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Optimizing surgical field visualization in total knee arthroplasty: a randomized controlled trial comparing esmarch bandages and simple leg elevation

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Abstract

Background This prospective randomized controlled study explores the effectiveness of two exsanguination techniques in total knee arthroplasty (TKA), comparing Esmarch bandages and simple leg elevation concerning surgical field visualization, intra-operative metrics, and post-operative outcomes.

Methods Patients who underwent primary unilateral TKA ($n = 100$) were randomized and equally divided into the Esmarch bandage (EM group) and simple leg elevation (LE group) groups. Surgical field visualization was assessed using the Fromme–Boezaart grading scale. The operative time, intra-operative blood loss, total blood loss, post-operative pain, leg swelling, and post-operative complications were also assessed.

Results Surgical field visualization was significantly better in the EM group for all steps except for wound closure. The overall surgical field scales were 1.16 ± 0.29 and 1.46 ± 0.34 in the EM and LE groups, respectively ($p < 0.001$). The operative time and intra-operative blood loss were not significantly different between the two groups. Post-operative pain levels on days 1 and 3, and total blood loss were comparable between the groups. The knee circumference significantly increased in the EM group compared to the LE group (4.6% vs. 2.9%; $p = 0.04$).

Conclusions Although Esmarch bandages enhance surgical field visualization, they do not reduce operative time or blood loss compared to simple leg elevation. However, the improved visualization is associated with increased post-operative knee swelling.

Trial registration Clinical Trials Gov (NCT03989648) (18/06/2019).

Keywords Esmarch bandages, Exsanguination, Simple leg elevation, Surgical field visualization, Tourniquet, Total knee arthroplasty

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Background

The concept of bloodless limb surgery was first introduced in 1873 by Friedrich von Esmarch through the use of elastic bandages for exsanguination. This technique was refined in 1908 by Harvey Cushing with the development of pneumatic tourniquet [1]. These innovations, particularly in TKA, significantly improve surgical visualization, reduce intra-operative blood loss, and shorten operative time [2].

The use of tourniquets in TKA remains a subject of ongoing debate. Proponents argue that tourniquets reduce intraoperative blood loss and improve bone-cement interdigitation [3]. However, recent studies have raised concerns about increased postoperative pain, delayed functional recovery, and a higher risk of complications such as thromboembolism and wound healing problems [4]. Meta-analyses suggest that while tourniquets reduce intraoperative bleeding, they do not significantly affect total blood loss due to increased postoperative hidden blood loss [5–7]. Nevertheless, over 90% of orthopedic surgeons continue to use tourniquets during TKA [2], reflecting ongoing reliance despite emerging evidence.

Exsanguination involves the expelling of blood from the distal to the proximal limb before inflating a pneumatic tourniquet [8]; this can be achieved using Esmarch bandages or by elevating the leg for 2 min [9]. Despite its wide usage, the Esmarch bandaging has been linked to complications such as pulmonary embolism [10–12], nerve paralysis [10], a significant decrease in venous outflow and venous capacitance [13], and skin tension blisters [14]. In contrast, simple leg elevation is less invasive and carries few risks [12, 13].

While both techniques are widely used in clinical practice, few studies have compared their efficacy in TKA, especially in terms of their impact on surgical field visualization, which is an important factor that may influence intraoperative precision, improve cementing technique, and reduce the risk of iatrogenic injury, especially for less experienced surgeons. Most existing studies have focused on blood loss, postoperative pain, or complications [13–15]. Chiu et al. demonstrated no significant differences in estimated blood loss or operative time between the two techniques; however, the Esmarch bandage led to a significant reduction in venous outflow and venous capacitance during the early postoperative period [13]. Zhang et al. reported that leg elevation was associated with reduced postoperative pain and fewer skin complications compared to Esmarch bandaging [14]. Our study aimed to fill this gap by evaluating the efficacy of these methods in providing clear surgical field visualization and their influence on intra-operative and early post-operative complications.

Methods

Study design

This prospective randomized controlled study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the University's Ethics Committee (Date 13/2/2019, COA028/2562). The study was registered at ClinicalTrials.gov (NCT03989648). Patients who underwent unilateral TKA between June 2019 and January 2022 were included. Informed consent was obtained from all participants. The participants did not receive any form of compensation.

Blocked randomization was performed with block sizes of four generated by a computer. Allocation concealment was performed using sequentially numbered, opaque, sealed envelopes, which were prepared by an independent coordinator. In the operating room, a circulating nurse opened the next envelope in sequence immediately before the exsanguination procedure. Both patients and outcome assessors were blinded to the exsanguination method.

Patients were admitted one day before surgery, and the following data were recorded: age, sex, operated side, BMI, American Society of Anesthesiologists physical classification system (ASA), underlying diseases, leg circumference at three locations (measured using a soft tape measure while supine with knees extended and muscles relaxed: thigh, 10 cm proximal to the superior border of the patella [16]; knee, at the midpoint of the patella; and calf, 20 cm proximal to the medial malleolus) [16], mechanical axis of the lower limb, varus or valgus deformity, Knee Society Score (KSS) [17], hemoglobin, and hematocrit.

Study population

Patients were recruited from the Orthopedic Department of our institution, including those diagnosed with primary osteoarthritis of the knee and admitted for primary unilateral TKA at our institution. The exclusion criteria were as follows: risk of venous thromboembolism (e.g., history of deep vein thrombosis [DVT], pulmonary embolism, hypercoagulability, chronic venous insufficiency, active malignancy, hormone replacement therapy, oral contraceptive therapy, or obesity class II with body mass index [BMI] ≥ 30 kg/m² [18, 19]), risk of increased intra-operative blood loss (e.g., on anticoagulant drugs and bleeding disorders), peripheral arterial disease, and history of previous knee surgery in the operated knee.

Study interventions

This study included 100 patients with primary osteoarthritis scheduled for unilateral TKA. All patients received information concerning the treatment and analysis procedures from a research assistant. Patients were randomized into the Esmarch bandage (EM group, 50 patients)

and simple leg elevation (LE group, 50 patients) groups (Fig. 1).

Anesthesia protocol

All patients received combined spinal epidural anesthesia (CSEA) with 2.8–3.2 mL of 0.5% heavy bupivacaine. An epidural catheter was inserted into the epidural space using a Tuohy epidural needle (16 G or 18 G) for post-operative analgesia. Continuous infusion of 0.0625% bupivacaine combined with fentanyl at a concentration of 2 mcg/mL was administered. The epidural catheter was removed on post-operative day 2. Intraoperative blood pressure was continuously monitored and maintained within a consistent target range across both groups.

Surgical procedure

TKA was performed by a single surgeon with the patient in the supine position. An appropriately sized pneumatic

cuff was applied to each thigh. The tourniquet pressure was determined using the Limb Occlusion Pressure (LOP) technique, which applies the minimum amount of tourniquet pressure to occlude the arterial blood flow in a limb at a specific time for a specific patient. A pulse sensor was attached to the toe, and the pressure at which the pulse disappeared was recorded as the LOP. Based on the patient's systolic blood pressure, the Zimmer A.T.S. 4000 Tourniquet System (Zimmer Biomet, Warsaw, IN, USA) automatically added a safety margin of 40–80 mmHg to account for blood pressure fluctuations, thereby calculating the recommended tourniquet pressure (RTP). This automated adjustment resulted in individualized RTP values, which were applied before surgical incision. Both LOP and RTP were automatically measured using the Zimmer A.T.S. 4000 Tourniquet System.

In the EM group (50 patients), an assistant surgeon lifted the patient's limb to 45° and wrapped it with a

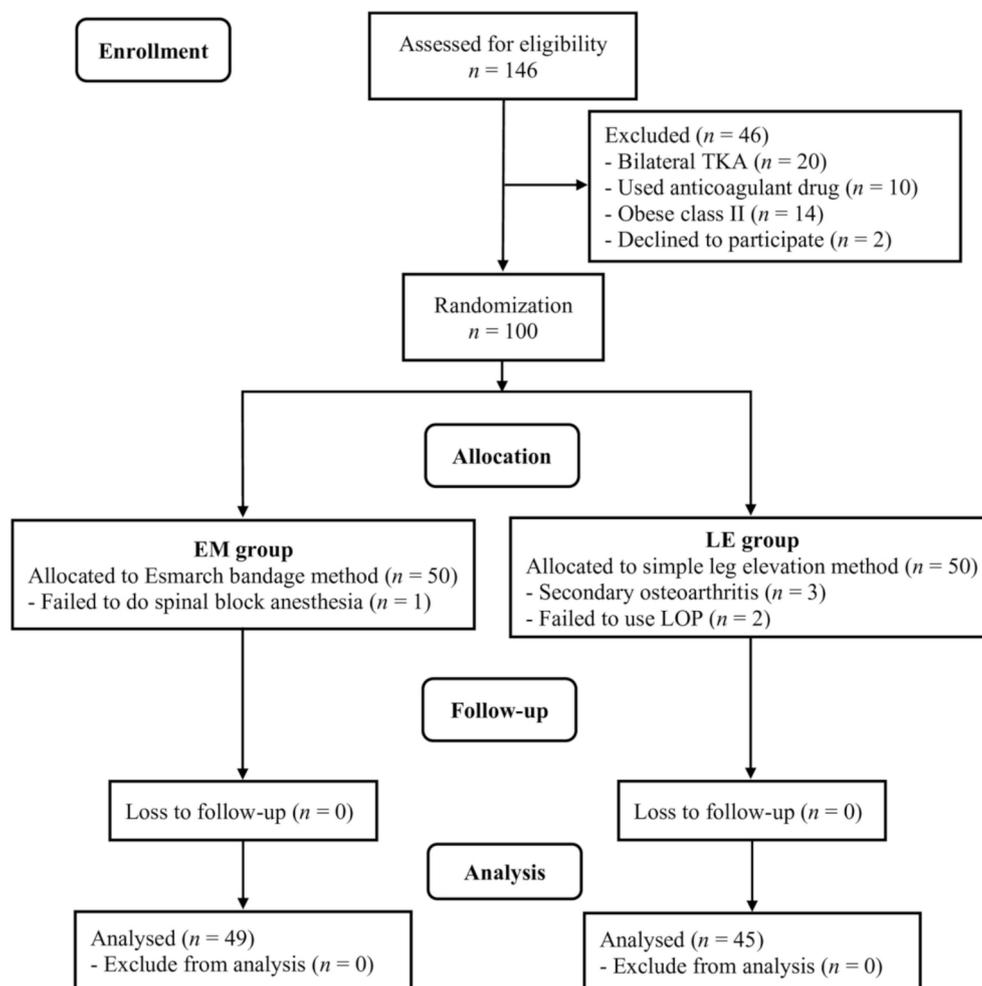


Fig. 1 CONSORT flow diagram illustrating the study design. This study aimed to compare the adequacy of exsanguination between the Esmarch bandages group (EM group) and simple leg elevation group (LE group) in total knee arthroplasty. LOP, limb occlusion pressure

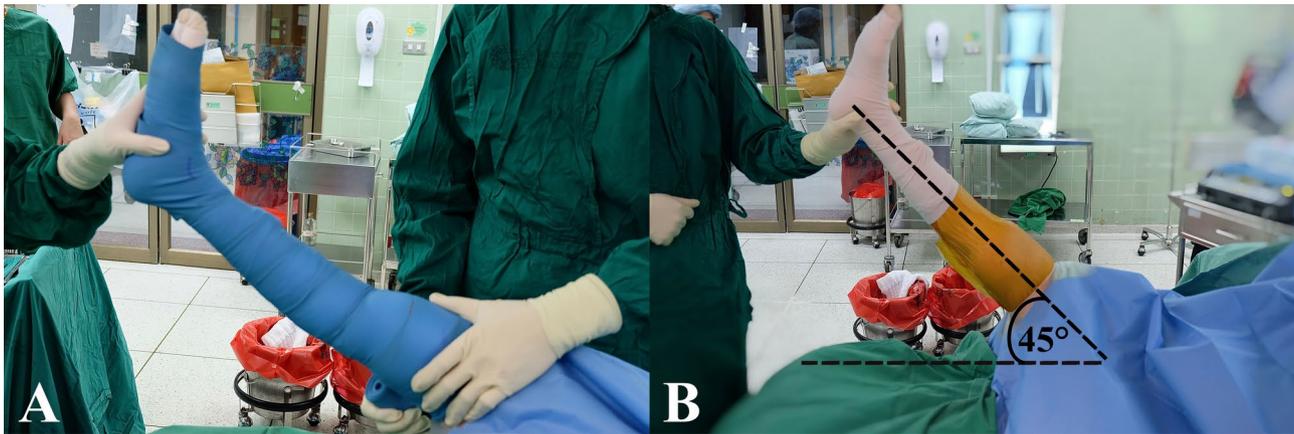


Fig. 2 Exsanguination methods. (a) Esmarch bandage method. The patient's limb was elevated to 45° and wrapped with an Esmarch bandage from the toes to the upper thighs under the protection of a stockinette. (b) Simple leg elevation method. The patient's limb was elevated to 45° for 2 min

Table 1 Category scale for assessment of surgical field

0	No bleeding.
1	Slight bleeding – no suctioning of blood required.
2	Slight bleeding – occasional suctioning require. Surgical field not threatened.
3	Slight bleeding – frequent suctioning required. Bleeding threatens the surgical field a few seconds after suction is removed.
4	Moderate bleeding – frequent suctioning required. Bleeding threatens the surgical field directly after suction is removed.
5	Severe bleeding – constant suctioning required. Bleeding appears faster than can be removed by suction. Surgical field severely threatened and surgery not possible.

standard Esmarch bandage from the toes to the upper thigh, under the protection of a stockinette (Fig. 2a). Esmarch bandage was removed from the surgical field after use. In the LE group (50 patients), the assistant surgeon elevated the patient's limb 45° for 2 min (Fig. 2b). Then, the tourniquet was inflated according to the RTP. The assistant surgeon was trained to avoid cues that could inadvertently reveal the exsanguination method. The surgeon, who assessed the surgical field visualization, entered the operating room only after the exsanguination process had been completed. Both the surgeon and research assistant were blinded to the methods of exsanguination. A skin incision (<9 cm) was made in the anterior midline. The mini-midvastus approach was used to access the knee joint without everting the patella. A fixed-bearing posterior-stabilized implant (Legion PS Total Knee System, Smith & Nephew, London, UK) with patellar resurfacing was used in all patients. The tibial, femoral, and patellar components were inserted using a cemented technique. A periarticular injection of 0.5% bupivacaine and 30 mg of ketorolac was administered. The knee joint was filled and left in place with 1 g of tranexamic acid before wound closure. A drain was not used in any patient. The surgical wound was sutured layer by layer, and the tourniquet was deflated after the skin suture was completed.

Post-operative management

A post-operative pain protocol involving multimodal analgesia and rehabilitation program was applied in both groups. Patients began ambulating with a walker on the first post-operative day. Discharge criteria included a steady gait, 90° knee flexion, full knee extension, and no dependence on intravenous pain medication.

Outcome measurement

The primary outcome was the visualization of the surgical field, assessed by the surgeon during four steps of TKA: approach to the knee joint, bone cutting, prosthesis placement with the cemented technique, and wound closure. A 6-point scale (0–5), adapted from Fromme et al. and Boezaart et al. [20–22], was used for evaluation (Table 1): 0, no bleeding; 1, slight bleeding without suctioning; 2, slight bleeding with occasional suctioning required; 3, slight bleeding with frequent suctioning required; 4, moderate bleeding that threatens the surgical field directly after suction is removed; and 5, severe bleeding with surgery not possible.

The secondary outcomes included measures related to intra-operative bleeding, including the operative time, defined as the duration from skin incision to completion of wound suture, and intra-operative blood loss, estimated from the blood collected in the suction bag. Reductions in hemoglobin and hematocrit levels compared to the preoperative values, as well as

total blood loss calculated using the Gross formula [23], were recorded. Complications of exsanguination were assessed, including post-operative pain on days 1 and 3, measured by the numerical rating scale (NRS), swelling of the operated leg on day 3, and hospitalization duration. Venous thromboembolism and surgical site infection were evaluated during the first post-operative month.

Sample size and statistical analysis

The sample size was calculated from our pilot study, which yielded mean surgical field scales of 1.406 (SD: 0.326) and 1.156 (SD: 0.48) for the EM and LE groups, respectively. Thus, 50 patients were required in each group, accounting for an alpha level of 0.05, a beta level of 0.2, and an anticipated dropout rate of 15%.

Statistical analyses were performed using SPSS version 23 (SPSS Inc., Armonk, NY, USA). Data were compared using the independent *t*-test or chi-square test, as appropriate. The level of significance was set at $p < 0.05$.

Results

Patients

A total of 146 patients were enrolled between June 2019 and January 2022. We excluded 46 patients: 20 had undergone bilateral TKA, 10 were receiving anti-coagulant drugs, 14 had obesity class II, and 2 declined to participate. Subsequently, 100 patients were randomized into the EM and LE groups. In the EM group, one patient was excluded because the anesthetist could not perform a spinal block. In the LE group, five patients were excluded: three had intra-operative evidence of

secondary osteoarthritis, confirmed by pathology as synovitis due to rheumatoid arthritis, and two experienced a machine error with the Zimmer A.T.S. 4000 Tourniquet System during the measurement of LOP and RTP, despite attempts to resolve the issue and repeat the measurements. The final analysis included 49 and 45 patients in the EM and LE groups, respectively, with no statistically significant differences in the demographic and pre-operative characteristics (Table 2).

Intra-operative outcomes

The mean surgical field scales were significantly higher in the LE group than in the EM group (1.46 ± 0.34 vs. 1.16 ± 0.29 ; $p < 0.001$). Specifically, the mean surgical field scales for the LE group were higher in the steps of approaching the knee joint, bone cutting, and prosthesis placement, with no significant difference in the wound closure step (Table 3).

On comparing the EM group with the LE group, operative time was slightly longer, although not statistically significant (89.4 ± 14.68 vs. 85.9 ± 10.2 min; $p = 0.18$); there were also no significant differences in the mean intra-operative blood loss (22.9 ± 10.8 vs. 23.4 ± 14.4 mL; $p = 0.82$) and tourniquet pressure ($p = 0.60$).

Post-operative outcomes

No differences were found in the reductions in hemoglobin and hematocrit and total blood loss, calculated using the Gross formula [23] (Table 4).

On post-operative day 1, pain scores were similar in both groups (mean NRS: 4.4 ± 2.4 vs. 4.7 ± 2.7 ; $p = 0.56$).

Table 2 Preoperative demographic data of the patients

	EM group (n = 50)	LE group (n = 50)	p-value
Age ^a (years)	70.1 ± 6.9	69.0 ± 7.0	0.42
Gender ^b (male: female)	9: 41	7: 43	0.59
Surgical side ^b (left: right)	28: 22	22: 28	0.23
BMI ^a (kg/m ²)	25.4 ± 2.6	24.5 ± 2.5	0.09
ASA ^b (I: II: III)	0: 35: 15	4: 35: 11	0.10
Underlying disease			
Hypertension ^b	39	31	0.08
Diabetes mellitus ^b	8	7	0.78
Dyslipidemia ^b	25	32	0.16
Others ^b	11	9	0.71
Thigh circumference ^a (cm)	42.5 ± 3.1	42.5 ± 4.3	0.99
Knee circumference ^a (cm)	37.7 ± 2.6	37.9 ± 2.8	0.71
Calf circumference ^a (cm)	32.6 ± 2.7	32.5 ± 3.3	0.86
Mechanical axis ^a (°)	varus 10.3 ± 10.1	varus 9.5 ± 6.3	0.67
Preoperative KSS ^a	41.8 ± 12.1	43.5 ± 13.6	0.53
Hemoglobin ^a (g/dL)	12.8 ± 0.9	12.7 ± 1.1	0.88
Hematocrit ^a (%)	38.7 ± 2.8	38.6 ± 3.0	0.86

^a presented as mean ± standard deviation

^b presented as number of knees

BMI = body mass index, ASA = American Society of Anesthesiologists classification, KSS = knee society score

Table 3 Intraoperative data of the patients

	EM group (n = 49)	LE group (n = 45)	p-value
Tourniquet pressure (mmHg)	256.8 ± 34.8	260.7 ± 36.2	0.60
Surgical field scale			
Approach to the knee joint	0.86 ± 0.40	1.18 ± 0.44	< 0.001*
Bone cutting	1.49 ± 0.62	2.09 ± 0.60	< 0.001*
Placement prosthesis with cement	1.27 ± 0.45	1.60 ± 0.58	0.003*
Wound closure	1.02 ± 0.25	0.98 ± 0.15	0.32
Overall	1.16 ± 0.29	1.46 ± 0.34	< 0.001*
Operative time (min)	89.4 ± 14.6	85.9 ± 10.2	0.18
Intraoperative blood loss (mL)	22.9 ± 10.8	23.4 ± 14.4	0.82

The results are presented as mean ± standard deviation

* indicates a significant difference (p -value < 0.05)

Table 4 Postoperative data of the patients

	EM group (n = 49)	LE group (n = 45)	p-value
Hemoglobin (g/dL)	11.5 ± 1.1	11.5 ± 1.1	0.87
ΔHemoglobin (g/dL)	-1.2 ± 0.9	-1.3 ± 0.7	0.62
Hematocrit (%)	34.8 ± 3.0	34.6 ± 3.0	0.77
ΔHematocrit (%)	-3.9 ± 2.8	-4.0 ± 2.2	0.76
Total blood loss (mL)	436.4 ± 262.5	436.4 ± 231.3	1.00
Postoperative pain (NRS)			
POD 1	4.4 ± 2.4	4.7 ± 2.7	0.56
POD 3	3.4 ± 2.0	3.0 ± 1.9	0.45
ΔPostoperative pain	-1.1 ± 2.4	-1.7 ± 2.9	0.27
Thigh circumference (cm)	46.7 ± 3.8	46.7 ± 3.8	0.93
ΔThigh circumference (%)	10.2	9.5	0.48
Knee circumference (cm)	39.4 ± 2.7	39.0 ± 3.1	0.50
ΔKnee circumference (%)	4.6	2.9	0.04*
Calf circumference (cm)	34.4 ± 2.7	34.6 ± 3.2	0.72
ΔCalf circumference (%)	5.6	6.0	0.75
Length of hospital stay (day)	6.3 ± 1.0	6.2 ± 1.0	0.43

The results are presented as mean ± standard deviation

* indicates a significant difference (p -value < 0.05).

Δ = differentiation between preoperative and postoperative data, NRS = numerical rating scale, POD = postoperative day

By post-operative day 3, the scores had decreased in both groups (mean NRS: 3.4 ± 2.0 vs. 3.0 ± 1.9; $p = 0.45$).

On post-operative day 3, the circumference of the operated leg was measured. The EM group demonstrated a significantly increased knee circumference compared with the LE group (increase rate: 4.6% vs. 2.9%; $p = 0.04$). The thigh was the most swollen area, which increased by 10.2% and 9.5% in the EM and LE groups, respectively.

The hospitalization duration did not differ between the groups. None of the patients were diagnosed with symptomatic pulmonary embolism, DVT, or surgical wound infection within 1 month post-operatively.

Discussion

This prospective randomized controlled trial compared the efficacy of exsanguination between Esmarch bandages and simple leg elevation in TKA. Our findings

revealed that surgical field visualization was statistically better in the EM group; however, both groups demonstrated similar operative times and intra-operative blood loss, consistent with the findings of Chiu et al. and Zhang et al. [13, 14], suggesting that the choice of exsanguination technique does not significantly impact these key surgical outcomes. Additionally, post-operative pain levels on days 1 and 3, and total blood loss were comparable between the groups, while post-operative knee circumference, indicating swelling, was significantly greater in patients treated with the Esmarch bandages.

There is a growing shift away from routine tourniquet use in TKA, driven by the evolution of modern surgical pathways such as fast-track protocols and Enhanced Recovery After Surgery (ERAS). These approaches emphasize reduced pain, early mobilization, and fewer complications. Although tourniquets have traditionally

been used to reduce intraoperative blood loss and improve cementation, they have been associated with increased postoperative pain, impaired early functional recovery, and a higher risk of thromboembolic events—outcomes that run counter to the goals of ERAS [24, 25]. Advances such as systemic and topical tranexamic acid, meticulous hemostasis, and optimized perioperative care have allowed many centers to achieve low blood loss without a tourniquet, supporting its selective rather than routine use in modern TKA [26, 27].

Currently, there is no standardized method for evaluating surgical field visualization in TKA. Hasanain et al. [2] categorized the visual field as poor, acceptable, or good when comparing tourniquet and tourniquet-less techniques. Kim et al. [28] assessed the efficacy of tourniquets in achieving a bloodless surgical field as a failure or success. In our study, we used a detailed and intelligible 6-point scale adapted from Fromme et al. and Boezaart et al. [20–22], which offers several advantages. It enables a more detailed and objective assessment by accounting for the frequency of suctioning required and the impact of bleeding on the surgical process. This level of detail provides greater sensitivity for detecting subtle differences between techniques and enhances reproducibility across observers.

Surgical field visualization was slightly superior in the EM group overall and during the steps of approaching the knee joint, bone cutting, and prosthesis placement. According to Blond et al. [29], the Esmarch bandage induced more effective exsanguination than leg elevation in terms of the median percentage reduction in the regional blood volume (65% vs. 42%; $p < 0.001$). Although the mean difference in surgical field scales between groups in our study was 0.3 points on a 6-point scale, the calculated effect size (Cohen's $d \approx 0.95$) represents a large effect, suggesting potential clinical relevance. We believe that even modest improvements in visualization may enhance surgical precision during critical steps such as the approach to the knee joint and bone cutting, particularly for less experienced surgeons, in technically challenging cases, or to reduce the risk of iatrogenic injury.

Post-operative pain and complications are major determinants of patient satisfaction following TKA. In our study, no significant differences in pain scores were observed between the groups on post-operative days 1 and 3. This finding aligns with the results of a randomized controlled trial conducted by Mitrichev et al., which found no significant difference in cumulative pain scores after tourniquet deflation among healthy volunteers who underwent either the Esmarch bandage or leg elevation method [30]. This contrasts with findings from Zhang et al. [14], who reported lower pain levels in the leg elevation group during the first post-operative week. This difference in findings may be attributed to variations

in surgical technique or pain management protocols. Although both groups received the same multimodal analgesia, we did not record the frequency or dosage of use, which is a limitation in detecting subtle differences in pain. Moreover, despite concerns about the potential for Esmarch bandages to develop preexisting DVT and cause life-threatening, this may be attributed to our rigorous patient selection process, effective prophylaxis measures including early ambulation, intermittent pneumatic compression, and low-dose aspirin, and the relatively small sample size, which may limit the detection of rare complications [10–12, 30].

The use of Esmarch bandages may be associated with skin complications. In a study by Zhang et al., skin tension blisters were significantly more frequent in the EM group than in the LE group after TKA (9.3% vs. 2.5%; $p = 0.031$) [14]. They hypothesized that the Esmarch bandage could cause skin friction during exsanguination and soft tissue injury during compression. In our study, post-operative knee circumference was significantly greater in the EM group than in the LE group. This finding is supported by the results of Chiu et al., who reported that venous outflow and venous capacitance were significantly decreased on post-operative days 2 and 6 in the EM group compared to the LE group [13]. The greater postoperative swelling in the EM group may result from impaired venous return caused by the compressive nature of the bandage. Although the difference in knee circumference between groups was small, it remains clinically relevant due to its potential association with skin complications.

Currently, TKA without a tourniquet or with limited use of a tourniquet is becoming popular [3, 31]. However, many surgeons still use tourniquets to achieve better visualization, decrease intraoperative blood loss, and improve cementation [2, 3]. Our study provides valuable data on exsanguination methods for surgeons who use tourniquets during TKA. Although the use of an Esmarch bandage can enhance surgical visualization during TKA, it has been associated with increased postoperative knee swelling. Therefore, we recommend that surgeons reconsider their routine use and apply it selectively based on individual patient factors.

This double-blind randomized controlled trial is the first to evaluate and compare the adequacy of exsanguination for surgical field visualization during TKA. However, it had some limitations. First, we excluded patients at risk of venous thromboembolism, intra-operative blood loss, and peripheral arterial disease, thereby limiting the applicability of our findings. Second, although the limb was elevated to 45°, this angle was estimated visually as the midpoint between 0° and 90° without the use of a goniometer. This may have introduced minor variability in positioning. In future studies, we recommend using a

goniometer or digital inclinometer to ensure standardized and reproducible limb elevation. Third, although intraoperative blood pressure was maintained within a target range across all patients, we did not record pressure values at the exact time of each surgical step, which may have influenced surgical field bleeding. Fourth, we assessed leg swelling using circumferential measurements, which is a noninvasive and quick clinical tool but an imprecise estimation. Precise tools, such as bioimpedance spectroscopy and handheld three-dimensional scanning, should be used in future studies [32]. Fifth, we did not evaluate analgesic drug consumption for post-operative pain control. Nevertheless, both groups followed the same post-operative pain protocol consisting of multimodal analgesia, and the same drug was used for breakthrough pain. Sixth, the findings of this study may not be generalizable to patients with high BMI, those with increased intra-operative blood loss, or individuals with peripheral arterial disease, as these groups were excluded from the study's criteria. Finally, follow-up data were collected for only 3 months. Long-term results, such as prosthesis loosening, should be evaluated in future studies.

Conclusions

In conclusion, the Esmarch bandage provided superior surgical field visualization but showed no advantage in reducing operative time or blood loss. However, the improved visualization is associated with increased post-operative knee swelling.

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Author contributions

ST: study conception and design, SC: data collection, SC, NH, and ST analysis and interpretation of results, SC: draft manuscript preparation, All authors reviewed the results and approved the final version.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

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