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Reduced opiate use after total knee arthroplasty using computer-assisted cryotherapy

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Abstract

Purpose Despite multimodal pain management and advances in anesthetic techniques, total knee arthroplasty (TKA) remains painful during the early postoperative phase. This trial investigated whether computer-assisted cryotherapy (CAC) is effective in reduction of pain and consumption of opioids in patients operated for TKA following an outpatient surgery pathway.

Methods Sixty patients scheduled for primary TKA were included in this prospective, double-blind, randomized controlled trial receiving CAC at 10–12 °C (Cold-group, $n = 30$) or at 21 °C (Warm-group, $n = 30$) during the first 7 days after TKA according to a fixed schedule. All patients received the same pre-, peri- and postoperative care with a multimodal pain protocol. Pain was assessed before and after every session of cryotherapy using the numerical rating scale for pain (NRS-pain). The consumption of opioids was strictly noted during the first 4 postoperative days. Secondary outcomes were knee swelling, visual hematoma and patient reported outcome measures (PROMs). These parameters were measured pre-, 1, 2 and 6 weeks postoperatively.

Results In both study groups, a reduction in NRS-pain after every CAC session were seen during the postoperative period of 7 days. A mean reduction of 0.9 and 0.7 on the NRS-pain was seen for respectively the Cold- ($P = 0.008$) and Warm-group (n.s.). A significant ($P = 0.001$) lower number of opioids were used by the Cold-group during the acute postoperative phase of 4 days, 47 and 83 tablets for respectively the Cold and Warm-group. No difference could be observed for secondary outcomes and adverse effects between both study groups.

Conclusions Postoperative CAC can be in added value in patients following an outpatient surgery pathway for TKA, resulting in reduced experienced pain and consumption of opioids during the first postoperative days.

Keywords Computed assisted cryotherapy · Cold therapy · Total knee arthroplasty · Outpatient surgery · PROMS · Equianalgesics · Opioids · Multimodal · Pain protocol

Introduction

Total knee arthroplasty (TKA) is a major orthopedic intervention accompanied by tissue damage and an inflammatory response, manifesting as local swelling and edema, reduced range of motion (ROM), stiffness and reduced quadriceps strength [2, 17, 30]. Despite multimodal pain management and advances in anesthetic techniques, a TKA is associated with pain and discomfort for most patients.

Currently, cold therapy for pain reduction is an accepted and frequently used treatment in daily practice after trauma or surgery since the time of Hippocrates. Although the mechanism is not well understood, cold therapy has been used for centuries in treatment for pain and swelling. Cryotherapy involves the application of cold to the skin surrounding the injured soft tissues and in joint surgery is supposed to

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reduce the intra-articular temperature [22]. Cold will reduce the local blood flow by vasoconstriction and, therefore, the local inflammatory reaction, swelling and heat experience. Moreover, it will slow the conduction of nerve signals potentially reducing pain transmission [3, 21].

Several cryotherapy modalities are available, from traditional ice packs to third-generation advanced computer-assisted devices with continuous controlled cold therapy. The advantage of these latter devices would be controlled temperature modulation with cooling at a specific and continuous temperature for a prolonged time. In addition to guaranteeing a steady temperature, these devices also allow a progressive increase of the temperature during the course of treatment to avoid cold-induced vasodilatation. Furthermore, they are less labor-intensive because there is no need to fill them with cold water or ice [27].

Cryotherapy is the standard care in some countries and is rarely used in others [4]. Conflicting evidence regarding the value of this treatment from randomized trials may contribute to that practice disparity [2]. Even though some studies show excellent results regarding computer-assisted cryotherapy (CAC), the quality of the available literature is not convincing and level I evidence is still missing. Cryotherapy may improve the ROM at the knee in the first 1–2 weeks after surgery [1, 26]. Furthermore, according to the manufacturer of the cooling device, CAC should provide less pain, less swelling and shorter length of stay. However, no studies were found that looked at the effect of cryotherapy on pain sensation and consumption of opioids in patients undergoing a TKA following an outpatient surgery pathway. Well-designed randomized controlled trials are required to improve the quality of the evidence.

The main objective of this prospective-double-blind randomized controlled trial is to assess the effect of CAC on pain sensation and consumption of opioids in patients undergoing a TKA following an outpatient surgery pathway. It was hypothesized that CAC can achieve a pain-reducing effect after TKA during the first 7 days.

Materials and methods

Between 2015 and 2016, patients who were to undergo TKA for a painful and disabled knee joint resulting from osteoarthritis, were invited to participate in this double blind, prospective, randomized, controlled trial at a single institution (Orthopedic department of Zuyderland Medical Center, Sittard-Geleen, The Netherlands). To provide a more homogeneous group of patients to be studied, the patient group was restricted to those patients who were scheduled to undergo primary TKA replacement due to a proven painful osteoarthritis of the knee, who need to obtain pain relief and improve function and who were able and willing to follow instructions and to return for follow-up evaluations. Patients with a general or an active knee infection, revision TKA, extension deficit of the knee of more than 15° and/or a flexion less than 110°, rheumatoid arthritis, pregnancy and patients who were not able to understand and complete the procedure due to cognitive dysfunction or language barrier were excluded.

Pre-, per- and postoperative protocols and patient selection criteria were described in detail in previous study for outpatient surgery (OS) pathway [18–20, 28, 29]. According to a standardized pain protocol, patients received premedication 2 h before operation acetaminophen 1 g, meloxicam 15 mg and gabapentin 600 mg. Patients were operated under spinal or general anesthetic treatment by one experienced knee surgeon (NK), performing a minimum of 150 TKA procedures annually. Patients were operated using a midline anterior incision with a medial parapatellar arthrotomy and with the use of Patient Specific Instruments (Signature, Zimmer Biomet, Warsaw, IN, USA) for the implantation of a cemented CR TKA (Vanguard CR, Zimmer Biomet, Warsaw, IN, USA). No tourniquet was used during surgery. Before skin closure, hemostasis was controlled using diathermia. The wound margins were infiltrated with 140 cc ropivacaine (0.2%) as local infiltration anesthesia (LIA). No adrenaline was used during LIA, since it was shown that adrenaline could be omitted from the LIA-mixture [29]. No wound drains were used. All wounds were closed with a barbed suture wire (V-Loc, Covidien, USA) The surgical wound was covered with a hydrocolloid dressing (Aquacel® Surgical, ConvaTec Inc.) for 7 days and a compressive dressing was applied in the operating room. This latter was replaced by a thin elastic compressive tubular dressing (Tubigrip, Mediq Medeco Inc.) before leaving the hospital to allow cryotherapy to be applied and penetrate to the skin. A strict urinary nurse-led bladder scan management protocol was used for the prevention of postoperative urinary retention [19]. All patients were planned to be discharged on the day of surgery.

On the day of surgery, a CAC-system was delivered at the patient's home. The advanced cooling device here used (Zamar Therapy Cube, Vrsar, Croatia) can guarantee a fixed temperature during a prolonged time. During these 7 days postoperatively they cooled the operated knee according to a fixed protocol. During inpatient clinic, immediately after surgery all patient received 6 h of continuous cooling at 10–12 or 21 °C for patients in the Cold- and Warm-group, respectively. These two temperatures setting were chosen as efficient cryotherapy requires cooling of the skin tissue to specific temperature levels (< 13.2 °C) to achieve reduction in pain, according to Chesterton et al. [7].

In the Cold-group, patients received immediately after surgery cryotherapy at 10 °C. In the evening and during the first night at home, patients received an additional 4 h

of CAC. The day after surgery the fixed protocol consisted of 2 h of cryotherapy in the morning at 10 °C, followed by 2 h in the afternoon at 10 °C. During the second evening and night patients received one session of 4 h of CAC at 12 °C. From then, patients were allowed to use CAC (12 °C) additionally in case of extreme pain during the nights. The schedule was repeated up to postoperative day 7. In the warm group, patients were following exactly the same cooling protocol but with another temperature setting of 21 °C for all cooling sessions.

Besides the CAC therapy, the patients received normal conservative 'standard of care' treatment, including analgesics, physical therapy, etc. Use of analgesic was allowed according to our pain protocol. Postoperatively, we used tramadol (50 mg) as a rescue analgesic for severe breakthrough pain and daily low molecular heparin injections (Fondaparinux, Arixtra, Glaxo-SmithKline) were used as thrombosis prophylaxis up to 6-weeks after surgery. All patients were instructed for knee exercises for the early postoperative period. Thereafter the same rehabilitation program was employed for all patients, consisting of full weight bearing and active range of motion exercises at day of surgery. No continuous passive motion devices were used. Subsequent follow-up took place after 1, 2 and 6-weeks. During each evaluation, a clinical follow-up examination was performed by the outcome assessor. After a follow-up period of 6-weeks the study ended.

To make sure CAC therapy was blinded to the patients, orthopaedic surgeon, investigator and other persons direct and indirect involvement in the study, randomization and preparation of the CAC systems for both 11 and 21 °C, were performed by an independent trial nurse (AD). Randomization was performed using computer, web-based generated randomized numbers (http://www.random.org). Randomization was unblinded after study completion or in case of a suspected unexpected serious adverse reaction (SUSAR).

The main outcome of this study was experienced pain, measured with a Numerical Rating Scale for pain (NRS-pain, from 0 to 10, 10 being 'worst pain'). Pain was measured before and after each time that CAC was used during the first 7 days postoperative according to a fixed time schedule. This score was noted in a pain diary up to 7 days after TKA. Secondary endpoints were the consumption of rescue medication (Tramadol), which was noted in the pain diary. Length of hospital stay (days) was evaluated as time between hospital admission and discharge. The presence of visual hematoma and knee swelling was examined and rated by an independent trial nurse during each follow-up (AD). To investigate the effect of CAC on knee swelling objectively the knee circumference was measured in centimeters at three fixed points: mid-patellar, 7 cm distally and 7 cm proximally. The average circumference was calculated before surgery, after 1, 2 and 6-weeks. Adverse events (AEs) were classified as patient related [e.g. postoperative nausea and vomiting (PONV)], thromboembolic events and wound disorders (e.g. persistent wound leakage), surgical related (e.g. infection) and/or prosthesis related (e.g. loosening). Besides the difference of the temperature of the CAC, pre-, per- and postoperative procedures and pain protocol were identical in both groups as well as the completed operative and clinical case report forms. Finally, patient reported outcome measures (PROMs) were obtained preoperative and 6 weeks postoperative including the Oxford Knee Score (OKS; 12–60, 12 being the best outcome) [16], the Western Ontario and McMaster Universities Arthritis Index (WOMAC; 0–100, 100 being the best outcome) [24] and the quality of life was assessed by the EuroQoL-5D questionnaire [6].

All data were collected in a database by the blinded researcher (ET) and an independent physiotherapist (YB) at fixed times during follow-up.

The study was approved by an independent medical ethics committee (METC Zuyd, No. 15-T-135) and registered online at the Dutch Trial Register (http://www.trialregister.nl, No. NTR5565) and conducted in accordance with the guidelines for Good Clinical Practice (GCP).

Statistical analysis

Sample size calculations were performed based on the assumption that both CAC groups (10–12 or 21 °C) significantly improve the mean NRS-pain score by 1.5 postoperative with a standard deviation of 2 on a NRS-pain score of 10 points. With an alpha of 0.05 and 1-beta error of 0.8, this study required 26 patients in each group to be able to reject the null hypothesis that the population means of two groups are different, with a power of 80%. The probability of Type II error associated with this test of a null hypothesis is 0.05 with two tails. To compensate for a possible 10% loss to follow-up, the total number of patients needed for the RCT was 60. The Shapiro–Wilk test showed that the data were normal distributed. Student's *t* tests were performed on significant interactions. Chi-square tests were used for categorical variables. A generalized linear mixed model (GLMM) approach was used for the PROMS, to cope with any missing data being collected preoperative and during the 2-, 6-, and 12-week follow-up [8]. *P* value was considered to be statistically significant at $P \leq 0.05$ for all analysis. All statistical analyses were performed with use of SPSS version 21.0 for windows (Inc., Chicago, IL). Results are presented as either with frequencies (%), or mean with a standard deviation (SD).

Results

Seventy consecutive patients were eligible for enrollment. Two patients had previous surgery of the knee, four patients participated in another study, one was living in another country, two declined to participate and one other

patient had reprieved the operation; therefore, they were excluded from the trial. Subsequently, 60 patients were included. An overview of the number of patients recruited, enrolled and analyzed in this study is presented in Fig. 1 in the manner recommended by consolidated standards of reporting trials [23].

Patient demographics and operation data were not significantly different between the two groups (p = n.s., Table 1). There were no bilateral cases. The mean time required for the surgical procedure was 56.7 min (15.2). The majority received spinal anesthesia (n = 52, 86.7%), others general anesthesia (n = 8, 13.3%). Seven of the 60 patients (4.2%), 4 (13.3%) and 3 (9.0%) patients from respectively the Warm- and Cold-group, were not discharged as planned on the day of surgery. Reasons for prolonged hospitalization were impaired sensibility of the lower extremity after spinal anesthesia (n = 3, 1.8%), bleeding from the wound (n = 1, 0.6%), insecure mobilization (n = 1, 0.6%), dizziness (n = 1, 0.6%) and on request of the patient (n = 1, 0.6%). All of these seven patients were discharged 1 day after surgery. One other patient was seen in the emergency room at the day of surgery because of post-operative hemorrhage. Hospitalization was not necessary; replacement of the bandage was enough.

NRS-pain scores before and after every session of CAC were noted for each day during the postoperative period of 7 days. The reductions between both NRS-pain scores for every cooling session are shown in Fig. 2 for both the Cold- and Warm-group. During the first week, both cohorts had lower NRS-scores after every cooling session. A mean reduction of 0.9 and 0.7 on the NRS-pain were seen for the Cold- and Warm-group, respectively. This reduction in NRS-pain was only significant for the Cold-group (P = 0.008).

With regard to consumption of tramadol during the first 4 days after surgery, a lower number of tablets and it were used by the Cold-group, as shown in Table 2. Patients who were treated with cryotherapy at 10–12 °C consumed up to 2.6 times less opioids during the early days after surgery in comparison with patients who were treated with cryotherapy at 21 °C. The difference in consumption of tramadol was seven tablets or approximately 350 mg less per day for the Cold-group. During the early postoperative 4 days the total number of doses that were required was much higher in the Warm-group. A cumulative amount of 2350 and 4150 mg

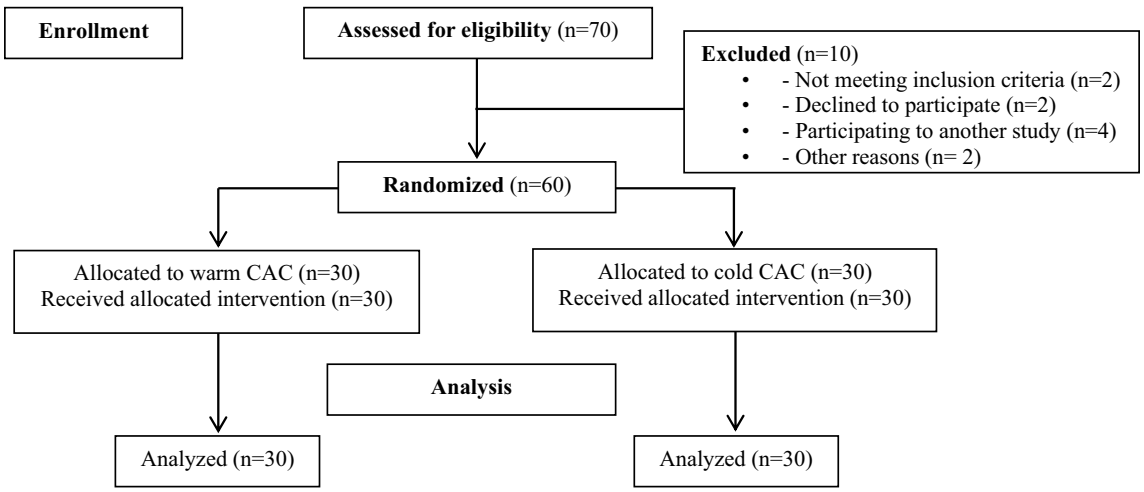

Fig. 1 Diagram of the number of patients enrolled and analyzed in this study recommended by CONSORT

Table 1 Baseline were not significantly different between the two groups

	Cold group (10–12 °C)	Warm group (21 °C)	*P* value
Age at index surgery, years	65.5 (6.2)	64.7 (6.8)	n.s
Females, *n*	13 (43.3)	15 (50.0)	n.s
Left knees, *n*	11 (36.7)	13 (43.3)	n.s
BMI, kg/m^2	27.7 (3.6)	27.4 (3.6)	n.s
ASA classification, I/II	17 (56.7)/13 (43.3)	15 (50)/15 (50)	n.s
Blood loss, ml	236.2 (101.7)	213.4 (78.9)	n.s
OR time, min	56.8 (15.8)	56.3 (14.8)	n.s

Data are presented as mean (SD) or absolute numbers (%) for both groups

BMI body mass index, *ASA* American Society of Anesthesiologists, *OR* operative data and operation room

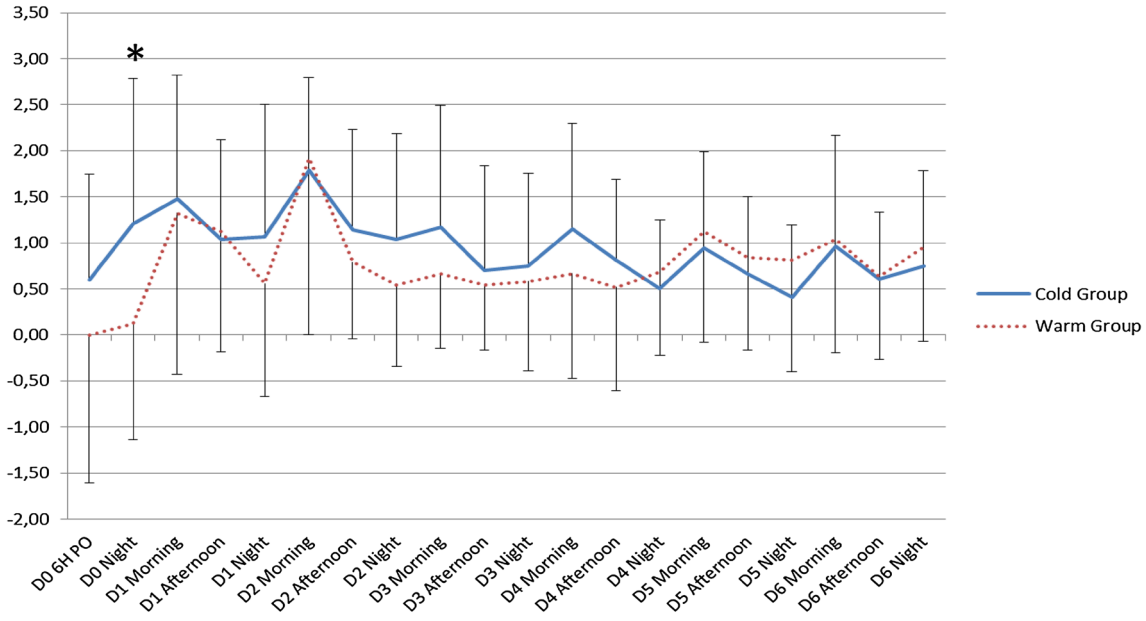

Fig. 2 Deviation of NRS-pain score between before and after each cooling session for every day postoperative. Whiskers are standard deviations (*$P = 0.0288$; $D =$ day)

Table 2 Number of tablets tramadol (equivalents mg) used in the early postoperative phase for both study groups

Number of tablets tramadol	Cold group (10–12 °C)	Warm group (21 °C)	Δ	*P* value
POD 0 (mg)	5 (250)	13 (650)	8 (400)	n.s
POD 1 (mg)	16 (800)	26 (1300)	10 (500)	0.034
POD 2 (mg)	11 (550)	19 (950)	8 (400)	n.s
POD 3 (mg)	9 (450)	13 (650)	4 (200)	n.s
POD 4 (mg)	6 (300)	12 (600)	6 (300)	n.s
Total (mg)	47 (2350)	83 (4150)	36 (1800)	0.001

Δ The difference between both groups at each postoperative day (POD)

were used in the Cold- and Warm-group, respectively ($P = 0.001$) (Table 2).

No significant difference could be observed in the mean knee circumference between both groups (See Table 3).

After 7 days less hematoma around the operated knee was seen in the Cold-group ($n = 5$, 16.7%) in comparison with the Warm-group ($n = 6$, 20%) (n.s.). (See Table 4).

Pre-operatively, at 2-, 6- and 12-weeks of follow-up, both groups had comparable PROMS (See Table 5).

No differences in knee instability or wound healing problems were assessed. Only one patient developed an allergic reaction to the Aquacel plaster at the first day surgery. No additional care was necessary. Only one patient in the Cold-group required cessation of the cryotherapy due to discomfort, which was not directly related to cryotherapy. The

Table 3 Mean difference (in cm) in knee circumference before and after surgery during the follow-up

	Cold group (10–12 °C)	Warm group (21 °C)	*P* value
Supra patellar			
Pre 1-WPO	3.7 (1.6)	3.8 (2.0)	n.s
Pre 2-WPO	3.5 (1.8)	3.1 (2.4)	n.s
Pre 6-WPO	1.9 (1.4)	2.5 (1.7)	n.s
Mid patellar			
Pre 1-WPO	3.0 (1.9)	3.2 (1.9)	n.s
Pre 2-WPO	2.4 (1.8)	2.7 (1.7)	n.s
Pre 6-WPO	1.7 (1.7)	1.9 (1.7)	n.s
Infrapatellar			
Pre 1-WPO	3.2 (1.5)	2.6 (1.9)	n.s
Pre 2-WPO	2.7 (1.7)	2.0 (2.2)	n.s
Pre 6-WPO	1.9 (1.3)	2.0 (1.9)	n.s

Outcomes were not significantly different between the two groups

WPO week postoperative

Table 4 Number of patients (*n*) with the presence of visual hematoma during the clinical follow-up

Presence of hematoma	Cold group (10–12 °C)	Warm group (21 °C)	*P* value
1-WPO	15 (50.0%)	21 (70.0%)	n.s
2-WPO	11 (36.7%)	10 (33.3%)	n.s
6-WPO	1 (3.0%)	0 (0%)	n.s

WPO week postoperative

Table 5 Mean (SD) and *P* values are presented for the PROMs for both groups for each different follow-up visits (WPO = weeks postoperative). Tested with a generalized linear mixed model (GLMM) [8]

	Cold group		Warm group		*P* value
	Mean	SD	Mean	SD	GLMM
EQ-5D (index)					
Pre	0.791	0.063	0.796	0.085	n.s
2-WPO	0.815	0.080	0.818	0.085	
6-WPO	0.865	0.080	0.853	0.076	
12-WPO	0.904	0.085	0.879	0.089	
EQ-5D (VAS)					
Pre	70.2	19.2	69.8	18.9	n.s
2-WPO	79.0	11.2	75.2	12.4	
6-WPO	82.9	10.0	80.9	10.9	
12-WPO	80.8	12.1	75.6	19.1	
NRS					
Pre	5.7	2.3	5.9	2.3	n.s
2-WPO	2.8	1.5	3.1	2.4	
6-WPO	1.7	1.3	2.1	1.7	
12-WPO	2.0	2.3	1.9	1.8	
OKS					
Pre	36.1	8.6	36.6	10.9	n.s
2-WPO	29.6	6.3	25.1	8.1	
6-WPO	25.8	5.8	25.1	8.7	
12-WPO	21.5	6.1	22.7	8.1	
WOMAC					
Pre	68.1	18.1	60.3	21.8	n.s
2-WPO	69.9	13.6	75.4	18.3	
6-WPO	81.6	9.8	81.2	12.6	
12-WPO	90.2	9.7	85.8	13.6	

WPO week postoperative

patient had an unsatisfied feeling and decided to stop the therapy. No SUSARs' were seen. Patient compliant rates for the cryotherapy and rehabilitation program were similar in both study groups.

Discussion

The most important finding of the present study was that postoperative computer-assisted cryotherapy (CAC) is effective in terms of pain control after TKA as it was associated with reduced pain and reduced use of analgesics during the early postoperative period.

There was a reduction in NRS-pain after every cooling session in both study groups. However, this mean reduction was only statistical significant for the Cold-group. Similar to these findings, pain reductions in the acute postoperative phase were reported by others [1, 2, 21, 25]. However, Ruffili et al. found no superiority in reducing pain compared with traditional icing [25].

Furthermore, effect of cryotherapy on the need for opioids was investigated in this trial. Cryotherapy has been frequently used as an adjunct to opioids after orthopedic surgery [10]. Though both study groups had improved pain relief after CAC, the perception of pain may be influenced by medication. Therefore, consumption of analgesic was more objective than the subjective NRS-pain score. In this trial, the consumption of the opioids given as rescue medication was up to 2.6 times more in the Warm-group than in the Cold-group. This difference was only significant on the first day after surgery, knowing that the worst phase of postoperative pain and inflammation occurs during the first days postoperatively [32]. This immediate post-operative pain and its associated opiate use is considered to have a negative influence on the postoperative rehabilitation [1] due to side effects (e.g. nausea, dizziness). A slower rehabilitation after TKA can result in an increased length of stay and costs [9]. As the consumption of addictive opioids was reduced by CAC, these clinical relevant side effects can be reduced or even be prevented. Lower consumption of opioids was previously seen in a multicenter RCT [31]. However, in a recent systematic review and meta-analysis of 11 RCTs on cryotherapy, Addie et al. showed no benefits for analgesic use [1, 2]. They reported no information about the standard pain medication that was given as it influences the pain experience, and thus the effect of cryotherapy. Furthermore, data was pooled including results from different cryotherapy systems. In this randomized trial the same third generation CAC system was used in all patients. CAC had several advantages compared to other cooling modalities. Using CAC, the joint can be cooled circular for a prolonged time at a continuous temperature. It is easily applicable and non-invasive treatment modality for the patient, which can be used in a home setting. No serious adverse effects of CAC were observed in either group as complications were infrequently reported in the literature. Cryotherapy was generally found to be safe and not associated with any serious adverse events. In this study, only one patient in the cold group required cessation of the cryotherapy due to discomfort, which was not directly related to CAC. This is in line with Sadoghi et al. [26], they recorded no adverse effect in their clinical trial. In previous literature, adverse events were reported in $< 1\%$ with knee joint cryotherapy. Discomfort, local skin reactions, superficial infections, cold injuries, and thrombolytic events were mentioned in the literature [1]. Though the skin is not the target of cryotherapy, frostbite can be a serious complication after cold application as described by Dundon et al. [10]. Because of a decreased tissue oxygenation and necrosis cold application can be associated with tissue and wound problems or even need for addition surgery. It typically begins to occur around temperatures of 10 °C [10, 32]. Precautions

to avoid frostbite during cryotherapy must be taken. Dundun et al. recommend cessation of at least 20 min every 2 h [10]. In this trial, all patients were wearing a thin elastic compression dressing during every cooling session. No case of frostbite was noted. Three patients in the Cold-group reported discomfort as a generalized cold feeling during the long cooling session of 4 h in the evening. All the patients in this study used an elastic compression dressing for just 1 week. They used the cooling device in combination with the compression. According to Kullenberg et al. simultaneous application of cold and compression is a better treatment than cold application alone in terms of haemarthrosis and edema formation [21].

No significant difference could be established in the secondary outcomes in this study. According to Dundon et al. cryotherapy may improve edema control in the postoperative period, which was associated with improved functional outcome [10]. Also Sadoghi et al. reported significant benefits in terms of early post-operative remobilization with respect to early ROM [26]. In the current study no difference concerning knee swelling, hematoma and PROMs was observed. However, there was a great patient satisfaction for both study groups. All patients reported pain relief, a mandatory rest period between rehabilitation exercises and a comfortable acute recovery using CAC. Moreover, a number of patients underwent TKA to the contralateral knee approximately 6-months later; all of them had a great desire to use the CAC device again.

In previous studies cryotherapy was only applied in in-hospital setting, in contrast to the current study, all patients got a TKA in an outpatient pathway. CAC in in-hospital setting may be associated with a shorter hospital stay as in previous studies the postoperative stay was significantly shortened by the use of cold therapy [21]. However, CAC is not a standard used procedure in most clinics and it is associated with extra economic costs compared to traditional ice packs and/or frequently used opioids. In case of a shorten hospital stay, CAC maybe cost-effective. Last but most important, using CAC can reduce or even prevent the consumption and thus side effect of opioids. Possible unpleasant side effects of opioids (e.g. PONV, constipation, dizziness, lethargy and potential addition) often require additional care.

Current randomized controlled trial had several strengths. This study was performed in one single center, evaluations were all done by the same investigator (ET) so bias of inter-observer variability in these results would not be expected. Likewise, one single experienced surgeon (NK) performed all surgeries using the same surgical approach, anesthesia techniques, implant, pain protocol and rehabilitation program. Routine use of gabapentinoids is no longer in our pain protocol, since Hamilton et al. found that this has no added value to in the management of acute pain following TKA [14]. Though, acceleration of knowledge development ensures that the half-life of scientific evidence has decreased, we should readapt our pain protocol with the recent literature and include gabapentinoids again [15]. Both patient groups were screened and studied under the same conditions in a RCT. Second, we monitored the consumption of analgesics to objectify the pain sensations and NRS-pain scores, which allows a more detailed analysis of the different parameters. Moreover, to our knowledge none of previous published trials studied patient self-reported function and quality of life. These outcomes measurements are of greater clinical importance to patients than the range of motion for example [2]. Though we could not report any benefit in terms of PROMs using cryotherapy, patient satisfaction improved in both groups. At least, this study strengthens the evidence on a topic that is of high clinical significant to the daily practice of TKA surgery and during rehabilitation.

Despite being well designed and monitored, this study does have some limitations. First, the main endpoint of this study was pain, measured with the NRS-pain score. In contrast to the Visual Analogue Scale for pain (VAS), only the numbers themselves are valuable outcome. This means that there are only 11 answers possible on a 0–10 point NRS. It thus allows a less accurate discrepancy of pain levels compared to VAS, where the range of possible numbers is unlimited [13]. With the NRS it is easily to administer pain verbally [33] as pain perception may differ within a time-period. Asking patients to rate their pain on average over a past short period of time is more valuable than pain at the specific time point [5]. On the other hand a change on the NRS of 20% between two follow-up moments was clinically relevant [11, 12], though it was not statistically significant between both temperature groups. Second, a lot of factors (e.g. social and work situation, history of a prior injury or osteoperative use of morphine medication) may influence pain perception. These factors were not included in this study, which is a limitation.

Skin and/or intra-articular temperature was not measured to confirm effective cooling [22]. It was not our intention to be invasive in measuring the intra-articular temperature changes, but the aim was to observe clinical outcomes of CAC. Second, two different temperature settings (10–12 vs. 21 °C) were compared. The initial aim of this study was to compare a CAC intervention to a placebo control treatment. Though, the IRB disagreed this setting. Therefore, we chose for an ineffective temperature setting of 21 °C. A placebo-effect was not expected to influence these results. Finally, one of the main purposes of outpatient surgery is to keep hospital costs low. Though this study did not address the cost of implementing this new technology, as CAC may be associated with extra economic costs compared to traditional ice packs and/or frequently used opioids. These costs should be considered with a view to the safety of the use of opioids in the home situation.

Conclusion

Postoperative computer-assisted cryotherapy is effective in patients following an outpatient surgery pathway for total knee arthroplasty, resulting in reduced experienced pain and consumption of opioids during the first postoperative days.

Author contributions Elke Thijs: Designed the study, gathered and analyzed all the data, wrote the initial draft of the manuscript and managed the study. Martijn G.M. Schotanus: Designed the study, analyzed the data, wrote and revised the manuscript and managed the study. Yoeri F.L. Bemelmans: Gathered data, wrote and revised the manuscript. Nanne P Kort: Conceived the study and revised the manuscript.

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Compliance with ethical standards

Conflict of interest One author, Nanne Kort, is a paid consultant for Zimmer-Biomet, Europe. The other authors certify that they have no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Ethical approval The study was approved by the ethics committee of Zuyderland-Zuyd, Number 15-T-135 and registered online at the Dutch Trial Register (http://www.trialregister.nl, No. NTR5565).

Informed consent For this type of study formal informed consent was obtained from each included patient.

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