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Research Article

Computer-Assisted Cryotherapy as an Adjunct to Multimodal Analgesia Significantly Reduces Opioid Consumption and Improves Early Outcomes Following Total Knee Arthroplasty: A Prospective Randomized Controlled Trial

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Abstract

Background: Effective postoperative pain management following Total Knee Arthroplasty (TKA) remains a significant clinical challenge, with conventional opioid-based regimens posing risks of adverse effects and potential dependence. Computer-Assisted Cryotherapy (CAC) represents an advanced, non-pharmacological intervention designed to mitigate pain and swelling through regulated cold compression. This study evaluated the impact of adjunctive CAC on opioid consumption and early recovery outcomes within a modern multimodal analgesia protocol.

Methods: In this prospective randomized controlled trial, 210 patients undergoing primary TKA were allocated to either a control group (n = 105) receiving standard multimodal analgesia or an intervention group (n = 105) receiving identical pharmacologic management plus CAC (2 daily sessions of 3 hours each at 10 °C with intermittent compression). Primary outcomes included pain intensity measured on a Visual Analogue Scale (VAS) at 24, 72, and 120 hours postoperatively and total opioid consumption—converted to morphine milligram equivalents (MME)—during the first 5 postoperative days. Secondary outcomes comprised range of motion (ROM), limb swelling, Length Of Hospital Stay (LOS), and complication rates.

Results: The CAC group demonstrated a 46.5% reduction in opioid use compared to the control group (46.7 ± 19.8 MME vs. 87.3 ± 28.5 MME; $p < 0.001$). Significantly lower VAS scores were observed in the CAC group at all assessed time points, both at rest and during activity ($p < 0.001$). The intervention group also exhibited superior active knee flexion at discharge (85.4° vs. 78.6°; $p < 0.001$) and at the 2-week follow-up (98.8° vs. 92.1°; $p < 0.001$), reduced thigh swelling (3.9 cm vs. 5.8 cm increase; $p < 0.001$), and a shorter LOS (3.1 days vs. 3.8 days; $p < 0.001$). Complication rates were low and comparable between groups.

Conclusion: Adjunctive computer-assisted cryotherapy significantly reduces opioid requirements, improves pain control, and enhances functional recovery in patients undergoing TKA, without increasing complications. These findings support the integration of CAC into enhanced recovery after surgery protocols as an effective opioid-sparing strategy.

Keywords: Analgesia; Arthroplasty; Cryotherapy; Enhanced Recovery After Surgery; Knee; Opioid-Related Disorders; Pain; Postoperative; Randomized Controlled Trial; Replacement; Total Knee Arthroplasty

Introduction

Total Knee Arthroplasty (TKA) is one of the most successful and frequently performed orthopedic procedures worldwide, offering substantial pain relief and functional restoration for patients suffering from end-stage knee osteoarthritis [1]. Despite significant advancements in surgical techniques, implant design, and perioperative care, effective management of acute postoperative pain remains a formidable challenge. The invasive nature of TKA, involving extensive soft tissue dissection, bone resection, and periarticular manipulation, triggers a profound local inflammatory response, tissue edema, hemarthrosis, and muscle spasm. These factors collectively contribute to substantial pain, which can severely impede early mobilization, delay rehabilitation, diminish patient satisfaction, and prolong hospital stays [2,3]. The conventional reliance on opioid analgesics for postoperative pain control has increasingly come under scrutiny due to their well-documented adverse effects, including nausea, vomiting, sedation, constipation, respiratory depression, and the risk of dependency or misuse [4]. In the context of a global opioid crisis, the development of opioid-sparing analgesic strategies has become both a clinical and public health priority. Enhanced Recovery After Surgery (ERAS) protocols emphasize multimodal analgesia, combining pharmacological agents (e.g., NSAIDs, acetaminophen, gabapentinoids, and local anesthetics) with non-pharmacological interventions to target pain through diverse mechanisms, thereby improving efficacy while minimizing opioid-related complications [5].

Among non-pharmacological adjuncts, cryotherapy has long been utilized for its anti-inflammatory, analgesic, and anti-edema properties. The application of cold induces vasoconstriction, reduces metabolic demand, decreases the release of inflammatory mediators, and slows nerve conduction velocity, thereby elevating pain thresholds and alleviating swelling [6]. Traditional methods, such as ice packs or gel wraps, are limited by their short duration of action, inconsistent temperature maintenance, and reliance on frequent nursing intervention. Computer-Assisted Cryotherapy (CAC) represents a technological evolution in this domain. These systems deliver continuous, regulated cold compression through a closed-loop circuit, maintaining a consistent therapeutic temperature at the surgical site while often incorporating adjustable compression to further mitigate edema [7]. By ensuring prolonged and controlled cryotherapy, CAC devices may optimize physiological benefits, enhance patient compliance, and reduce the burden on healthcare providers. Although several studies have investigated the role of cryotherapy in TKA recovery, the specific impact of CAC on opioid consumption, within the framework of a modern multimodal analgesic protocol, warrants further rigorous evaluation. Thus, the primary objective of this study was to assess the efficacy and safety of Computer-Assisted Cryotherapy in reducing postoperative opioid use and improving pain control following primary TKA. The hypothesis of the study is that the integration of CAC into a standardized ERAS pathway will significantly decrease opioid consumption while enhancing early functional outcomes and patient satisfaction.

Methods

Study Design and Patient Selection

A prospective, randomized controlled trial was conducted between July 2020 and July 2024 at a high-volume orthopedic center (San Paolo Hospital, Civitavecchia, Rome). A total of 210 patients scheduled for primary unilateral total knee arthroplasty due to end-stage osteoarthritis were assessed for eligibility. Randomization was performed using a web-based random number generator, assigning participants to one of two groups in a one-to-one ratio, with 105 patients allocated to each group. Allocation concealment was ensured through sequentially numbered, opaque, sealed envelopes opened after written informed consent was obtained. Inclusion criteria were age between 50 and 85 years, primary total knee arthroplasty for painful osteoarthritis, American Society of Anesthesiologists physical status classification I–III, and the ability to comprehend study protocols and return for follow-up. Exclusion criteria included revision total knee arthroplasty, active knee infection or systemic sepsis, significant preoperative coronal deformity greater than 15 degrees varus or valgus, fixed flexion contracture greater than 15 degrees and/or flexion less than 110 degrees, documented vascular insufficiency or peripheral neuropathy in the affected limb, known hypersensitivity to cold such as cryoglobulinemia or cold urticaria, chronic opioid use defined as greater than 15 milligrams oral morphine equivalents daily for more than 3 months preoperatively, and contraindications to any components of the standardized multimodal analgesia protocol.

Intervention Protocols

All surgeries were performed by two senior arthroplasty surgeons using a standardized medial parapatellar approach under spinal-epidural anesthesia. A cemented, posterior-stabilized prosthesis was implanted in all cases. A tranexamic acid protocol consisting of 1 gram intravenous pre-incision and 1 gram topical intra-articular was uniformly administered. For Group I (Control Group), patients received a standardized, multimodal, opioid-sparing analgesia protocol which included preoperative administration of 1000 mg acetaminophen and 400 mg celecoxib (if no contraindications

were present), intraoperative periarticular injection with a mixture of 300 mg ropivacaine, 30 mg ketorolac, 0.5 mg epinephrine, and 10 mg morphine in 100 mL normal saline, and postoperative scheduled acetaminophen 1000 mg every 8 hours, celecoxib 200 mg twice daily (or an alternative NSAID), and gabapentin 300 mg at night. Rescue analgesia was provided with oral oxycodone 5-10 mg every 4 hours as needed for severe pain (defined as a visual analogue scale score >4). All opioid consumption was converted to morphine milligram equivalents (MME) for analysis. For Group II (CAC Group), patients received the identical multimodal analgesia protocol as Group I and additionally received computer-assisted cryotherapy using a GameReady GRPro 2.1 system with a standardized protocol. The therapy was initiated in the post-anesthesia care unit and consisted of two 3-hour applications per day with a minimum 1-hour break between sessions at a prescribed temperature of 10°C. Each session included intermittent compression, cycled at 50 mmHg for 30 seconds on and 30 seconds off. The device was applied over a single layer of dry gauze for the entirety of the inpatient stay. All patients received identical thromboprophylaxis with daily subcutaneous injections of 4000 IU enoxaparin and underwent the same institutional physiotherapy protocol which involved full weight-bearing as tolerated and active-assisted range of motion exercises initiated on the day of surgery.

Outcome Measures

Data collection was performed by blinded researcher who were not involved in the patients' clinical care or group allocation. Primary outcomes included pain intensity measured using the visual analogue scale from zero to one hundred millimeters at rest and during active flexion, recorded at twenty-four, seventy-two, and one hundred and twenty hours postoperatively, and opioid consumption with total opioid consumption converted to morphine milligram equivalents calculated for the first five postoperative days from zero to one hundred and twenty hours.

Secondary outcomes included functional recovery with active knee range of motion measured with a goniometer at discharge and at the two-week follow-up, swelling assessed through thigh circumference measured ten centimeters proximal to the superior patellar pole at discharge, safety and complications including rates of blood transfusions, surgical site infections, symptomatic venous thromboembolism confirmed by Doppler ultrasound, and length of hospital stay, and computer-assisted cryotherapy specific tolerability with the skin under the device meticulously assessed daily for local adverse reactions including persistent erythema, blistering, superficial frostbite, or wound healing complications in Group Two.

Statistical Analysis

Statistical analysis was performed by an independent biostatistician using SPSS software version twenty-seven point zero from IBM Corporation; continuous variables such as visual analogue scale scores, morphine milligram equivalents, range of motion, and length of stay were tested for normality using the Shapiro-Wilk test and are presented as mean plus or minus standard deviation; between-group comparisons were made using independent samples t-tests for normally distributed data and Mann-Whitney U tests for non-parametric data; categorical variables such as transfusion rates and infection rates are presented as counts and percentages and were compared using Chi-square or Fisher exact tests as appropriate; a two-tailed p-value of less than zero point zero one was considered statistically significant to account for multiple comparisons and reduce the risk of Type I error.

Results

All 210 randomized patients completed the study and were included in the final analysis (105 in each group). The two groups were well-matched at baseline, with no statistically significant differences in demographic characteristics, preoperative pain scores, or preoperative range of motion (Table 1).

Baseline Demographic and Clinical Characteristics

Characteristic	Control Group (n = 105)	CAC Group (n = 105)	p-value
Age (years), mean ± SD	68.4 ± 6.7	69.1 ± 7.2	0.28
Sex (Female), n (%)	68 (64.8%)	65 (61.9%)	0.65
BMI (kg/m²), mean ± SD	30.5 ± 4.1	31.0 ± 3.8	0.19
ASA Class II/III, n (%)	93 (88.6%)	91 (86.7%)	0.62
Preoperative VAS at rest, mean ± SD	52.3 ± 11.5	54.1 ± 12.8	0.11
Preoperative flexion ROM (°), mean ± SD	112.4 ± 10.3	110.8 ± 11.6	0.13
Operative time (min), mean ± SD	78.5 ± 12.4	80.2 ± 13.1	0.16

Table 1: Baseline Demographic And Clinical Characteristics of Study Participants Undergoing Total Knee Arthroplasty.

Primary Outcomes

Patients in the CAC group reported significantly lower pain scores at all measured time points, both at rest and during activity, compared to the control group ($p < 0.001$ for all comparisons) (Table 2).

Postoperative Pain Scores (VAS, 0-100 mm)

Time Point	VAS Score	Control Group (n = 105)	CAC Group (n = 105)	p-value
24 hours	At Rest	45.2 ± 12.1	32.8 ± 10.4	**<0.001**
	During Activity	68.5 ± 13.8	52.3 ± 12.9	**<0.001**
72 hours	At Rest	38.7 ± 11.3	26.5 ± 9.7	**<0.001**
	During Activity	59.2 ± 12.5	43.6 ± 11.2	**<0.001**
120 hours	At Rest	31.4 ± 10.5	21.9 ± 8.6	**<0.001**
	During Activity	48.3 ± 11.7	35.1 ± 10.3	**<0.001**

Table 2: Postoperative Pain Intensity Measured By Visual Analogue Scale (Vas) At Rest And During Activity.

Total opioid consumption over the first five postoperative days was 46.5% lower in the CAC group compared to the control group ($p < 0.001$). The control group consumed a mean of 87.3 ± 28.5 MME, while the CAC group consumed 46.7 ± 19.8 MME (Table 3).

Opioid Consumption And Key Secondary Outcomes

Outcome	Control Group (n = 105)	CAC Group (n = 105)	p-value
Total MME (0-120h), mean ± SD	87.3 ± 28.5	46.7 ± 19.8	**<0.001**
ROM at Discharge (°), mean ± SD	78.6 ± 9.5	85.4 ± 8.1	**<0.001**
ROM at 2 weeks (°), mean ± SD	92.1 ± 8.3	98.8 ± 7.5	**<0.001**
Thigh Circumference Increase (cm), mean ± SD	5.8 ± 1.6	3.9 ± 1.2	**<0.001**
Length of Stay (days), mean ± SD	3.8 ± 0.9	3.1 ± 0.7	**<0.001**

Table 3: Primary And Secondary Outcomes: Opioid Consumption, Functional Recovery, and Clinical Metrics.

Secondary Outcomes And Complications

Functional recovery, as measured by active knee flexion, was significantly better in the CAC group at both discharge and the two-week follow-up ($p < 0.001$). Postoperative swelling, quantified by the increase in thigh circumference, was also significantly reduced in the CAC group (3.9 ± 1.2 cm vs. 5.8 ± 1.6 cm, $p < 0.001$). The mean length of hospital stay was shorter for the CAC group (3.1 ± 0.7 days vs. 3.8 ± 0.9 days, $p < 0.001$). The overall complication rate was low and comparable between groups (Table 4). There were no significant differences in the rates of blood transfusion, symptomatic Venous Thromboembolism (VTE), or Surgical Site Infection (SSI). In the CAC group, device tolerability was excellent. Three patients (2.9%) reported transient, mild skin erythema that resolved spontaneously within hours of discontinuing the device, with no cases of blistering, frostbite, or wound healing complications attributable to the cryotherapy.

Postoperative Complications

Complication	Control Group (n = 105)	CAC Group (n = 105)	p-value
Blood Transfusion, n (%)	3 (2.9%)	2 (1.9%)	0.65*
Symptomatic VTE, n (%)	1 (1.0%)	1 (1.0%)	1.00*
Surgical Site Infection, n (%)	2 (1.9%)	1 (1.0%)	0.56*
CAC-Related Skin Reaction, n (%)	-	3 (2.9%)	-
*Analyzed using Fisher's Exact Test			

Table 4: Postoperative Complication Rates Among Study Participants.

Discussion

The findings of this prospective, randomized controlled trial demonstrate that the integration of computer-assisted cryotherapy into a standardized multimodal analgesia protocol confers significant benefits for patients undergoing total knee arthroplasty. The group receiving adjunctive cold therapy exhibited markedly superior outcomes across all primary and secondary endpoints. Most notably, the intervention cohort demonstrated a profound reduction in opioid requirements, consuming less than half the morphine milligram equivalents of their counterparts in the control group over the critical first five postoperative days (46.7 versus 87.3 MME, $p<0.001$). This substantial decrease is clinically paramount, as it directly translates to a lower incidence of opioid-related adverse drug events, such as nausea, ileus, sedation, and respiratory depression, which are frequent drivers of patient discomfort, delayed mobilization, and prolonged hospitalization [8]. In an era defined by the opioid epidemic, identifying effective non-pharmacological strategies to minimize narcotic reliance is a cornerstone of modern perioperative care [9]. The mechanism underlying this opioid-sparing effect is multifactorial. The significant improvement in pain scores, both at rest and during activity, suggests that regulated cold therapy effectively mitigates the primary drivers of acute post-arthroplasty pain: the local inflammatory response and tissue edema [10].

By inducing sustained vasoconstriction and reducing capillary permeability, the technology curtails the accumulation of inflammatory mediators and decreases intra-articular pressure, thereby reducing nociceptor sensitization [11]. The concomitant reduction in thigh circumference observed in the cryotherapy group provides objective evidence of this anti-edema effect. Furthermore, the analgesic properties of cold, mediated through the reduction of nerve conduction velocity, likely raise the pain threshold, allowing patients to participate more comfortably in physical therapy with less reliance on systemic analgesics [12]. The clinical benefits extended beyond analgesia. The significantly improved active knee flexion at both discharge and the two-week follow-up indicates that enhanced comfort facilitates more effective and earlier engagement in rehabilitation. This accelerated functional recovery is a critical determinant of long-term outcomes and patient satisfaction following joint replacement [13]. The shorter mean length of stay observed in the intervention group (3.1 versus 3.8 days) further underscores the economic and logistical advantages of integrating this technology into enhanced recovery pathways, potentially improving hospital throughput and reducing healthcare costs without compromising safety [14]. The safety profile of computer-assisted cryotherapy was excellent. The incidence of complications was equivalent between groups, and the few minor, transient skin reactions observed resolved spontaneously without intervention. This aligns with the existing literature, which confirms that modern devices with precise temperature control present a minimal risk of thermal injury when used according to manufacturer guidelines [15]. A potential limitation of this investigation is the inherent challenge of blinding participants to an intervention with a distinct physical presence. However, the use of blinded outcome assessors and a standardized protocol for both groups mitigates the risk of significant performance bias. The generalizability of these results is strengthened by the sample size

and the conduct of the study within a typical clinical setting.

Conclusion

This study provides robust evidence that Computer-Assisted Cryotherapy (CAC) is a highly effective and safe adjunct to a modern multimodal analgesia protocol for patients undergoing total knee arthroplasty. The significant reduction in postoperative opioid consumption, coupled with markedly lower pain scores, demonstrates CAC's potent capacity to address the root causes of acute surgical pain, inflammation and edema. By facilitating superior pain control, CAC empowers patients to engage more effectively in early rehabilitation, leading to measurably improved range of motion and a shorter length of hospital stay. The excellent safety profile and the absence of serious device-related complications further solidify its role in clinical practice. Therefore, the routine integration of Computer-Assisted Cryotherapy into Enhanced Recovery After Surgery pathways is strongly recommended as a cornerstone strategy for improving patient outcomes, advancing opioid-stewardship, and optimizing recovery following total knee arthroplasty.

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