Comparison of exsanguination and hemostasis devices for Limb surgery: a multicenter randomized controlled study

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Abstract

Background Excessive intraoperative bleeding remains a challenge in limb surgeries. The exsanguination tourniquet ring has emerged as a potential solution for effective exsanguination and hemostasis. This study aims to evaluate its efficacy and safety compared to the conventional exsanguination and hemostasis approach (pneumatic tourniquet combined with Esmarch bandage).

Methods This randomized controlled trial evaluates the exsanguination tourniquet ring's effectiveness and safety versus the conventional approach in 220 participants undergoing various limb surgeries. Allocation included experimental and control groups, assesses through efficacy (including intraoperative and total blood loss, hemoglobin levels, and exsanguination and hemostasis effectiveness) and safety (adverse event occurrence) indicators.

Results The experimental group ($n = 110$) utilizes the exsanguination tourniquet ring, while the control group ($n = 110$) employs the conventional approach. As for intraoperative blood loss, the experimental group is non-inferior to the control group (p-value < 0.001). While no significant difference is found in total blood loss (for the full analysis set, p-value = 0.442; for the per protocol set, p-value = 0.976) and differences in postoperative and preoperative hemoglobin levels (for the full analysis set, p-value = 0.502; for the per protocol set, p-value = 0.928). Regarding exsanguination and hemostasis effectiveness, the full analysis set reveals significantly superior ratings in the experimental group compared to the control group (p-value = 0.002 < 0.05), while the per protocol set analysis indicates no significant difference between the groups (p-value = 0.504). As for safety indicators, adverse events related to the device are minimal in two groups, with only one severe event unrelated to the device.

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Conclusions The exsanguination tourniquet ring is an effective and safe device for intraoperative blood loss control in various limb surgeries.

Trial registration Comparison of Exsanguination and Hemostasis Devices for Limb Surgery A Prospective Multicenter Randomized Controlled Study, ChiCTR2300077998, 11/27/2023.

Keywords Exsanguination tourniquet ring, Exsanguination, Tourniquets, Hemostasis, Surgical, Clinical trials, Controlled as topic

Background

In surgical procedures involving the extremities, effective exsanguination and hemostasis play pivotal roles in ensuring a clear operative field and minimizing blood loss [1]. Exsanguination, the removal of blood from a limb, and hemostasis, the control of bleeding, are critical steps that facilitate optimal visualization, aid in precision, and contribute to improved patient outcomes [2, 3]. The meticulous management of these processes is paramount to the success of limb surgeries, enabling surgeons to operate with precision and enhancing postoperative recovery.

Since Cushing's pioneering introduction of tourniquet use in 1904, hemostatic tourniquets have boasted a century-long history in surgical practice [4, 5]. Their application, spanning extremity surgeries, has significantly evolved. In limb surgeries, the synergistic employment of exsanguination and tourniquets, such as the combination of Esmarch bandage and pneumatic tourniquet, maximizes control over intraoperative bleeding [6]. This conjoint approach ensures a clear operative field, precise anatomical visualization, shorter anesthesia durations, and reduced blood loss.

Exsanguination tourniquet ring is composed of an elastic contraction ring, elastic fabric sleeve, color tape, handle, straps, and plastic cushion pieces [7]. The elastic contraction ring is designed with a contracted diameter smaller than the minimum size of the limb (including the distal part). During application onto the limb, the elastic contraction ring is squeezed and stretched by the limb's expansion, generating tension. This tension, in turn, applies pressure back onto the limb, compressing it and transmitting the compressive force to the blood vessels. As a result, blood within the vessels is displaced and blood flow is obstructed, thereby yielding an exsanguination and hemostasis effect [8–11].

While the exsanguination tourniquet ring has demonstrated advantages in surgical visualization [7] and procedural efficiency [9] after years of clinical use, a comprehensive assessment of its effectiveness and safety across various limb surgeries remains lacking. Although its innovative design addresses some limitations, a systematic evaluation is essential to validate its utility and ascertain potential benefits for diverse surgical contexts.

Despite the proven benefits of exsanguination and tourniquet rings in surgical procedures, gaps in empirical evidence still exist concerning their comparative effectiveness and safety profiles against conventional methods across a broad spectrum of limb surgeries. Recent advancements have raised questions about the optimal approach to exsanguination and hemostasis, particularly regarding patient outcomes, procedural efficiency, and long-term safety [7].

Given these considerations, our study seeks to bridge this knowledge gap by undertaking a prospective multicenter randomized controlled trial, aimed at elucidating the comparative effectiveness and safety of the exsanguination tourniquet ring and the conventional exsanguination and hemostasis device (pneumatic tourniquet combined with Esmarch bandage) in diverse types of limb surgeries. This investigation aims to provide comprehensive insights into the utility and potential advantages of the exsanguination tourniquet ring, offering guidance for surgical practices involving limb procedures.

The primary hypothesis of this study is that the exsanguination tourniquet ring is non-inferior to the conventional combination of pneumatic tourniquet and Esmarch bandage in terms of controlling intraoperative blood loss in limb surgeries. We further hypothesize that the use of the exsanguination tourniquet ring will result in similar or fewer adverse events compared to the conventional method, thus providing a safer and equally effective alternative for hemostasis during limb surgeries.

Methods

Selection and recruitment of participants

Our study was a prospective, multicenter randomized controlled trial. The recruitment period for the trial was from October 12, 2018, to June 20, 2019. The trial concluded as scheduled after enrolling a sufficient number of participants to meet the predefined sample size requirements, ensuring adequate power for statistical analysis. Recruitment ceased on June 20, 2019, transitioning into data compilation and statistical analysis until July 25, 2019. The trial was not prematurely terminated but rather completed in accordance with the planned timeline and objectives, focusing on the thorough assessment of the intervention's efficacy and safety within the recruited cohort. This multicenter trial allocated cases based on

competitive enrollment among participating institutions, with each center enrolling no fewer than 20% of the total sample size. The study involved three clinical research units: the Second Affiliated Hospital of Zhejiang University, School of Medicine; Zhejiang Provincial People's Hospital; and Hangzhou First People's Hospital, Zhejiang University School of Medicine.

Participants should meet all of the following criteria for inclusion: (1) Age between 18 and 78 years; (2) Underwent limb surgery requiring exsanguination and hemostasis; (3) Anticipated surgical duration within 60 min; (4) Upper arm circumference between 24 and 40 cm or mid-thigh circumference between 28 and 60 cm; (5) Were willing to participate, comply with study requirements, follow-up arrangements, and sign informed consent.

Exclusion criteria were applied if participants met any of the following conditions: (1) Female patients pregnant or lactating during screening; (2) Severe skin damage on limbs; (3) Known inadequate peripheral blood flow, edema, or deep venous thrombosis; (4) Patients with limb infections or malignancies; (5) Patients who experienced severe discomfort, such as cardiovascular risks or respiratory difficulties, from prior tourniquet use; (6) Inability to stabilize systolic blood pressure below 180 mmHg preoperatively; (7) Participation in other drug or device clinical trials within the last month of screening; (8) Other circumstances deemed unsuitable by the investigator.

Three primary reasons for patient exclusion from the final analysis were identified and implemented to maintain the integrity and validity of the trial results: (1) Patients with randomization errors; (2) Patients with no efficacy and safety data post-device treatment; (3) Patients with serious protocol violations not exempted by the principal investigator.

The studies involving human participants were reviewed and approved by Institutional Review Board of the Second Affiliated Hospital of Zhejiang University, School of Medicine (2018-046), Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College (2018QX011), and Hangzhou First People's Hospital, Zhejiang University School of Medicine (2018-027). Informed consent was obtained from all patients for being included in the study. Additionally, this study was registered as a clinical trial with the registration number ChiCTR2300077998 and the date of trial registration 11/27/2023, ensuring adherence to international clinical research standards and enhancing the transparency of our research methods and ethical compliance.

Study devices, anesthesia, group allocation, randomization, and blinding

The exsanguination tourniquet ring was provided by Cixi BLD Medical Instrument Co., Ltd. The pneumatic tourniquet was provided by Zhejiang Guangci Medical Device Co., Ltd. The application of exsanguination and hemostasis techniques strictly adhered to the respective product manuals and surgical standards.

The types of anesthesia include general anesthesia, brachial plexus block anesthesia, and continuous epidural anesthesia.

Participants were allocated into two groups based on the intervention method: the experimental group, where the exsanguination tourniquet ring was utilized, and the control group, receiving the conventional exsanguination and hemostasis approach (pneumatic tourniquet combined with Esmarch bandage).

Given the nature of the interventions, which made blinding of participants and surgeons impractical, the focus was on maintaining the integrity of the allocation concealment process. A block randomization method was used. Investigators (who did not participate in the inclusion of cases and the experimental research process) set the seed number to generate a series of random numbers on SPSS software (Version 16.0), where every two random numbers constitute a block. The generated random numbers were randomly divided into blocks using the Visual Binning function of SPSS. divided into 2 groups. Subjects were entered into the corresponding groups in the order of enrollment time. The grouping list is kept by investigators and is strictly confidential. This method ensured that the allocation sequence was concealed from the researchers until the moment of assignment, preserving the randomization's impartiality. An independent biostatistician, not involved in the clinical aspects of the trial, generated the allocation sequence. The participants were enrolled by research staff at participating sites after confirming eligibility and obtaining informed consent. The assignment of participants to their respective interventions was facilitated through the centralized randomization service, ensuring that the assignment was impartial and that the enrolling staff and participants were immediately aware of the group allocation. Outcome assessors and data analysts remained blinded to the group assignments to minimize bias in the evaluation of results and data interpretation.

Although the interventions differed in terms of the device used, efforts were made to standardize the procedural aspects surrounding their application. This included uniform training for surgical teams on the application and removal of both devices, standardizing the timing of application relative to surgical start, and the criteria for removal. Additionally, the overall management of the surgery, including anesthesia type, surgical technique, and postoperative care, was standardized across both groups to ensure that the only significant variable was the exsanguination and hemostasis method. The aim was to minimize any potential confounding factors and ensure that any differences in outcomes could

be attributed with greater confidence to the interventions being studied rather than to differences in surgical management.

Outcome measures (efficacy and safety indicators)

The assessment criteria encompassed both efficacy and safety indicators.

Efficacy indicators included the primary efficacy indicator (intraoperative blood loss) and the secondary efficacy indicators (postoperative and preoperative hemoglobin comparison, total blood loss, and exsanguination and hemostasis effectiveness). Intraoperative blood loss was calculated as the difference between the mass of soaked gauze and the dry gauze weight, plus the volume in the suction bottle. Total blood loss was determined by the preoperative patient blood volume (PBV) multiplied by the preoperative hematocrit minus postoperative hematocrit. PBV for males was calculated as $0.3669 \times$ height $(m)^3 + 0.0322 \times$ weight $(kg) + 0.6041$. For females, PBV was $0.3561 \times$ height $(m)^3 + 0.0331 \times$ weight $(kg) + 0.1833$. Exsanguination and hemostasis effectiveness was classified into three categories: excellent, good, and bad. An "excellent" rating required meeting the following criteria: (1) No bleeding during surgery, with clear visibility of anatomical layers; (2) After decompression, there was slight indentation on the skin, without redness, swelling, or blisters. Limb blood circulation immediately recovered, with no numbness or other neural functional impairments. A "good" rating involved: (1) Reasonably clear surgical site during the operation, with minor bleeding permitting basic anatomical dissection; (2) After decompression, the skin showed noticeable indentation, mild redness, and a few small blisters, while limb blood circulation immediately recovered without any numbness or other neural functional impairments. A "bad" rating applied when: (1) Evident bleeding at the surgical site hampered anatomical dissection and surgical procedures; (2) Following decompression, the skin displayed numerous blisters, some of which might have ruptured, leading to limb congestion, swelling, and numbness.

Safety indicators primarily involved the occurrence rate of adverse events. During the utilization of research medical devices, adverse medical incidents, whether device-related or not, were classified as adverse events. Mild adverse events referred to slight discomfort experienced by subjects without hindering daily activities and were well tolerated. Moderate adverse events caused significant discomfort and interfered with regular activities. Severe adverse events hindered routine activities. Serious adverse events entailed instances resulting in death or significantly deteriorating health status during the clinical trial. Device-related adverse events were defined as reactions conforming to known reaction patterns of the used product, following a reasonable temporal sequence after treatment, being unable to be explained by other causes, possibly disappearing or alleviating after treatment cessation, and recurrence unable to be attributed to unrelated factors or the subject's pre-existing medical condition.

Statistical methods

Quantitative variables that adhered to a normal distribution were analyzed using either the *t*-test or *t'* test. For non-normally distributed quantitative data, non-parametric tests were employed. Qualitative or ordinal indicators were statistically described by presenting frequency distributions. Categorical variable comparisons were assessed using the chi-squared test or Fisher's exact test. For ordinal indicator comparisons, the Wilcoxon signed-rank test was used. In the comparison of the primary efficacy indicator (intraoperative blood loss), the analysis employed the Least Squares Means (LSMEAN) method with Analysis of Covariance (ANCOVA), accounting for center effects. One-sided 95% confidence intervals (CI) for the between-group difference were computed separately for the experimental and control groups. Non-inferiority of the experimental group over the control group was considered when the lower limit of the CI was greater than -10 mL.

Sample size estimation was performed based on the primary efficacy indicator (intraoperative blood loss) using a non-inferiority design. The calculation was conducted using PASS software (Version 11.0.7). Parameters for this calculation included a standard deviation (σ) of 24 mL for intraoperative blood loss, a one-sided alpha level (α) of 0.025, and a power of test (1-β) of 0.80. The non-inferiority margin (δ) was set at -10 mL. The required sample size per group was calculated to be 92 participants to ensure adequate power to detect the specified non-inferiority margin. Taking into account an anticipated dropout and exclusion rate of 24%, the total sample size required for the study was 228 participants, with 114 participants in each group.

This multicenter trial employed competitive enrollment to allocate cases among participating centers, ensuring that no single center contributed less than 20% of the total sample size. This approach facilitates a broad representation of patient populations and increases the generalizability of the study findings.

Results

Study population for analysis

The entire study actually included a total of 220 enrolled participants (110 in the experimental group and 110 in the control group). Among them, 214 participants successfully completed the trial, while 6 participants discontinued. Ultimately, 188 cases were included in the per protocol set (PPS) and all 220 cases were included in the

Table 1 Cases enrolled, completed, and analyzed dataset

Subject distribution	Exp. group size (%)	Ctrl. group size (%)	Total (%)
Enrollment	110 (50.00)	110 (50.00)	220 (100.00)
Completion	107 (50.00)	107 (50.00)	214 (100.00)
Discontinuation	3 (50.00)	3 (50.00)	6 (100.00)
FAS	110 (50.00)	110 (50.00)	220 (100.00)
PPS	100 (53.19)	88 (46.81)	188 (100.00)
SS	110 (50.00)	110 (50.00)	220 (100.00)

Exp. Group, Experimental Group; Ctrl. Group, Control Group; FAS, Full Analysis Set; PPS, Per Protocol Set; SS, Safety Analysis Set

Table 2 Demographic characteristics of the two study groups

Characteristics		Exp. group (*N*=110)	Ctrl. group (*N*=110)	Statistic	*p*-value
Age (years)	Mean (SD)	45.07 (16.22)	46.79 (13.81)	0.84	0.400
	Median	45.06	48.83		
	Min, Max	18.19, 72.84	19.37, 77.56		
Height (cm)	Mean (SD)	165.25 (7.83)	167.60 (9.38)	2.012	0.045
	Median	165.00	168.00		
	Min, Max	150.00, 185.00	138.00, 193.00		
Weight (kg)	Mean (SD)	63.98 (11.14)	67.58 (13.22)	2.172	0.031
	Median	65.00	65.50		
	Min, Max	42.00, 95.00	40.00, 124.00		
Gender	Male (%)	50 (45.45)	66 (60.00)	4.668	0.031
	Female (%)	60 (54.55)	44 (40.00)		
Ethnicity	Han Ethnicity (%)	109 (99.09)	110 (100.00)	/	1.000*
	Others (%)	1 (0.91)	0 (0.00)		
Marital Status	Married (%)	87 (79.09)	97 (88.18)	3.321	0.068
	Unmarried (%)	23 (20.91)	13 (11.82)		

*, Fisher's exact test; exp. Group, Experimental Group; ctrl. Group, Control Group; SD, Standard Deviation

Table 3 Past medical history of the two study groups

Characteristics		Exp. group (*N*=110)	Ctrl. group (*N*=110)	Statistic	*p*-value
Surgical History	Yes (%)	49 (44.55)	55 (50.00)	0.456	0.499
	No (%)	61 (55.45)	55 (50.00)		
Allergy History	Yes (%)	16 (14.55)	12 (10.91)	0.655	0.418
	No (%)	94 (85.45)	98 (89.09)		
Allergic Constitution	Yes (%)	2 (1.82)	1 (0.91)	/	1.000*
	No (%)	108 (98.18)	109 (99.09)		
History of Significant Organ Dysfunction	Yes (%)	0 (0.00)	0 (0.00)	/	/
	No (%)	110 (100.00)	110 (100.00)		

*, Fisher's exact test; Exp. Group, Experimental Group; Ctrl. Group, Control Group

Table 4 Surgical sites of the two study groups

Surgical sites	Exp. group (*N*=110)	Ctrl. group (*N*=110)	Statistic	*p*-value
Upper Extremity (%)	32 (29.09)	37 (33.64)	0.528	0.468
Lower Extremity (%)	78 (70.91)	73 (66.36)		

Exp. Group, Experimental Group; Ctrl. Group, Control Group

safety analysis set (SS). Data from three participating centers were collected, resulting in a comprehensive dataset for analysis, as detailed in Table 1.

During the course of the trial, a total of 32 participants were excluded due to significant protocol violations. These violations included cases where surgical duration exceeded 90 min, hemostatic drugs were used during the surgery, or hemostasis was terminated prior to the conclusion of the surgical procedure. Other deviations from the protocol were primarily related to laboratory tests that were not completed within the specified time or instances where certain laboratory assessments were missing.

Baseline analysis

The baseline characteristics of the two groups were compared, including demographic variables such as age, height, weight, gender, ethnicity, and marital status. Except for gender, height, and weight, no statistically significant differences were observed in the comparison of other indicators between the groups. Details are provided in Table 2. Comparison of medical history (surgical history, allergy history, allergic constitution, and history of significant organ dysfunction) between the two groups also showed no statistically significant differences, as presented in Table 3. Similarly, comparison of surgical sites (upper extremity and lower extremity) between the two groups did not yield any statistically significant differences, as shown in Table 4.

Primary efficacy indicator analysis

In this study, a non-inferiority analysis was conducted for the primary efficacy indicator (intraoperative blood loss). The non-inferiority margin was set at -10 mL. According to the full analysis set (FAS) analysis, the intraoperative blood loss in the experimental group and the control group was 12.57±30.32 mL and 23.17±52.64 mL, respectively, with a 95% CI of (-∞, -1.026). The non-inferiority analysis showed a *p*-value<0.001, indicating that the experimental group is non-inferior to the control group.

The PPS analysis showed that the intraoperative blood loss in the experimental group and the control group was 8.49±15.18 mL and 12.94±17.93 mL, respectively, with a 95% CI of (-∞, -0.497). The non-inferiority analysis showed a *p*-value<0.0001, further supporting the non-inferiority of the experimental group to the control group. Consistency between PPS and FAS analyses was observed, as presented in Table 5.

Secondary efficacy indicator analysis

In the FAS analysis, the total blood loss in the experimental group and the control group were 141.73±126.54 mL and 147.85±114.45 mL, respectively, with no statistical significance (*p*-value=0.442). In the PPS analysis, the total blood loss in the experimental group and the control group were 146.35±128.39 mL and 139.05±109.45 mL, respectively, also with no statistical significance (*p*-value=0.976). PPS analysis results were consistent with FAS analysis. Table 6 presented the detailed information.

Regarding the hemoglobin levels, the FAS analysis indicated that the preoperative hemoglobin levels were 137.81±19.06 g/L and 142.08±16.30 g/L in the experimental and control groups, respectively. The postoperative hemoglobin levels were 126.69±18.46 g/L and 130.06±14.66 g/L, showing statistically significant differences when compared to the preoperative levels (both *p*-value<0.001). In the PPS analysis, the preoperative hemoglobin levels were 138.67±18.86 g/L and 142.08±15.88 g/L in the experimental and control groups, respectively. The postoperative hemoglobin levels were 127.05±18.14 g/L and 130.60±14.21 g/L, again demonstrating statistically significant differences (both *p*-value<0.001). PPS results were consistent with FAS analysis. Specific details were outlined in Table 7.

Furthermore, in the FAS analysis, the differences in postoperative and preoperative hemoglobin levels in the experimental and control groups were (-11.12)±10.58 g/L and (-12.02)±8.93 g/L, respectively, with no statistically significant differences (*p*-value=0.502). Similarly, in the PPS analysis, the differences in postoperative and preoperative hemoglobin levels in the experimental and control groups were (-11.62)±10.78 g/L and (-11.48)±8.93 g/L, respectively, also without statistical significance (*p*-value=0.928). PPS results were consistent with FAS analysis. Details were provided in Table 8.

Lastly, the analysis of exsanguination and hemostasis effectiveness, based on FAS analysis, showed that the effectiveness ratings of excellent, good, and poor in the experimental group were 100%, 0%, and 0%, respectively, compared to 91.82%, 6.36%, and 1.82% in the control

Table 5 Intraoperative blood loss (mL) of the two study groups

	FAS		PPS	
	Sample size	Intraoperative blood loss	Sample size	Intraoperative blood loss
Exp. Group	110	12.57±30.32	100	8.49±15.18
Ctrl. Group	110	23.17±52.64	88	12.94±17.93
Statistic		3.56		6.10
p-value		<0.001		<0.001
95% CI		(-∞, -1.026)		(-∞, -0.497)

Exp. Group, Experimental Group; Ctrl. Group, Control Group; FAS, Full Analysis Set; PPS, Per Protocol Set; CI, confidence intervals

Table 6 Total blood loss (mL) of the two study groups

	FAS		PPS	
	Sample size	Total blood loss	Sample size	Total blood loss
Exp. Group	109	141.73±126.54	99	146.35±128.39
Ctrl. Group	106	147.85±114.45	85	139.05±109.45
Statistic*		0.769		0.031
p-value		0.442		0.976

*, the Z value in Wilcoxon Signed Rank Test; Exp. Group, Experimental Group; Ctrl. Group, Control Group; FAS, Full Analysis Set; PPS, Per Protocol Set

Table 7 Preoperative and postoperative hemoglobin levels (g/L) of the two study groups

	FAS		PPS	
	Exp. group (*N*=109)	Ctrl. group (*N*=106)	Exp. group (*N*=99)	Ctrl. group (*N*=85)
Preoperative Hemoglobin	137.81±19.06	142.08±16.30	138.67±18.86	142.08±15.88
Postoperative Hemoglobin	126.69±18.46	130.06±14.66	127.05±18.14	130.60±14.21
Statistic*	10.970	13.865	10.720	11.854
p-value	<0.001	<0.001	<0.001	<0.001

*, Paired *t*-test; Exp. Group, Experimental Group; Ctrl. Group, Control Group; FAS, Full Analysis Set; PPS, Per Protocol Set

Table 8 Preoperative and postoperative hemoglobin difference (g/L) of the two study groups

	FAS		PPS	
	Exp. group (*N*=109)	Ctrl. group (*N*=106)	Exp. group (*N*=99)	Ctrl. group (*N*=85)
Preoperative-Postoperative Hemoglobin Difference	(-11.12)±10.58	(-12.02)±8.93	(-11.62)±10.78	(-11.48)±8.93
Statistic		0.67		0.09
p-value		0.502		0.928

Exp. Group, Experimental Group; Ctrl. Group, Control Group; FAS, Full Analysis Set; PPS, Per Protocol Set

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Table 9 Exsanguination and hemostasis effect of the two study groups

	FAS			PPS		
	Excellent (%)	Good (%)	Bad (%)	Excellent (%)	Good (%)	Bad (%)
Exp. Group	110 (100.00)	0 (0.00)	0 (0.00)	110 (100.00)	0 (0.00)	0 (0.00)
Ctrl. Group	101 (91.82)	7 (6.36)	2 (1.82)	84 (95.45)	4 (4.55)	0 (0.00)
Statistic	3.053			0.669		
p-value	0.002			0.504		

Exp. Group, Experimental Group; Ctrl. Group, Control Group; FAS, Full Analysis Set; PPS, Per Protocol Set

Table 10 Occurrence of adverse events in the two study groups

	Group	Happening (%)	Not happening (%)	Statistic	*p*-value
Total	Exp. Group	41 (37.27)	69 (62.73)	0.318	0.573
	Ctrl. Group	37 (33.64)	73 (66.36)		
Probably associated with Instruments	Exp. Group	7 (6.36)	103 (93.64)	1.676	0.195
	Ctrl. Group	3 (2.73)	107 (97.27)		

Exp. Group, Experimental Group; Ctrl. Group, Control Group

group, with statistical significance (*p*-value=0.002<0.05). However, in the PPS analysis, the effectiveness ratings in the experimental group were 100%, 0%, and 0%, compared to 95.45%, 4.55%, and 0% in the control group, with no statistical significance (*p*-value=0.504). Details were provided in Table 9.

Safety analysis

During the course of the trial, a total of 78 subjects experienced 126 adverse events. Among the 220 subjects enrolled (110 in the experimental group and 110 in the control group), 41 subjects in the experimental group (37.27% incidence rate) and 37 subjects in the control group (33.64% incidence rate) experienced at least one adverse event, with no statistically significant difference between the two groups (*p*-value=0.573). A total of 10 subjects experienced 15 adverse events possibly related to the device during the trial, with 7 subjects in the experimental group experiencing 11 events and 3 subjects in the control group experiencing 4 events, showing no statistically significant difference (*p*-value=0.195). Details were presented in Table 10. Adverse events related to the investigational device included limb numbness, swelling, and ecchymosis, while no occurrences of ineffective hemostasis, increased bleeding, tourniquet pain, tourniquet shock, muscle nerve injury, or blood vessel damage were observed.

Apart from one instance of a serious adverse event, the remaining adverse events in this study were of mild or moderate severity. The details of this serious adverse event are as follows: The patient signed the informed consent on December 11, 2018, successfully screened and enrolled in the clinical trial on December 12, 2018, and was assigned to the control group. The patient's diagnoses upon enrollment were "1. Right popliteal cyst; 2. Left inguinal hernia postoperative, 3. Hypertension." Surgery was performed on the same day, lasting for 1 h and

9 min, with hemostasis lasting for 1 h and 12 min, and a blood loss of 10 mL during the procedure. At 02:45 on December 14, 2018, the patient exhibited symptoms of chest tightness, dyspnea, and rapid breathing, with blood oxygen saturation at 85%. Appropriate treatment was administered but yielded no effect. The family requested discharge. On December 20, 2018, it was learned that the patient had passed away on December 14, 2018. The researchers determined that this incident was unrelated to the investigational device. Therefore, no device defect that might have led to a serious adverse event was identified in this study.

Discussion

The exsanguination tourniquet ring demonstrated non-inferiority to the conventional exsanguination and hemostasis device in terms of the primary efficacy indicator (intraoperative blood loss). The results from both FAS and PPS analyses were consistent. The FAS analysis indicated a reduction of 45.75% in average intraoperative blood loss, while the PPS analysis showed a reduction of 34.39%. In a study involving 134 cases of long bone fracture surgery, Christopher Domes et al. [12] reported a 42% reduction in blood loss with the exsanguination tourniquet ring compared to the pneumatic tourniquet. Similarly, Jean-Yves Jenny et al. [13], in a study of 72 cases of knee arthroplasty, reported an 8.9% reduction in blood loss using the exsanguination tourniquet ring compared to the pneumatic tourniquet. These findings aligned closely with our results, although our study encompassed a more comprehensive range of surgical procedures, including fractures, benign bone tumors, arthritis, and popliteal cysts, all of which required limb exsanguination and hemostasis. However, A. Pereira et al. 's [14] study on 76 patients with carpal tunnel syndrome yielded contrasting results, indicating no significant difference in blood loss between the use of the pneumatic tourniquet

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and the exsanguination tourniquet ring. This discrepancy could partly be attributed to the diversity of surgical types in our study, where the original data suggested substantial variations in intraoperative blood loss across different surgical procedures. Additionally, the variance might stem from differences in evaluation methods. While they employed surgeon-rated scoring for assessing intraoperative blood loss, our evaluation was based on a more meticulous approach involving postoperative dressing quality minus preoperative dry dressing quality plus the volume of blood collected in the suction bottle. Our method of assessing intraoperative blood loss was more rigorous, whereas their approach appears more analogous to our evaluation of the exsanguination and hemostasis efficacy.

In the SS analysis, our study indicated that 6.36% (7/110) of participants in the experimental group experienced adverse events possibly related to the device, while 2.73% (3/110) of participants in the control group encountered similar adverse events. These events included limb numbness, swelling, and bruising. Interestingly, in a study focusing on total knee arthroplasty, Sanjay Bhalchandra Londhe et al. [15] reported that the utilization of conventional hemostasis devices resulted in a local skin complication rate of 20% (10/50), characterized by occurrences of local bruising or blister formation. Conversely, when employing the exsanguination tourniquet ring, the rate of local skin complications was observed to be 0% (0/50). Their mentioned bruising complication aligned with the adverse events we discussed in relation to the device, possibly implying a subordinate relationship. Furthermore, their reported blister formation coincided with one aspect of our evaluation of exsanguination and hemostasis effectiveness. Our findings had effectively demonstrated the exceptional hemostatic efficacy of the exsanguination tourniquet ring, manifested in two key aspects: (1) During surgery, there was minimal bleeding and ecchymosis at the surgical site, along with a clear visualization of anatomical layers; (2) Following decompression, the skin displayed only slight indentation, devoid of redness and blisters, while the restoration of limb circulation was immediate and there were no numbness or other neural functional impairments. Discrepancies between their results and ours might be attributed to sample size, variations in surgical procedures, and other factors. Additionally, Viktor Feldman et al. [9] reported cases of pulmonary embolism in 2 trauma patients (fractures of the patella and tibial plateau) following the use of the exsanguination tourniquet ring. Further assessment was required to comprehensively evaluate the safety profile of the exsanguination tourniquet ring.

Our findings enhance the current understanding of hemostasis techniques in limb surgeries, showing that the exsanguination tourniquet ring can reduce intraoperative blood loss more effectively compared to traditional methods. This supports the potential for broader clinical application, particularly in surgeries where precision and rapid postoperative recovery are crucial. By aligning our results with existing literature, which also documents reduced complications with modern hemostasis methods, we provide a compelling case for re-evaluating surgical standards to incorporate these newer technologies. Such a shift could significantly improve patient outcomes, reduce hospital stays, and potentially lower healthcare costs associated with surgical complications.

Our study's design and execution, while meticulous, naturally encompass several limitations that warrant further discussion to provide a balanced understanding of the results. The variability in intraoperative blood loss across different surgical types, as mentioned, not only affected the precision of our results but also suggests a potential confounder: the surgical technique itself. Surgical techniques vary widely in complexity and duration, factors that could independently influence blood loss irrespective of the hemostasis method used. This introduces a layer of complexity that could obscure the direct effects of the hemostasis devices. Additionally, the broad age range of participants (18 to 78 years) covers a wide spectrum of physiological profiles, which could significantly affect outcomes such as blood loss and recovery. Older patients or those with co-morbidities might respond differently to hemostasis methods, potentially skewing efficacy and safety profiles. While our exclusion criteria aimed to minimize this variability, they might also limit the generalizability of our findings to all potential surgical candidates, particularly those with underlying conditions like severe limb skin damage or deep venous thrombosis. Another limitation stems from our method of measuring blood loss, which, despite being standardized, may still suffer from measurement biases inherent in surgical settings. For instance, the quantification of blood on surgical drapes and in suction devices can be imprecise, leading to potential underestimation or overestimation of actual blood loss. Regarding potential biases, our study might also be influenced by selection bias. Although randomized, the allocation to experimental or control groups could still harbor hidden biases based on unmeasured or unaccounted-for participant characteristics. Moreover, while we attempted to blind outcome assessors and data analysts, the complete blinding of participants and surgeons was not feasible, which might introduce performance bias where knowledge of the treatment received could subtly influence care practices or reporting of outcomes.

In future studies, we aim to address these issues by stratifying participants more finely by age, comorbidities, and specific surgical criteria to better isolate the effects of

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the hemostasis methods. Additionally, employing more robust methods to measure blood loss and enhancing the blinding process where possible will help mitigate measurement and performance biases. Lastly, expanding the assessment to include postoperative pain [15–17], infection rates [18], and incidence of thrombotic events [19] will provide a more comprehensive view of the relative efficacy and safety of the hemostasis methods used, thereby enriching the clinical relevance of our findings.

Conclusions

In conclusion, our study demonstrated that the exsanguination tourniquet ring provides precise hemostatic efficacy in limb surgeries, showing non-inferior performance to conventional exsanguination and hemostasis devices in terms of intraoperative blood loss. Specifically, the experimental group using the tourniquet ring matched the control group employing traditional methods, with no significant difference observed in total blood loss or in changes between preoperative and postoperative hemoglobin levels. Furthermore, in terms of exsanguination and hemostasis effectiveness, the FAS analysis highlighted a statistically significant superiority of the experimental group over the control group, although this difference was not observed in the PPS analysis. Safety outcomes were also favorable, with minimal adverse events reported in both groups, and only one severe event that was determined to be unrelated to the use of the device. Despite these positive results, our study has limitations such as its restricted focus on certain types of surgeries and a narrow demographic, which may limit the generalizability of our findings. Future research will aim to address these limitations by refining participant stratification based on age, comorbidities, and specific surgical criteria to better isolate the effects of hemostasis methods. Employing more robust methods for measuring blood loss and enhancing the blinding process will aim to reduce measurement and performance biases. Expanding evaluations to include metrics such as postoperative pain, infection rates, and the incidence of thrombotic events will offer a more comprehensive assessment of the relative efficacy and safety of the hemostasis methods used, thus enhancing the clinical relevance of our study results.

Abbreviations

FAS	Full analysis set
PPS	Per protocol set
SS	Safety analysis set
CI	Confidence interval
LSMEAN	Least Squares Means
ANCOVA	Analysis of Covariance
PBV	Patient blood volume

Author contributions
JJX and KQZ carried out experiments. SNX, JQX, and ZMY analyzed the data. BBS and TSL wrote the manuscript. WFZ, QB, and WXY designed the study and revised the manuscript. All authors reviewed and approved the final version of the manuscript.

Data availability
All data generated or analyzed during this study are included in this manuscript and its supplementary information files. The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by Institutional Review Board of the Second Affiliated Hospital of Zhejiang University, School of Medicine (2018-046), Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College (2018QX011), and Hangzhou First People's Hospital, Zhejiang University School of Medicine (2018-027). Informed consent was obtained from all patients for being included in the study.

Consent for publication
Not applicable.

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Competing interests
The authors declare no competing interests.

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References
1. de la Herrero B, Roa-Esparza J, Cearra I, et al. The Prevention of Ischemia-Reperfusion Injury in Elderly rats after lower limb Tourniquet Use. Antioxid (Basel). 2022;11(10):1936. Published 2022 Sep 28.
2. Bourquelot P, Levy BI. Narrow elastic disposable tourniquet (Hemaclear®) vs. traditional wide pneumatic tourniquet for creation or revision of hemodialysis angioaccesses. J Vasc Access. 2016;17(3):205–9.
3. Bosman HA, Robinson AH. Pneumatic tourniquet use in foot and ankle surgery–is padding necessary? Foot (Edinb). 2014;24(2):72–4.

4. Ding L, Ding CY, Wang YL, et al. Application effect of pneumatic tourniquet with individualized pressure setting in orthopaedic surgery of extremities: a meta-analysis. J Adv Nurs. 2019;75(12):3424–33.
5. Yatsun V. Application of hemostatic tourniquet on wounded extremities in Modern Trench Warfare: the View of a vascular surgeon [published online ahead of print, 2022 Jul 13]. Mil Med. 2022;usac208.
6. Chen P, Chen H, Yang M. Comparison of high ligation of great saphenous vein using pneumatic tourniquets and conventional method for great saphenous vein varicosis. Med (Baltim). 2020;99(35):e21975.
7. Lee TS, Park KK, Cho BW, Lee WS, Kwon HM. Silicone ring tourniquet could be a substitute for a conventional tourniquet in total knee arthroplasty with a longer surgical field: a prospective comparative study in simultaneous total knee arthroplasty. BMC Musculoskelet Disord. 2023;24(1):363. Published 2023 May 9.
8. Franzone JM, Yang JH, Herzenberg JE. Reuse of single-use HemaClear Exsanguination tourniquets: a technique note. J Long Term Eff Med Implants. 2017;27(1):59–65.
9. Feldman V, Biadsi A, Slavin O, et al. Pulmonary embolism after application of a sterile Elastic Exsanguination Tourniquet. Orthopedics. 2015;38(12):e1160–3.
10. Tang DH, Olesnicky BT, Eby MW, Heiskell LE. Auto-transfusion tourniquets: the next evolution of tourniquets. Open Access Emerg Med. 2013;5:29–32. Published 2013 Dec 4.
11. Ladenheim E, Krauthammer J, Agrawal S, Lum C, Chadwick N. A sterile elastic exsanguination tourniquet is effective in preventing blood loss during hemodialysis access surgery. J Vasc Access. 2013;14(2):116–9.
12. Domes C, O'Hara NN, O'Toole RV, Schloss MG, Hannan ZD, Pensy RA. Use of the HemaClear™ elastic tourniquet reduces blood loss in operative treatment of humeral shaft fractures. Injury. 2023;54(2):584–8.
13. Jenny JY, Bahlau D, Wisniewski S. Silicone ring tourniquet or pneumatic cuff tourniquet for total knee arthroplasty. Int Orthop. 2016;40(9):1803–6.
14. Pereira A, Hendriks S, Facca S, Bodin F, Gay A, Liverneaux P. Evaluation of a new tourniquet for hand surgery: comparison of 76 carpal tunnel syndrome cases operated using a hemaclear(®) Model-F tourniquet versus a pneumatic tourniquet. Chir Main. 2015;34(2):73–8.
15. Bhalchandra Londhe S, Vinod Shah R, Sanjay Londhe S, Agrawal PO, Antao NA, Churhe S. Comparison of local pain and tissue reaction between conventional pneumatic tourniquet and disposable silicone ring tourniquet during total knee arthroplasty. J Clin Orthop Trauma. 2020;15:152–5. Published 2020 Sep 9.
16. Drosos GI, Kiziridis G, Aggelopoulou C, et al. The Effect of the Silicone Ring Tourniquet and Standard Pneumatic Tourniquet on the motor nerve conduction, Pain and grip strength in healthy volunteers. Arch Bone Jt Surg. 2016;4(1):16–22.
17. Mohan A, Baskaradas A, Solan M, Magnussen P. Pain and paraesthesia produced by silicone ring and pneumatic tourniquets. J Hand Surg Eur Vol. 2011;36(3):215–8.
18. Bae K, Kim G, Aldosari AM, Gim Y, Kwak YH. Sterile silicone Ring tourniquets in Limb surgery: a prospective clinical trial in Pediatric patients undergoing orthopedic surgery. J Pers Med. 2023;13(6):979. Published 2023 Jun 10.
19. Migliorini F, Maffulli N, Eschweiler J, Knobe M, Tingart M, Betsch M. Tourniquet use during knee arthroplasty: a bayesian network meta-analysis on pain, function, and thromboembolism. Surgeon. 2022;20(4):241–51.

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