were limited to the first postoperative week may be affected by limited ability of the study personnel to monitor cryotherapy use and compliance after the first postoperative week. Additionally, the present review did not conduct a meta-analysis of data as this was not feasible given the high level of heterogeneity among the studies. Therefore, its conclusions are qualitative and not subject to the rigor of data analysis.

It is worth highlighting that all improvements in the assessed parameters were found only within the first postoperative week. None of the studies that evaluated outcomes at longer intervals found significant differences in pain, swelling, or ROM at 2 weeks, 6 weeks [17,22], or 12 weeks [19] postoperatively between cryotherapy and noncryotherapy groups. Previous studies have shown similar findings, demonstrating that the benefit of cryotherapy is seen mostly in the immediate postoperative period, and there is less benefit after 1 week postoperatively for pain, ROM, and swelling [3,25] This, combined with our findings, indicates that surgeons should expect cryotherapy to decrease pain only during the first postoperative week, although this may not be a clinically significant decrease. Beyond the first postoperative week, cryotherapy shows no statistically significant benefit in any of the assessed parameters.

The lack of consistent and meaningful improvements in ROM and swelling found is consistent with previous studies that have demonstrated no significant improvement in these parameters when using cryotherapy in the immediate postoperative period [11,12]. Prior research has similarly failed to demonstrate CAC's superiority in improving immediate postoperative ROM and swelling compared to traditional ice packs [5,8–10,21,22]. Therefore, cryotherapy's utility in improving short- and long-term outcomes regarding ROM and swelling cannot be confirmed at this time.

Our findings are representative of the current body of evidence on this topic in that the majority of studies suggest that cryotherapy indeed reduces immediate postoperative pain [3,13]. The determination of MCID for pain control is controversial given the multifactorial nature of pain [24]. Currently, no MCID has been established for postoperative TKA pain, making the interpretation of pain ratings in this setting difficult. Regardless, no studies in this review achieved injury-nonspecific MCID [23] for NPRS or VAS [24]

Table 1
Summary of Findings.

Study (Author, Year)	No. of Patients	Modality		Parameters Assessed	Time points of Evaluation	Salient Finding for Each Parameter Assessed	Favored Cohort
		Control (n)	Study (n)				
Yuksel et al (2022) [19]	100	Standard rehabilitation (34)	(1) Kinesio tape (KT) group: standard rehab + kinesio taping (33); (2) Cryotherapy (CT) group: standard rehab + cold packs (33)	Pain, edema, range of motion (ROM), quadriceps femoris and hamstring muscle strength, timed-up-and-go, 10-minute walk test, Iowa Level of Assistance Scale, Hospital for Special Surgery knee score, and Short Form-12	Discharge, Postoperative 3rd mo	1) No significant differences in ROM 2) CT group had significantly less swelling at discharge compared to the KT group ($P < .05$). 3) Both KT and CT groups were superior to control group ($P < .05$). No significant difference between KT group and CT group in pain at discharge ($P = .072$). 4) All groups were similar in all parameters at the 3rd postoperative month ($P < .05$)	Cold pack superior to kinesio tape and control groups
Sadoghi et al (2018) [20]	97	Conventional cold packs: ST group (51)	Continuous cooling: CT group (46)	ROM, pain intensity (Numerical Rating Scale) at rest and in motion, knee girth (midpatellar, 7 cm proximal to the patellar base, 7 cm distal to the apex of the patellae), pain medication consumption	Admission day, 2nd, 4th, and 6th postoperative days	1) No significant difference in swelling 2) Pain in motion significantly decreased on postoperative day 2 in CT group (3.7 points ± 2.1), compared to 4.6 ± 2.1 for the ST group ($P = .034$). No significant differences in pain at rest between groups. 3) ROM: CT group superior to ST group on postoperative day 6 (86 degrees ± 7 versus 80 degrees ± 14) ($P = .021$). No significant difference on days 2 or 4. 4) Nonstatistically significant decrease in hydromorphone consumption in the CT group compared to the ST group.	Continuous cold flow device
Zhong et al (2021) [21]	80	Conventional cold pack: WIP group (40)	Mirabilite ice pack: MIP group (40)	Pain (Visual Analogue Scale), swelling, ROM, length of hospital stay, and serum C-reactive protein levels	24 h, 48 h, and 72 h post-operatively	1) Statistically significant lower knee girth at 48 h ($P < .05$) and 72 h ($P < .05$) postoperatively in the MIP group compared to WIP group 2) Pain ratings (VAS) were significantly lower in the MIP group when compared to the WIP group at 48 h and 72 h postoperatively ($P = .018$). 3) ROM was statistically significantly higher in MIP group ($P = .024$)	Mirabilite ice pack
Thijs et al (2019) [17]	60	Warm group (30)	Cold group (30)	Opioid use, knee swelling, visual hematoma, and patient reported outcome measures.	1 wk, 2 wk, and 6 wk postoperatively Opioid use was measured for the first 4 postoperative days.	1) No significant differences in ROM or swelling 2) Significant reduction in pain after each cryotherapy session within the first postoperative wk for the cold group only. Mean reduction was 0.9 on Numerical Rating Scale ($P = .0008$). Nonsignificant reduction in the warm group was observed. 3) Cold group consumed significantly less pain medication over the first postoperative week versus the Warm group ($P = .001$).	10-12 degrees C computer-assisted cryotherapy
Chen et al (2020) [18]	60	Control group: CPM and no programmed cryotherapy (30)	Intervention group: CPM + programmed cryotherapy (30)	Pain (Numerical Rating Scale), Short Form - McGill Pain Questionaire, ROM, joint circumference, thigh circumference, calf circumference	POD1 and POD4 or until the patients were discharged	1) No significant differences in swelling or pain 2) ROM: Intervention group had significantly higher flexion ROM on postoperative day 4 only (98 degrees versus 91 degrees) ($P = .007$).	CPM and programmed cryotherapy
Brouwers (2021) [22]	102	Regular group: R-group (51)	Cold (computer-assisted cryotherapy) group: C-group (51)	Pain (Numerical Rating Scale), opioid use, active range of motion, timed-up-and-go, joint girth (circumferential	Patient satisfaction was measured at 1-, 2-, and 6-wk postoperatively (WPO). Pain and opioid use was evaluated each day for the first seven	1) No significant differences in swelling or ROM 2) C-group used significantly less oxycodone than R-group during the first postoperative week ($P = .001$)	Computer-assisted cryotherapy

measurements), patient reported outcome measures (Knee Injury Osteoarthritis Outcome Score (KOOS) and Work Osteoarthritis or Joint-Replacement Questionnairre (WORQ)), patient satisfaction	postoperative days. KOOS and WORQ were assessed preoperatively, 2-WPO, and 6-WPO. timed-up-and-go, active range of motion, and joint circumference (proximal to patella, midpatella, and distal to patella) were assessed preoperatively and at 6-WPO.	3) C-group reported less pain at rest and during loading activities within the first postoperative week ($P < .05$)

pain ratings. However, the majority of the studies still demonstrated a statistically significant decrease in pain compared to noncryotherapy alternatives. Therefore, cryotherapy proves to be a safe tool for decreasing postoperative TKA pain, but expectations regarding the magnitude of its effect on pain should be tempered when discussing postoperative pain management with patients. Prior studies have similarly shown conflicting evidence regarding the superiority of CAC or traditional ice packs in reducing pain [5,8–10,12,26,27]. Therefore, the superiority of CAC or ice packs in the first postoperative week pain reduction is inconclusive at this time.

The findings of our study demonstrate that opioid use is significantly decreased in response to cryotherapy during the immediate postoperative period. This may relate to opioids being most used in the first postoperative week, which is the time in which cryotherapy is most effective. These findings contrast with a previous systematic review and meta-analysis that concluded cryotherapy had no significant effect on postoperative narcotic consumption [25]. This difference might be due to a high level of heterogeneity among studies. Also, in contrast to previous data suggesting that CAC temperature settings do not play a role in opioid consumption [28], the findings of this review suggest that CAC devices which are set to 10-12 °C significantly reduce opiate consumption compared to those set to 21 °C [17]. This difference could be due to the use of different temperatures in the prior study (23.89 °C and 7 ° C). In short, cryotherapy, be it CAC or traditional ice pack, seems to reduce opioid consumption and colder temperatures (10-12 °C) may augment this benefit.

Conclusion

This systematic review provides clarification regarding the benefits of cryotherapy use after TKA. Current evidence supports the use of cryotherapy for opioid consumption during TKA recovery in the first postoperative week. Pain is also decreased, but this may not be clinically relevant. Swelling and ROM appear to receive no significant benefit from the use of cryotherapy in this setting. Recent research has tried to establish optimized delivery methods. However, heterogeneous protocols make comparison challenging. Future research should focus on outcomes evaluated in the first postoperative week, consider multiple delivery methods and, importantly, the ease and cost of application for patients.

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