BS Structured Summary

Article: Pre-operative Cryo-compression in Total Knee Arthroplasty

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Structured Summary: Pre-operative Cryo-compression in Total Knee Arthroplasty

Original Article: Preoperative knee joint hypothermia reduces inflammation and recovery time and increases range of motion after total knee arthroplasty: A randomized controlled trial

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INTRODUCTION / BACKGROUND

Cryotherapy, in its classic form of ice combined with compression wraps, has been established as effective treatment after total knee arthroplasty (TKA) for decades. Its physiological mechanisms are multiple and well characterized: cold exposure triggers vasoconstriction, which reduces local metabolism and inflammatory response, decreases capillary permeability and edema, activates pain control pathways, and creates an environment unfavorable to bacterial growth. When combined with compression, cooling penetrates more effectively into deep tissues and prevents fluid accumulation by reducing vascular-tissue pressure gradients.

Joint cooling correlates with lower prostaglandin E2 production and reduction of synovial inflammatory mediators — interleukin-6 (IL-6), interleukin-1 beta (IL-1β), and vascular endothelial growth factor (VEGF) — in arthritic knees. Previous studies have demonstrated that post-operative cryotherapy reduces opioid requirements, improves 6-minute walk test, and enhances patient satisfaction after TKA. However, the pre-operative application of cryotherapy in TKA remains a largely unexplored area.

Given that TKA triggers an intense systemic inflammatory response — with peak biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and fibrinogen in the first 72 hours — the authors hypothesized that performing the procedure under deep joint hypothermia could attenuate this post-operative inflammatory response and, consequently, accelerate recovery. The biological premise is coherent: starting surgery with already "cooled" tissue creates a less reactive environment at the moment of surgical trauma, potentially modulating the inflammatory cascade from the outset.

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Against this gap in the literature, this study from the group of Prof. Andrea Baldini (IFCA Florence) investigated whether the application of cryo-compression for 1.5h before TKA, using the Zamar ZT Clinic PRO device, would maintain deep tissue hypothermia during the procedure, attenuate the inflammatory response and tissue damage, and improve post-operative outcomes — compared to the standard protocol of post-operative cryo-compression alone. This represents the first dedicated investigation of pre-operative cryo-compression application in TKA, within modern ERAS (Enhanced Recovery After Surgery) protocols.

OBJECTIVE

To investigate whether the application of pre-operative cryo-compression for 1.5h before TKA would be able to (1) maintain deep tissue hypothermia during the surgical procedure, (2) attenuate the inflammatory response and tissue damage, and (3) improve post-operative outcomes — specifically pain, swelling, and functional recovery parameters — compared with exclusively post-operative cryo-compression.

METHODS

Single-centre, parallel-group randomized controlled trial conducted between June 2021 and May 2022 according to CONSORT guidelines. 100 patients were randomized 1:1 (50 intervention + 50 control). Inclusion criteria: unilateral primary knee osteoarthritis, Kellgren-Lawrence Grade IV (bone-on-bone). Exclusion criteria: coagulation disorders, psychiatric conditions, allergies to protocol medications, or intolerance to cryo-compression. Allocation sequence generated by independent statistician in blocks of 4 to ensure balance between groups.

Partial blinding: outcome assessors, statisticians, physiotherapy team, and internal medicine personnel were blinded to allocation. Complete blinding of patient and surgeon was not feasible given the nature of the intervention. Sample size calculation by G*Power with assumed medium effect size (0.5), alpha 5%, 80% power — supporting 50 patients per group.

Intervention: the intervention group received pre-operative cryo-compression at 5°C for 1.5h before surgery using the Zamar ZT Clinic PRO device, maintained until surgical field preparation. Post-operatively, all patients (intervention and control) received daily 4-5h cryotherapy sessions, continued for 2 weeks, with the same equipment and settings. Early full weight-bearing mobilization was initiated after selective spinal anesthesia wore off.

Standardized surgical technique — same surgical team followed identical protocol: midline skin incision, medial parapatellar arthrotomy, pneumatic tourniquet during bone preparation and cementation phase. All received perioperative tranexamic acid and corticosteroids. In all cases the Persona® Medially Congruent (MC) Total Knee system (Zimmer Biomet) was implanted with tibia-first personalized alignment approach. Identical DVT prophylaxis protocol in both groups.

Primary outcomes: difference in inflammatory markers (ESR, CRP, fibrinogen) between cohorts. Secondary: pain (VAS), PROMs (KSS, OKS), and range of motion (ROM). Additional measurements: knee circumference, skin and bone temperature (infrared thermometer —

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bone temperature measured intraoperatively after arthrotomy to confirm deep hypothermia), time to reach rehabilitation milestones for hospital discharge. Statistical analysis: non-parametric tests (Mann-Whitney U, Wilcoxon) after Shapiro-Wilk; linear mixed-effects models for temporal variation of biomarkers; Cliff's delta for effect size; MCID calculated by the 0.5 SD approach.

MAIN RESULTS

Cohort and baseline: 100 patients completed 20-day follow-up with no losses or protocol deviations. Female predominance (73%), median age 74 years (IQR 68-77), median BMI 28.4. There was significant imbalance between groups: control group had more women (86% vs 60%; p=0.003) and higher baseline fibrinogen (median 521 vs 457 mg/dL; p<0.001). Remaining baseline variables (age, BMI, maximum flexion, OKS, KSS, CRP) without significant differences.

Finding 1 — deep tissue hypothermia confirmed: pre-operative cryo-compression achieved measurable and deep hypothermia. Median skin temperature of the operated knee immediately before incision: 15.7°C (IQR 13.0-18.6) — significantly lower than contralateral (Z=-4.5; p<0.001). Bone temperature after arthrotomy: 21.4°C (IQR 19.0-22.0) — also significantly different (Z=-4.9; p<0.001). This is the first objective documentation, by intraoperative infrared thermometry, that 1.5h of pre-operative cryo-compression manages to cool not only the skin but the underlying bone.

Finding 2 — attenuation of inflammatory response: significantly lower ESR in the intervention group at POD1 (6 vs 14; p=0.001) and POD2 (16 vs 25; p=0.032). Mixed-effects model analysis confirmed significant reduction of fibrinogen increment in the intervention group (β=-24.6; p=0.011). CRP showed a trend toward less elevation in the intervention group (β=-9.8; p=0.10), without reaching significance — likely due to undersizing for this specific biomarker. Robust positive correlation between pre-incision skin temperature and post-operative inflammatory markers: CRP (r=0.3; p<0.01) and fibrinogen (r=0.4; p<0.01) — the colder the tissue at incision, the smaller the subsequent inflammatory response.

Finding 3 — clinical and functional outcomes: maximum flexion at POD20 significantly greater in the intervention group (112.7±8.9° vs 105.9±10.1°; p=0.001; Cliff's delta 0.37). Time to reach rehabilitation milestones for hospital discharge 11.8% shorter in the intervention group (1.2±0.4 vs 1.3±0.4 days; p=0.007). VAS pain scores similar between groups throughout follow-up — both with median 0, reflecting the institution's already-optimized ERAS protocol. PROMs (KSS, OKS) without significant differences at POD20, with more than 93% of patients in both groups reaching MCID for KSS. No complications reported.

Limitations declared by authors: single-centre design, single cryotherapy device (Zamar), impossibility of complete blinding, gender imbalance between groups, short 20-day follow-up, significant baseline difference in fibrinogen (mitigated by delta variation analysis), sample calculation based on presumed medium effect. The authors themselves classify the level of evidence as IV despite the design being clearly an RCT (Level II) — likely conservative editorial decision given the single-centre nature and limited follow-up.

AUTHORS' CONCLUSION

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Pre-operative cryo-compression applied for 1.5h before TKA reduces early post-operative inflammation, accelerates rehabilitation milestones, and improves early range of motion. These findings highlight a potential role for hypothermia in knee surgery, justifying future investigations with larger samples and multi-centre designs to validate results and establish standardized protocols before widespread implementation.

💬 BS DISCUSSION

This is the first RCT that adds a **Knee Arthroplasty (TKA)** paper to our BS Papers series — and it opens a new and relevant front for the site, especially since it comes from Andrea Baldini's group, an international reference in knee surgery. The paper tests a provocative idea: what if cryotherapy, which we always use post-operatively, were more effective if it started BEFORE the skin is incised? The biological premise makes sense — starting surgery with already-cooled tissue means entering with the inflammatory cascade "attenuated" from the initial trauma. And the findings partially support this hypothesis: bone temperature of 21°C confirmed at the moment of arthrotomy (versus 36°C baseline), significantly lower ESR in the first two days, fibrinogen with attenuated increase by mixed-effects analysis, and — perhaps the most clinically relevant — flexion of 113° vs 106° at POD20, a significant 7° delta (p=0.001).

What does this mean for the BS surgeon? First, from a technical standpoint, the practicality of the intervention is notable. 1.5h of Zamar before surgery is compatible with day-hospital or same-day admission workflow. The patient can receive the cryo-compression sleeve in the room, in the pre-anesthetic area, or even during limb marking. There is no surgical cost, no additional technical complexity, no reported complication in this series. It is a "low-risk / potential-benefit" intervention — exactly the kind of addition that fits any ERAS protocol running here at BS. Second, the correlation between pre-incision skin temperature and post-operative inflammatory markers (CRP r=0.3; fibrinogen r=0.4) suggests a dose-response mechanism: the deeper the hypothermia achieved, the smaller the inflammatory response — which justifies protocoling the 1.5h duration as a minimum, not a ceiling.

There are, however, several points for honest discussion — and this is the kind of discussion we need to have in our community. First: the study is single-centre, with only 100 patients, and the authors prudently declare Level IV evidence (perhaps overcautious — the design is clearly an RCT). Second: Baldini's ERAS protocol is extremely high-standard — median VAS of 0 at all timepoints, discharge within 1 day. In centers with less optimized ERAS, the margin for "gain" may be even larger, or there may be confounding factors. Third: gender imbalance (86% women in control vs 60% in intervention, p=0.003) is a real methodological problem — women respond differently to pain, inflammation, and post-TKA kinematics. The authors honestly acknowledge this limitation. Fourth: the 20-day follow-up is short. To know whether this "early advantage" of 7° of flexion and 11.8% rehabilitation time translates into better outcomes at 6 months, 1 year, or 5 years, we need larger studies.

The most subtle and perhaps most important point: the study shows that pre-operative hypothermia is DIFFERENT from post-operative in mechanism. Both groups received

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identical post-op cryo (4-5h daily for 2 weeks, same device, same protocol). Therefore, any observed difference is specifically from the PRE-operative component. This is important because it debunks the alternative hypothesis that "more cryo = better". Timing seems to matter more than total dose — starting before surgical trauma alters the inflammatory cascade differently from trying to attenuate an already-established cascade. This is a concept worth attention: we may be at the start of a new category of "preconditioning" tissue treatment for knee surgery, analogous to what has been done in cardiology for decades.

For BS practice, three practical recommendations. First: incorporate this study into our ERAS discussion for TKA — especially in BS labs, where we discuss perioperative protocols. Second: if we are going to adopt the practice, standardize the Zamar protocol (5°C, 1.5h, until field preparation) and measure outcomes (early flexion, time to rehabilitation milestones, biomarkers if available). Third: await and seek multi-centre replications before claiming categorical superiority — but, given the low risk and modest cost, the benefit/risk ratio already favors adoption in real practice. This is the kind of paper that tends to be cited in international consensuses in the next 2-3 years; having the content in BS Papers from now positions the site as a reference in cutting-edge content for the Brazilian knee surgery community.

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