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COMPARISON OF THREE TOURNIQUET APPLICATION METHODS IN PRIMARY TOTAL KNEE ARTHROPLASTY SURGERY

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VILNIAUS UNIVERSITETAS

GIEDRIUS KVEDERAS

TRIJŲ KRAUJOTAKOS SUMAŽINIMO METODŲ PALYGINIMAS ATLIEKANT PLANINĮ CEMENTINĮ KELIO SĄNARIO ENDOPROTEZAVIMĄ

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CONTENTS

1. ABBREVIATIONS

ASA	American Society of Anesthesiologists physical status class
BMI	Body mass index
BSA	Body surface area
BVL	Blood volume loss
DVT	Deep vein thrombosis
ECG	Electrocardiogram
GDT	Goal directed therapy
H	Height
Hb	Hemoglobin
Hct	Hematocrit
KSS	Knee Society Score
mVLT	Mini volume loading test
NS	Not significant
NSAID	Nonsteroidal anti-inflammatory drugs
P	The estimated probability of rejecting the null hypothesis (H_0) of a study question when that null hypothesis is true
PACU	Post-anesthesia care unit
PD	Plasma dilution
PV	Plasma volume
RCL	Red cell volume loss
revGDT	Revised goal directed therapy protocol
RCT	Randomized clinical trial
RCV	Red cell volume
ROM	Range of motion
SD	Standard deviation
SV	Stroke volume
TKA	Total knee arthroplasty
TUG test	Timed Up and Go test
W	Weight
WOMAC VA 3.1	Western Ontario and McMaster Universities' proposed Osteoarthritis Index visual analogue scale

2. INTRODUCTION

2.1. Background

A pneumatic lower limb tourniquet is conventionally used in primary total knee arthroplasty (TKA) surgery in order to provide better visualization, dry surgery, facilitation of cementing technique and reduction of the duration of surgery.[1, 2] A recent meta-analysis showed that both total and intraoperative blood losses are lower using a tourniquet.[3] On the basis of the available evidence, the use of a tourniquet during primary TKA should be considered the standard of care.[4] However, soft tissues can suffer from ischemia by the direct pressure of the tourniquet. The tourniquet is also a risk factor for thromboembolism. It is associated with increased swelling and stiffness of joints, impaired wound healing, nerve palsy, vascular injuries, rhabdomyolysis and subcutaneous thigh fat necrosis as well as thigh pain. Thus, a relationship of risk to benefit of tourniquet application *per se* is continuously debated.[5]

The mostly used tourniquet application strategies can be classified into three main patterns: one is when the tourniquet is inflated before incision and deflated after the closure of the incision; another is when the tourniquet is inflated before incision and deflated after the hardening of the cement; the other is – the tourniquet is inflated before prosthesis placement and deflated after the hardening of the cement. There is no consensus regarding the optimal timing of tourniquet application[6], although it can have a major impact on perioperative blood loss[3]. The controversial results are published even in meta-analyses. In two meta-analyses Rama et al.[7] and Zan et al.[8] observed a statistically significant reduction in total blood loss when the tourniquet was left inflated until wound closure was complete comparing with the early release. Another meta-analysis by Zhang et al.[9] did not demonstrate significant differences between the two groups in the actual blood loss. Therefore, it appears to be highly desirable to reduce the tourniquet time to a minimum. Mittal et al.[10] compared functional outcomes between tourniquet application of short duration (during cement fixation only) and tourniquet application of longer duration

(from skin incision to just after cement fixation) and found that restriction tourniquet application to the period of cementing is associated with a significantly higher risk of transfusion. In opposite, Fan et al.[11] concluded that limited tourniquet use (from the cementation to the completion of the procedure) did not increase the blood loss. Tarwala et al.[12] suggested that there were no relevant clinical differences between patients who had a tourniquet inflated throughout the procedure compared with those who had it inflated only during cementation. Additional trials are required to clarify the roles of tourniquet and compare the effects of different methods of tourniquet applications in TKA [1].

The hypothesis of this clinical trial was that applying a tourniquet for a different duration this would have an impact on perioperative blood loss and influence time when the criteria of fit-to-discharge were achieved.

2.2. The aim of the study

The aim of this study was to analyse the influence of the three intraoperative tourniquet application methods on the perioperative blood loss in primary total knee arthroplasty patients:

- the tourniquet was inflated just before skin incision and deflated after the cement had hardened.
- the tourniquet was inflated just before the cement was laid and deflated after its solidifying.
- the tourniquet was inflated before skin incision and deflated following the wound closure and compressive dressing application.

2.3. Objectives of the study

1. To evaluate how three strategies of lower limb pneumatic tourniquet application affect the blood loss for TKA patients.
2. To evaluate impact of the different tourniquet strategies on frequency of transfusions.

3. To compare the short-term postoperative outcomes of different timing of tourniquet.
4. To estimate blood loss with different methods of blood loss calculation.
5. To evaluate the impact of the individualised perioperative fluid therapy on recovery after surgery.
6. To compare complications of different tourniquet strategies.

2.4. The scientific novelty of the study and implementation into the practice

There has been no research evaluating three most common tourniquet application methods in TKA. The effects of various tourniquet application strategies on perioperative blood loss have not been fully established. Previous studies have shown that calculating blood loss is more accurate than measuring obvious loss. However, research studies showed that normal blood volume calculated by formulas does not always fit the values obtained by direct measurements. All formulas for calculating blood loss have their deficiencies. Blood hemoglobin concentration (Hb) and hematocrit (Hct) used for blood loss calculations could vary due to patient's condition, recovery due to blood loss compensatory mechanisms, fluid therapy, day time changes. Therefore, it is hard to differentiate Hb and Hct changes resulting from mild or initial stage bleeding and similar changes induced by isoosmotic plasma dilution shifts. The accuracy of the most previous studies could be affected by use of only one method for the blood loss calculation. The literature recommends several formulas for calculation of fluid deficits, ongoing loss and maintenance requirements. The use of different methods could reduce probability of false positive or false negative results.

The different hydration situations could change values of Hb and Hct as well as results of estimated blood loss. The fluid administration may vary between 1 and 5 liters of fluids (crystalloids or crystalloids together with colloids) regardless of loss.[13] Nevertheless, excessive infusions result in haemodilution or controversially

limited fluid intake could increase Hgb concentration and shift blood loss results. No study was used to individualize fluid management in TKA for tourniquet comparing trials. Goal directed therapy (GDT) is a validated method for individual optimization of circulation within a fluid protocol in perioperative settings.[14] GDT is usually guided by flow-related parameters such as stroke volume (SV) or cardiac output.However, GDT protocols have recently been challenged since infused fluids in such programs could end up to larger volumes compared to standard of care.[15-17]Infused fluids, even if given in an individualized manner, are accumulated interstitially. Therefore, a stepwise infusion method (mini Volume Loading Test, mVLT) based on changes in haemodilution has been suggested as a supplement to GDT to detect imminent interstitial edema [18, 19]. A revised GDT protocol (revGDT) could, by intermittent small infusions, identify a point where haemodilution no longer increases (non responsiveness) and this would be an indication of when fluid is being allocated into surrounding tissues (edema). We proposed a revised goal directed fluid therapy protocol (revGDT) with a mini Volume Loading Test (mVLT) where calculation of plasma dilution (PD) induced by serial of lower volume (mini) fluid challenges was used to calibrate the state of hydration. Applying of revGDT twice before and after surgery could optimize hydration status of the patient and reduce bias of the Hb and Htc results.

The evaluation of the pain, range of motions, swelling or functional scores are the most popular in the tourniquet comparing studies. Most of them have found no or minimal differences between different tourniquet strategies. Moreover, these differences have become not significant during the time. The clinical relevance of those findings is not clear. The evaluation of the time when the fitness-to-discharge is achieved could be more clinically and financially rational.

The perioperative blood loss could vary depending on many factors, such as patient condition, knee deformity, type of implant, surgical technique, hypotensive anaesthesia, postoperative dressing, anticoagulant therapy or drain use and clamping. As well as the clinical results could depend on skin protection underneath, type and

pressure of tourniquet. The strict inclusion and exclusion criteria, standardised study protocol, one surgeon and one anaesthetist have led to the better detection of outcome differences between the groups in our study.

3. MATERIALS AND METHODS

3.1. Study Design and Settings

The protocol and subsequent amendments were approved by the Regional Ethical Committee of the Vilnius Regional Bioethics Committee, Vilnius, M.K. Ciurlionio 21/27, LT-03101, Lithuania (chairperson G. Andrulionis, approval No.158200-9-071-22). The trial was registered at Clinicaltrials.gov (identifier: NCT01355900). The study was performed at the Republic Vilnius University Hospital, Vilnius, Lithuania, from January 2010 to January 2014.

3.2. Study Subjects

The patients scheduled for TKA were screened for inclusion. Table 1 lists the exclusion criteria. All enrolled patients signed an informed consent form. CONSORT diagram of the trial is shown in Figure 1. One hundred thirty two participants were enrolled in the trial. One hundred twenty patients (101 females, 19 males) completed the study.

Table 1 Exclusion Criteria

- Age < 50 or > 80 years
- Body mass index < 20 or > 40 kg/m^2
- ASA I, ASA >= III physical status
- Rheumatoid arthritis
- Diabetes mellitus
- Current chronic anticoagulation therapy
- History of a bleeding disorder

- History of deep vein thrombosis (DVT), thromboembolic complications or acute cardiac insufficiency
- Anemia before surgery requiring blood transfusion
- Severe deformity of the knee: > 15° varus, > 20° flexion contracture
- Previous open-knee surgery
- Intravascular fluid infusion within 24 hours before surgery
- Chronic non-steroidal anti-inflammatory drug use (more than 6 months of daily use)
- Psychiatric illness (intake of other psychiatric medication than selective serotonin reuptake inhibitors)
- Alcohol intake greater than 5 units daily
- Active malignancy
- Contraindication to epidural catheter insertion
- Any contraindication to a catheter insertion into a radial artery
- Surgery performed not by a study surgeon
- Participation in another study
- Operative exclusion criteria:
    - Synovectomy
    - Patella replacement
    - Lateral retinacular of the patella release

3.3. Study Groups

The primary outcome was to determine the effect of three intraoperative tourniquet method use on total blood loss for patients undergoing TKA. The three tourniquet timing strategies were compared:

Group 1- the tourniquet was inflated just before skin incision and deflated after the cement had hardened.

Group 2- the tourniquet was inflated just before the cement was laid and deflated after its solidifying.

Group 3- the tourniquet was inflated before skin incision and deflated following the wound closure and compressive dressing application.

The secondary endpoints were the accuracy of noninvasive hemoglobin measurements and the influence of fluid therapy on outcomes. All three intervention groups received perioperative fluid therapy which included the pre- and post-operative administration of revGDT protocol. With the aim to evaluate the influence of revGDT on outcomes, a control Group 4 was included. The control group received crystalloid infusions solely at the discretion of an attending physician during the whole study. The identical tourniquet method was applied for Group 1 and Group 4 (Table 2).

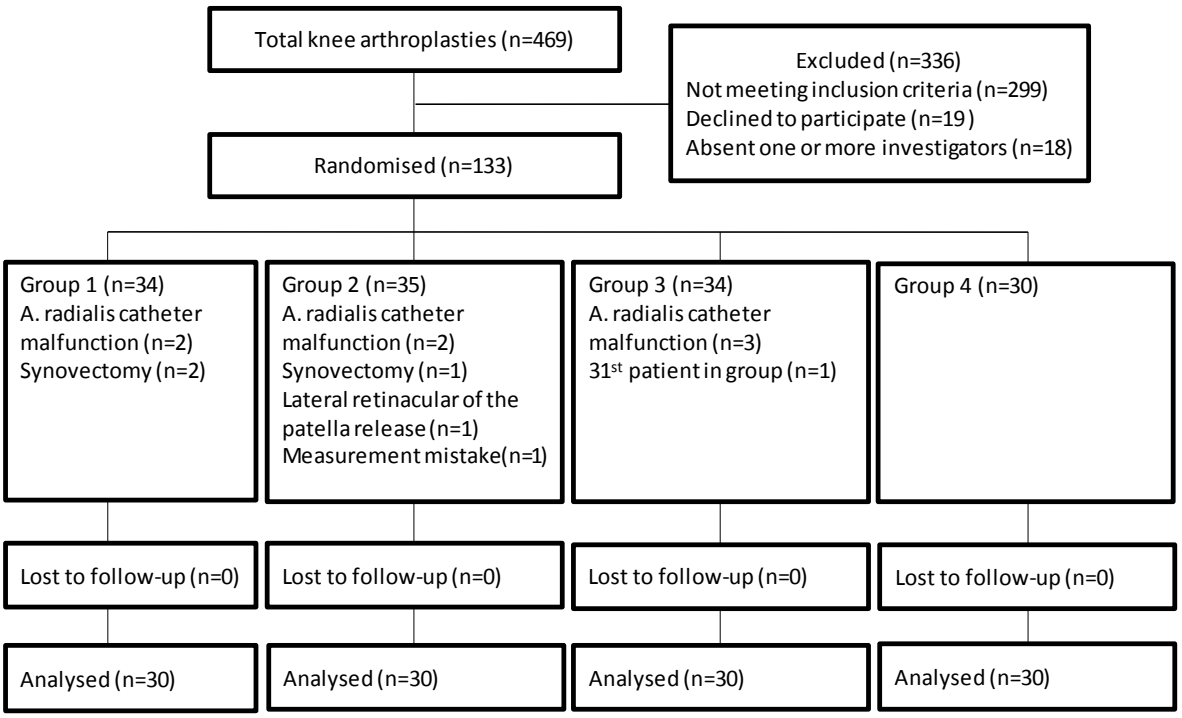


Fig. 1 CONSORT diagram of the trial. Group 1– patients who underwent total knee arthroplasty with tourniquet inflated just before the skin incision and deflated after the hardening of cement, Group 2– tourniquet inflated just before the cement application and deflated after its hardening, Group 3– tourniquet inflated before incision and deflated after the last suture of the skin, and Group 4 – tourniquet method was identical with Group 1, but patients of Group 4 received crystalloid

infusions solely at the discretion of an attending physician. Group 1, 2 and 3 received perioperative fluid therapy which included the pre- and post-operative administration of revGDT (revised goal directed therapy) protocol. CONSORT – Consolidated Standards of Reporting Trials.

Table 2 Study groups: tourniquet timing and fluid therapy protocol

Study Group	Tourniquet		Fluid therapy
	Inflation	Deflation	
1	Before skin incision	After the cement hardening	revGDT protocol
2	Before cement application	After the cement hardening	revGDT protocol
3	Before skin incision	After the last suture of the skin	revGDT protocol
4	Before skin incision	After the cement hardening	Standard

3.4. Blinding and Randomization

A block randomization list was generated prior to recruitment by a statistician not involved in the study. Every enrolled subject was assigned a computer-generated random number, consecutively from the list. The randomization schedule assigned random numbers to group codes. Patients were randomized in a 1:1:1:1 ratio to Group 1, Group 2, Group 3 or Group 4 (Figure 1). The intervention for each group is described in the text below. One hundred and forty opaque envelopes with random numbers containing the assigned treatment options were prepared and kept sealed in a safe. If a patient met the criteria for inclusion into the study, the operating surgeon requested the envelope with the lowest number and opened it to determine to which group the patient should be allocated. Blinding was not possible neither for the surgeon nor for the anaesthetist. The researchers who examined and collected the data were blinded to the patient allocation to study groups.

3.5. Preoperative examination

The enrolled patients completed the WOMAC VA 3.1 questionnaire (Western Ontario and McMaster Universities' proposed Osteoarthritis Index visual analogue scale). The Knee Society Score (KSS) was used to quantify the degree of pain and extent of disability before surgery. The range of motion (ROM) and flexion

contracture were measured. The TUG test was used to evaluate the preoperative degree of mobility. This test involves measuring the time a patient needs to get up from a chair, walk three meters, turn, walk back to the chair and then sit down again [20]. The stage of osteoarthritis of the knee was determined by radiology and was graded using the classification proposed by Holden et al. [21].

3.5.1. Monitoring and Preoperative blood sampling

Standard perioperative monitoring (ECG, pulse oximetry and non-invasive blood pressure measurement) was applied when the patient arrived at the operating theatre at 7:00 am. An antecubital intravenous line for fluid infusion was placed in one arm, and a radial artery cannula in the other arm for arterial blood sampling. Preoperative arterial blood samples for perioperative blood loss calculation purposes were obtained via a catheter in the radial artery just before starting the intravenous infusion prior to anaesthesia induction. Blood samples were analysed in the laboratory for arterial hemoglobin concentration (Hb) and hematocrit (Hct) by a haematology analyser (COULTER® LH750, Beckman Coulter, Inc., USA)with a precision coefficient of variation (CV) ≤ 0.8% for Hb.

3.5.2. Preoperative optimization of fluid status

A revised algorithm for goal-directed fluid therapy – the minimal volume loading test (mVLT) – was used, with the goal of optimizing the preoperative hydration status of the patients. Briefly, this test consists of three fluid challenges – three 5 ml/kg boluses of acetated Ringer's solution separated by periods of duration of 5 minutes without fluids. The minimization of dilution efficacy of the fluid challenges was used as a marker of optimized fluid status.

3.6. Surgery

3.6.1. Anaesthesia

An epidural catheter was inserted but not yet activated and spinal anaesthesia was administered in the L3-4 intervertebral space with 3.0 ml of 0.5% bupivacaine

solution and injection of an epidural test dose (3 ml of 2% lidocaine solution). Anaesthesia was administered by the same anaesthesiologist for all patients.

3.6.2. Tourniquet application

The automatic lower limb pneumatic tourniquet system (Automatic Tourniquet System A.T.S. 3000, Zimmer Orthopaedic Surgical Products, Dover, Ohio, USA) was applied to reduce blood loss during surgery. The skin under the tourniquet was covered by cast padding. The operated leg was elevated and exsanguinated before inflating the automatic pneumatic tourniquet. One of three tourniquet treatment strategies was used, as determined by the group allocation of the patient. The tourniquet was inflated just before skin incision and deflated after the cement had hardened for patients in Group 1. The tourniquet was inflated just before the cement was laid and deflated after its solidifying for patients in Group 2. Finally, the tourniquet was inflated before skin incision and deflated following the wound closure and compressive dressing application in Group 3. Control Group 4 was involved into the study to evaluate the influence of the individual fluid therapy on clinical results. The tourniquet strategy was the same as for Group 1, but the revGDT was not applied for patients in Group 4.

3.6.3. Surgical interventions

All operations were performed by the same senior surgeon. Anterior medial parapatellar incision and standard medial subvastus arthrotomy techniques were used. Intramedullary femoral and extramedullary tibial resection guides were used for all subjects. Holes in the distal femur made for intramedullary guides were filled with bone cement (Refobacin Bone Cement R, Biomet Orthopaedics Switzerland GmbH, Ried b. Kerzers, Switzerland) and deployed when the prosthesis (AGC V2 Posterior Cruciate Retaining Total Knee system, Biomet UK Ltd, Bridgend, UK) was placed. Electrocautery was used when needed. A suction drain was inserted into the joint on completion of surgery, and the line was clamped.

3.7. Postoperative evaluation

3.7.1. Postoperative period (24 hours)

All the patients were transferred to the PACU for a 24-h period of postoperative care. A cold pack was applied to the surgical site for 2-3 hours after arrival. The timing of the drain opening was the same in all groups. Aiming for postoperative intraarticular tamponade, a vacuum wound drainage was kept closed for three postoperative hours, after which it was released for about 10 minutes, clamped again and kept closed until 7:00 am the following morning. Then it was released, kept open for 1 hour, and then removed. The fluid therapy was targeted to achieve the zero fluid balance.

Postoperative arterial blood samples were obtained via the catheter in the radial artery at 7:00 am on the first postoperative day (about 24 hours after the preoperative sampling). Immediately after the postoperative blood sampling, the minimal volume loading test was applied again. The aim of this was to optimize the postoperative hydration status of the patient.

For the first 24 postoperative hours, continuous epidural analgesia was administered through an infusion pump syringe filled with 0.125% bupivacaine solution plus 2.0 micrograms ml^{-1} of fentanyl at a 4 ml/hr rate. The epidural infusion was stopped at 6:30 am the following day and the continuous epidural analgesia regimen was switched to a single-shot injection of 6-8 ml of 0.125% bupivacaine every 6 hours for the following 48 hours. Adjuncts – NSAIDs and opioids – were administered on an as-needed basis (VAS scale > 4). The epidural catheter was removed after 48 hours, and NSAIDs were administered as requested.

Patients were transferred from the PACU to the surgical ward at 9:00 am on the first postoperative day, and then were allowed a non-restricted solid food intake. The bladder catheter was removed and enforced mobilization was applied. Patients received daily functional training under the supervision of a physiotherapist. Administration of low molecular weight heparin bemiparin sodium (Zibor®, Madrid, Spain), 3.500 IU, was started 6 hours after surgery, and repeated at 24 hour intervals on the subsequent days.

Calculation of blood loss

Blood loss was estimated based on arterial hemoglobin concentration (Hb) and hematocrit (Hct). These parameters were used in three conventional formulae (see the Appendix) to calculate the estimated blood loss (EBL) as follows: (1) the 'classic' formula, which uses a simplistic calculation based on the ratio of preoperative and postoperative Hb, (2) the modified Gross formula, which is based on the fractional change of Hct, and (3) Shander's modification of the Gross formula. Each EBL formula had two versions (modifications) due to the use of two different formulas for the estimated normal blood volume: (1) Nadler's formula, and (2) the formula recommended by the Expert Panel on Radionuclides of the International Council for Standardization in Haematology [22], which takes the body surface area into account. Thus, six methods (sets of formulas) were deployed to calculate EBL during the 24 hours after the start of surgery. Additionally, the loss of red cell volume was calculated for each estimated blood loss. 7^{th} and 8^{th} methods of estimated red cell volume loss were calculated using the homeostatic red cell loss formula with two different formulas for the estimated normal blood volume.

3.7.2. Secondary outcome measures

The secondary outcome measure was the time when fitness-to-discharge was achieved.The following criteria were used during the six postoperative days to determine whether a patient was fit to discharge: (a) pain control solely by oral NSAIDs during the preceding 24 hours, (b) Timed Up and Go (TUG) test less than 20 s, (c) normal wound healing, and (d) body temperature below 37.7 C during the preceding 24 hours. The rate of donor blood transfusions during six postoperative days was recorded. Donor blood transfusion was performed according to guidelines for perioperative blood transfusion.

The additional secondary outcome measures were swelling of legs by calculation of the ratio between the post- and pre-operative circumference of the lower limbs at the level of the superior pole of the patella (site 1), as well as 10 cm above and below (site 2).

All perioperative complications were recorded.

3.8. Statistical analysis

The sample size for study was based on interim report.[23] It was determined that a sample size of 12 subjects per group achieved a 65% power to detect a difference of 94ml between means of estimated red cell volume loss with known group standard deviations of 80 and 106 and with a significance level of 0.05 using a two-sided Mann-Whitney test. Based on these data, 30 patients were required in each group to detect estimated blood loss difference at the significance level of 0.05 with a power of 0.95.

Kolmogorov-Smirnov test was used to analyse data normality. Data are presented as mean (SD) where appropriate (normally distributed data) and as median [25^{th};75^{th} percentiles] for non-normally distributed data. Mean values were compared using ANOVA with Bonferroni correction for multiplicity testing and when Levene's test for comparison of variances did not reject hypothesis on equality of variance between groups. Mann-Whitney-Wilcoxon,Kruskal-Wallis and Wilcoxon signed rank test were applied to non-normally distributed data. The categorical data were analyzed with Pearson χ^2 and Fisher's exact tests.Kaplan-Meier method was used to calculate the discharge from hospital rate. The date of discharge with the fit-to-discharge criteria was used for time-to-event analysis. The log-rank and Breslow tests were used to detect differences in the time of discharge from hospital between groups. Statistical analysis was performed using PASW (PASW Statistic 17, SPSS, IBM Corporation, NY). Analysis was performed with significance level alpha = 0.05 (two sided).

4. RESULTS

One hundred thirty two subjects were enrolled and one hundred twenty patients (101 females, 19 males) completed the study. Patient preoperative characteristics of the four groups were similar (Table 3).The tourniquet pressure, duration of surgery and tourniquet time are shown in Table 4. The operative tourniquet pressure was similar

in all groups. The duration of surgery was significantly longer (p=0.022) in Group 2 than in Group 3.

Table 3 Preoperative patient characteristics

Group	**1**	**2**	**3**	**4**	***p*-value**
Sex (male/female)	3/27	7/23	3/27	6/27	0.363[a]
Age (years)	69.2 [62.8 to 73.4]	70.4 [63.3 to 73.8]	70.0 [65.7 to 74.9]	70.0 [63.7 to 75.7	0.924[b]
BMI (kg/m^2)	33.1 (3.4)	32.0 (4.6)	32.2 (3.8)	30.8 (5.1)	0.328[c]
Timed Up and Go Test (s)	11 [10 to 14]	11 [9 to 13]	11 [10 to 14]	10 [9 to 12]	0.364[b]
Side (right/left)	12/17	15/15	18/12	13/17	0.423[d]
WOMAC VA 3.1, total (points)	1350 [1033 to 1568]	1410 [1103 to 1608]	1277 [1073 to 1478]	1234 [938 to 1510]	0.657[b]
KSS (points)	133 [96 to 126]	114 [99 to 132]	115 [108 to 122]	119 [103 to 128]	0.829[b]
Hb (g/l)	134.0 (10.3)	139.0 (9.2)	134.7 (8.8)	137.4 (12.9)	0.209[c]
Range of motion (degrees)	117 [109 to 126]	120 [111 to 126]	119 [110 to 126]	121 [110 to 128]	0.678[b]
Flexion contracture (degrees)	10 [6 to 12]	8 [3 to 11]	12 [8 to 11]	12 [8 to 13]	0.108[b]
Grade of osteoarthritis (II/III)	5/25	8/22	4/26	6/24	0.597[d]

Values are number, mean (SD) or median (25^{th} - 75^{th} percentiles), [a] Fisher's test, [b] Mann-Whitney-Wilcoxon, [c] Student's *t*-test, [d] Pearson χ^2 test

Table 4 Comparison of tourniquet pressure, operation time, tourniquet time

Group	1	2	3	4	p value
Tourniquet pressure (mmHg)	298 [255 to 328]	311 [299 to 344]	310 [284 to 360]	304 [246 to 329]	0.303[a]
Duration of tourniquet (min)	34 [32 to 40]	11 [10; 13]	60 [58; 69]	38 [32 to 43]	0.299[b]
Duration of surgery (min)	58 [55 to 65]	63 [59 to 66]	58 [55 to 64]	63 [58 to 70]	0.042[c]

Values are median (25^{th} - 75^{th} percentiles), p is the result from the Kruskal-Wallis[a] and Mann-Whitney-Wilcoxon[b, c] Test. [b] No significant difference between Group 1 and 4. [c] Duration of surgery was significantly longer in Group 2 than in Group 3.

4.1. Comparison of three tourniquet application methods (Group 1, 2 and 3)

4.1.1 Blood loss

The estimated loss of blood volume, loss of red blood cells and significance of difference between study groups are shown in Fig. 2 and Table 5-8. The estimated loss of blood volume in all groups was significantly different ($0.025<p<0.041$) and in Group 2 was higher than in Group 1 ($0.026<p<0.040$) or Group 3 ($0.014<p<0.026$) as calculated by all six blood volume methods (Fig. 2a and Table 5). The difference between all groups was detected as calculated by the 1^{st}, 3^{rd} and 5^{th} method for ratio of estimated blood volume loss with body weight (Fig 2b and Table 6). The ratio of estimated loss of blood volume with body weight in Group 2 was higher than Group 1 or Group 3 ($0.020<p<0.043$ and $0.031<p<0.049$, respectively).

The difference between all groups was shown as calculated for five estimated red cells (Fig. 2c and Table 7) and four of eight of the relative red cell volume loss (Fig. 2c and Table 8) calculation methods (the 1^{st}, 2^{nd}, 5^{th}, 6^{th}, 7^{th} and 1^{st}, 3^{rd}, 5^{th}, 7^{th} method, retrospectively). Blood loss in Group 2 was higher than in Group 1 as calculated by all eight red cell volume methods ($0.030<p<0.043$) and for seven of the

relative method calculation (the 1st, 2nd, 3rd, 4th, 5th, 6th and 7th method for ratio of estimated blood volume loss with body weight). Blood loss in Group 2 was higher than in Group 3 as calculated by six red cell volume methods (1st, 2nd, 5th, 6th, 7th and 8th method) and only for three of the relative red cell method calculation (1st, 5thand 7th method).

The blood loss between groups was not significantly different by all 28 calculation methods during revGDT protocol in any further steps ($0.225<p<0.615$) as well as 20min after the last bolus.

No significant difference ($p=0.334$) was observed comparing blood transfusion rate between groups (Table 9).

4.1.2. Fitness-to-discharge

The time to fit-to-discharge criteria achievement was different in Group 1, 2 and 3 (Breslow test, $p=0.044$). Fit-to-discharge criteria (Fig. 3a and Table 10) were met significantly more rapidly by patients in Group 1 than those in Group 3 (Breslow test, $p = 0.021$). The functional recovery (TUG test) was better and pain control solely by NSAIDs was achieved earlier in Group 1 than in Group 3 (Breslow test, $p=0.027$, log-rank test, $p = 0.048$, retrospectively, Fig. 3b and 3c). The wound healing was better in Group 2 than in Group 1 (log-rank test, $p=0.049$, Fig. 3d). The body temperature was similar in all groups (Fig. 2e).

4.1.3 Swelling of legs

The ratio between the post- and preoperative circumferences at the superior pole of the patella (site 1) of the operated leg was bigger in Group 3 than in Group 1 and Group 2 ($p= 0.007$ and 0.024, respectively; Table 11). The ratio between the post- and preoperative circumferences 10 cm above the patella (site 2) of both legs as well as at the superior pole of the patella (site 1) of the non-operated leg were similar in Group 1, 2 and 3.

Table 5 Estimated blood volume loss during the perioperative 24 h. A – calculated by method 1, B – calculated by method 2, C – calculated by method 3, D – calculated by method 4, E – calculated by method 5, F – calculated by method 6.

Group	Estimated blood volume loss, ml					
	A	B	C	D	E	F
1	1012 [796; 1151]	957 [774; 1098]	907 [737; 1026]	849 [711; 962]	869 [681; 952]	811 [648;892]
2	1175 [912; 1175]	1126 [918; 1386]	1044 [833; 1251]	977 [831; 1170]	978 [792; 1249]	905 [768; 1167]
3	910 [770; 1156]	891 [741; 1096]	826 [697; 1032]	784 [634;990]	806 [632; 892]	779 [600; 938]
Study groups comparing	p value					
1 vs. 2[a]	**0.033**	**0.040**	**0.032**	**0.038**	**0.037**	**0.026**
1 vs. 3[a]	0.679	0.813	0.584	0.756	0.712	0.824
2 vs. 3[a]	**0.015**	**0.019**	**0.014**	**0.023**	**0.020**	**0.026**
1, 2 and 3[b]	**0.029**	**0.037**	**0.025**	**0.041**	**0.037**	**0.035**

Values are median (25^{th} - 75^{th} percentiles), p is the result from the Mann-Whitney-Wilcoxon[a] and Kruskal-Wallis[b] Test, significant differences ($p<0.05$) are bolded.

Table 6 Ratio of estimated blood volume loss with body weight during the perioperative 24 h. A – calculated by method 1, B – calculated by method 2, C – calculated by method 3, D – calculated by method 4, E – calculated by method 5, F – calculated by method 6.

Group	Ratio of estimated blood volume loss with body weight, ml/kg					
	A	B	C	D	E	F
1	11.4 [9.0; 13.5]	10.6 [8.3; 14.0]	10.3 [8.3; 12.0]	9.4 [7.5; 12.2]	9.4 [7.9; 11.4]	9.6 [7.3; 11.2]
2	13.8 [11.2; 16.4]	13.2 [10.2; 16.8]	12.3 [10.2; 14.3]	11.8 [9.1; 14.2]	11.6 [9.3; 14.1]	10.7 [8.4; 13.4]
3	10.9 [9.4; 13.5]	10.8 [8.8; 13.4]	10.0 [8.3; 12.1]	9.7 [7.8; 11.7]	9.4 [7.8; 11.4]	9.2 [7.3; 10.7]
Study groups comparing	p value					
1 vs. 2[a]	**0.029**	**0.041**	**0.029**	**0.041**	**0.020**	**0.043**
1 vs. 3[a]	0.918	0.802	0.988	0.894	0.871	0.802
2 vs. 3[a]	**0.035**	**0.049**	**0.031**	**0.046**	**0.032**	**0.046**
1, 2 and 3[b]	**0.045**	0.067	**0.042**	0.065	**0.035**	0.068

Values are median (25^{th} - 75^{th} percentiles), p is the result from the Mann-Whitney-Wilcoxon[a] and Kruskal-Wallis[b] Test, significant differences ($p<0.05$) are bolded.

Table 7 Estimated red cell volume losses during the perioperative 24 h. A – calculated by method 1, B – calculated by method 2, C – calculated by method 3, D – calculated by method 4, E – calculated by method 5, F – calculated by method 6, G – calculated by method 7, H – calculated by method 8.

Group	Estimated red cell volume loss, ml							
	A	B	C	D	E	F	G	H
1	327 [258; 360]	313 [247; 344]	327 [258; 360]	308 [243; 339]	327 [258; 360]	308 [243; 339]	331 [256; 367]	313 [238; 335]
2	368 [301; 474]	347 [292; 447]	368 [301; 474]	342 [288; 440]	368 [301; 474]	342 [288; 400]	368 [308; 483]	342 [283; 441]
3	309 [237; 375]	300 [230; 360]	314 [248; 376]	300 [232; 368]	309 [237; 375]	295 [227; 375]	324 [237; 381]	299 [226; 345]
Study groups comparing	p value							
1 vs. 2[a]	**0.041**	**0.030**	**0.041**	**0.030**	**0.041**	**0.030**	**0.043**	**0.038**
1 vs. 3[a]	0.790	0.848	0.918	0.906	0.790	0.813	0.848	0.941
2 vs. 3[a]	**0.024**	**0.030**	0.062	0.065	**0.024**	**0.027**	**0.025**	**0.032**
1, 2 and 3[b]	**0.044**	**0.042**	0.077	0.065	**0.044**	**0.039**	**0.046**	0.050

Values are median (25^{th} - 75^{th} percentiles), p is the result from the Mann-Whitney-Wilcoxon[a] and Kruskal-Wallis[b] Test, significant differences ($p<0.05$) are bolded.

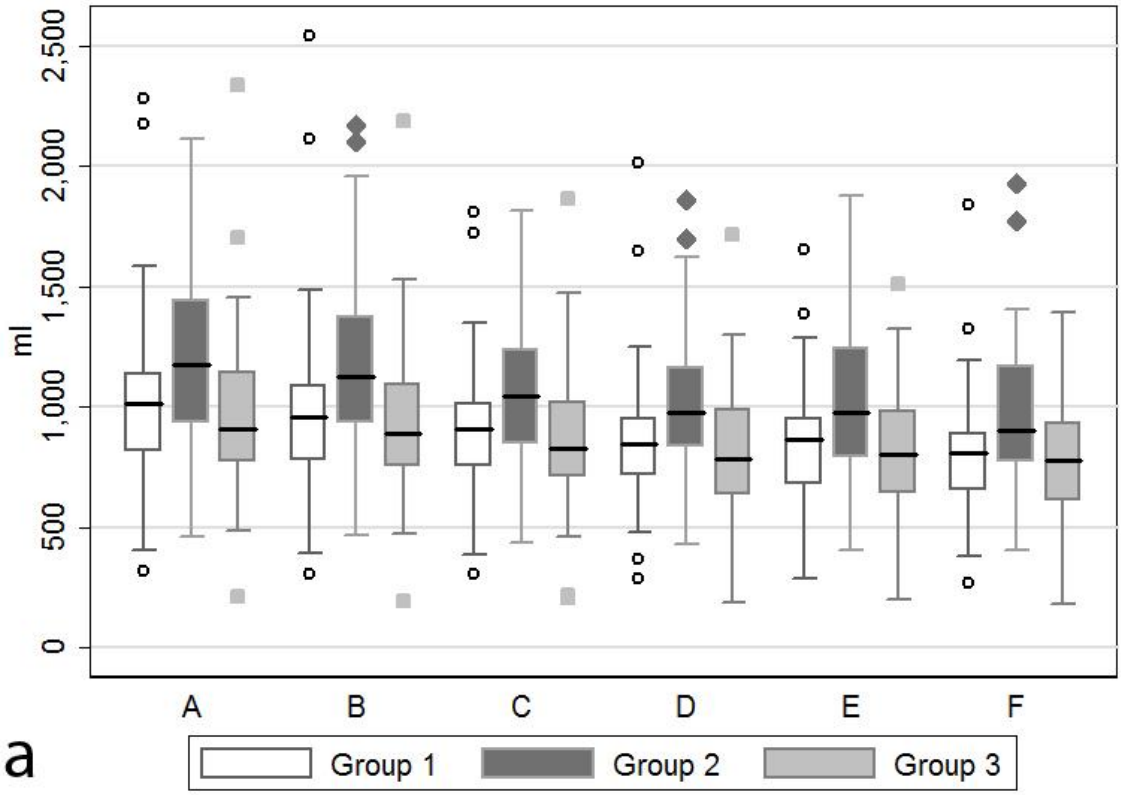
Table 8 Ratio of estimated red cell volume loss with body weight during the perioperative 24 h. A – calculated by method 1, B – calculated by method 2, C – calculated by method 3, D – calculated by method 4, E – calculated by method 5, F – calculated by method 6, G – calculated by method 7, H – calculated by method 8.

Group	Ratio of estimated red cell volume loss with body weight, ml/kg							
	A	B	C	D	E	F	G	H
1	3.6 [3.0; 4.2]	3.3 [2.8; 4.3]	3.5 [3.0; 4.2]	3.2 [2.8; 4.2]	3.5 [3.0; 4.2]	3.2 [2.8; 4.2]	3.6 [3.1; 4.3]	3.3 [2.8; 4.1]
2	4.3 [3.5; 5.3]	4.1 [3.2; 5.2]	4.3 [3.5; 5.3]	4.0 [3.1; 5.1]	4.3 [3.5; 5.3]	4.0 [3.1; 5.1]	4.4 [3.5; 5.3]	4.0 [3.1; 5.1]
3	3.6 [2.9; 4.3]	3.6 [2.8; 4.2]	3.8 [3.0; 4.3]	3.7 [2.8; 4.2]	3.6 [2.9; 4.3]	3.5 [2.7; 4.1]	3.8 [2.9; 4.4]	3.5 [2.7; 4.2]
Study groups comparing	p value							
1 vs. 2[a]	**0.019**	**0.038**	**0.019**	**0.038**	**0.019**	**0.038**	**0.020**	0.056
1 vs. 3[a]	0.790	0.790	0.535	0.595	0.790	0.848	0.712	0.626
2 vs. 3[a]	**0.031**	0.053	0.076	0.121	**0.031**	0.055	**0.030**	0.065
1, 2 and 3[b]	**0.032**	0.066	**0.048**	0.096	**0.032**	0.068	**0.032**	0.088

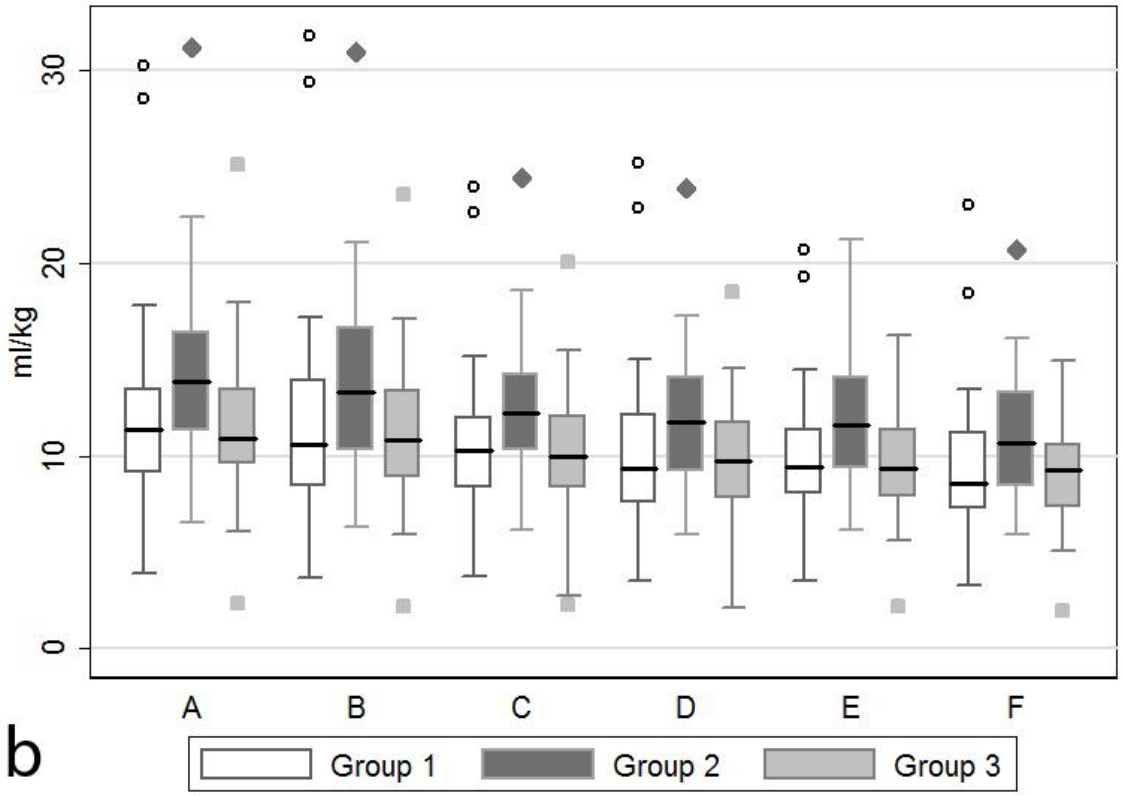
Values are median (25^{th} - 75^{th} percentiles), p is the result from the Mann-Whitney-Wilcoxon[a] and Kruskal-Wallis[b] Test, significant differences ($p<0.05$) are bolded.

Table 9 Comparison of the donor blood transfusion rate between groups.

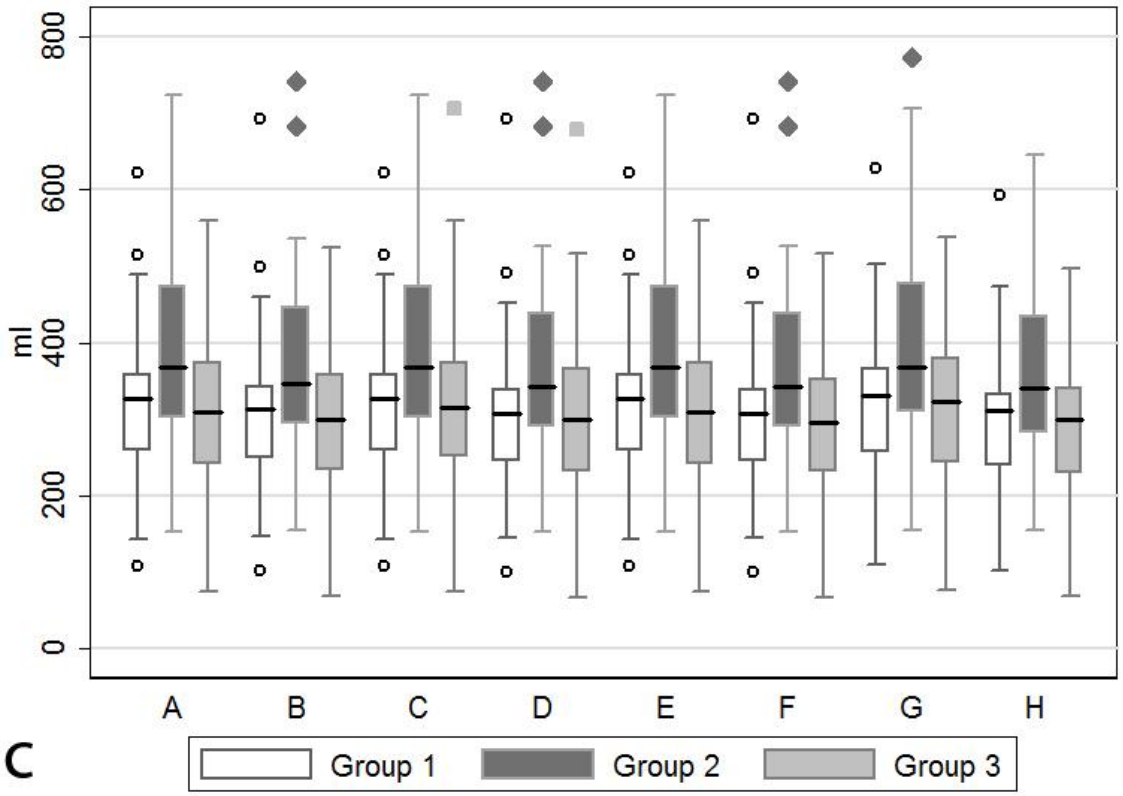
Group	Rate of donor blood transfusion (units)	
	2	3
1	3	
2	1	1
3		1



a


ml/kg
0
10
20
30
A
B
C
D
E
F
Group 1
Group 2
Group 3

b


ml
0
200
400
600
800
A
B
C
D
E
F
G
H
Group 1
Group 2
Group 3

C

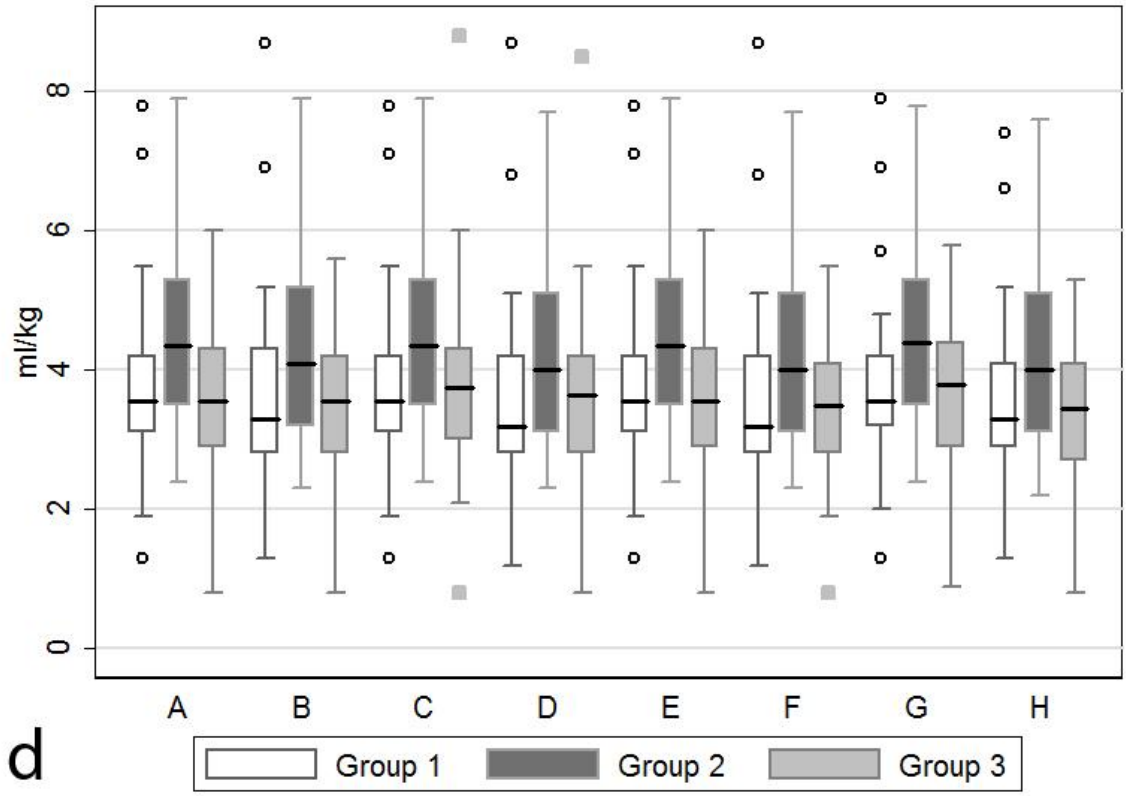
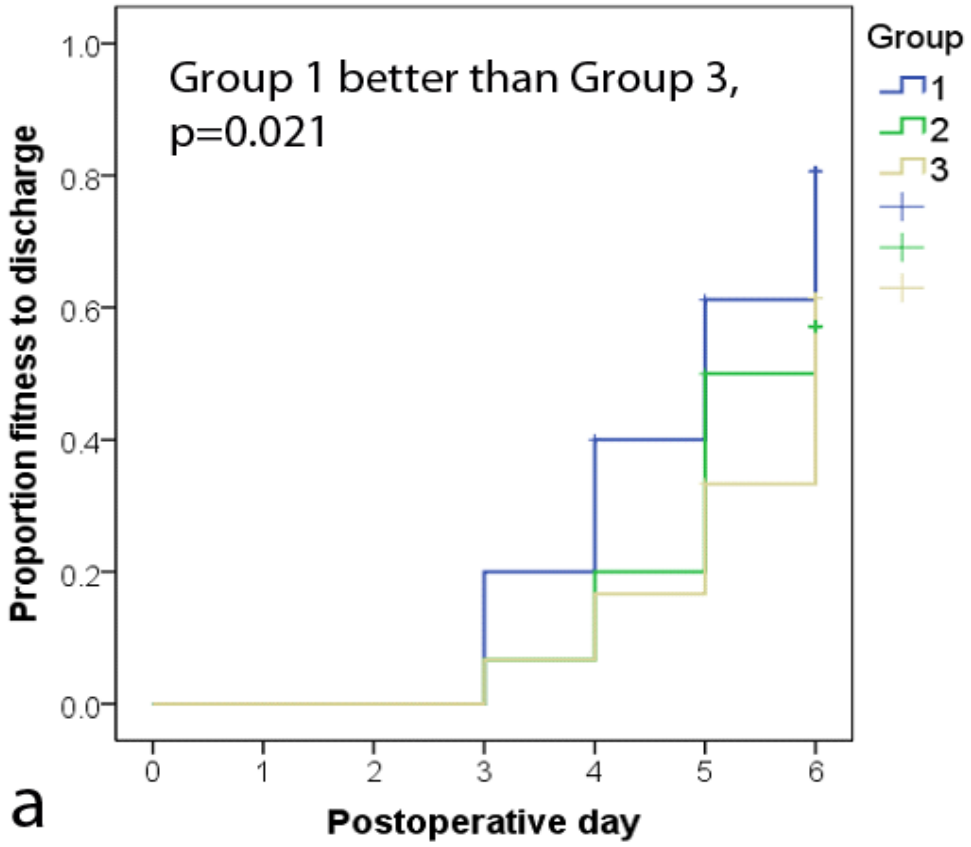
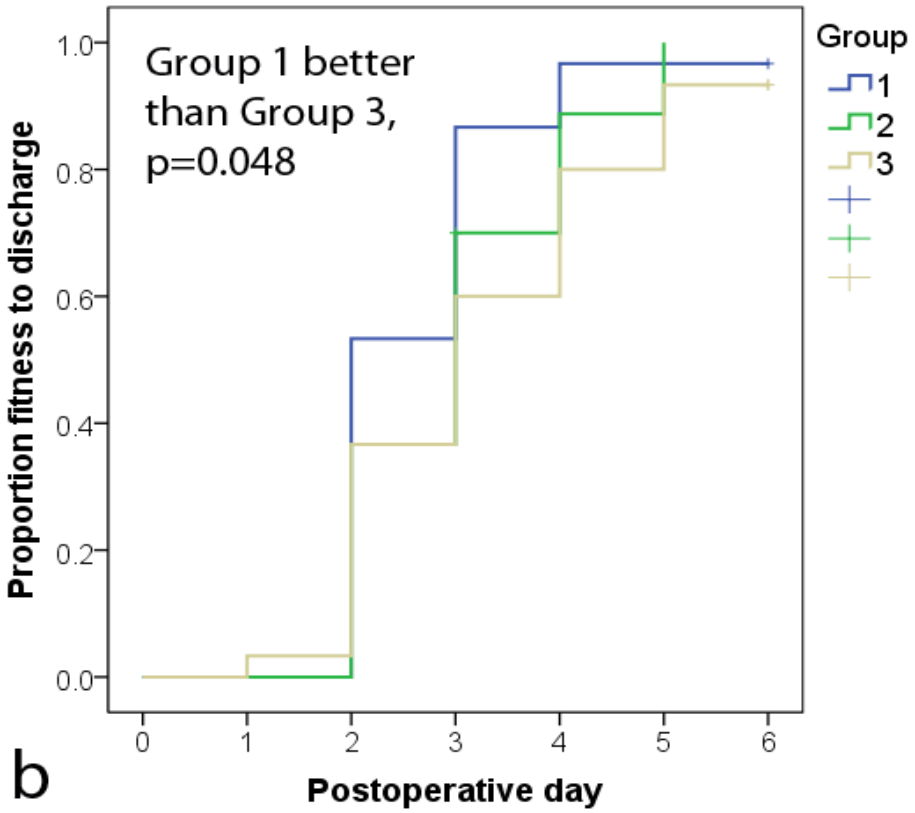


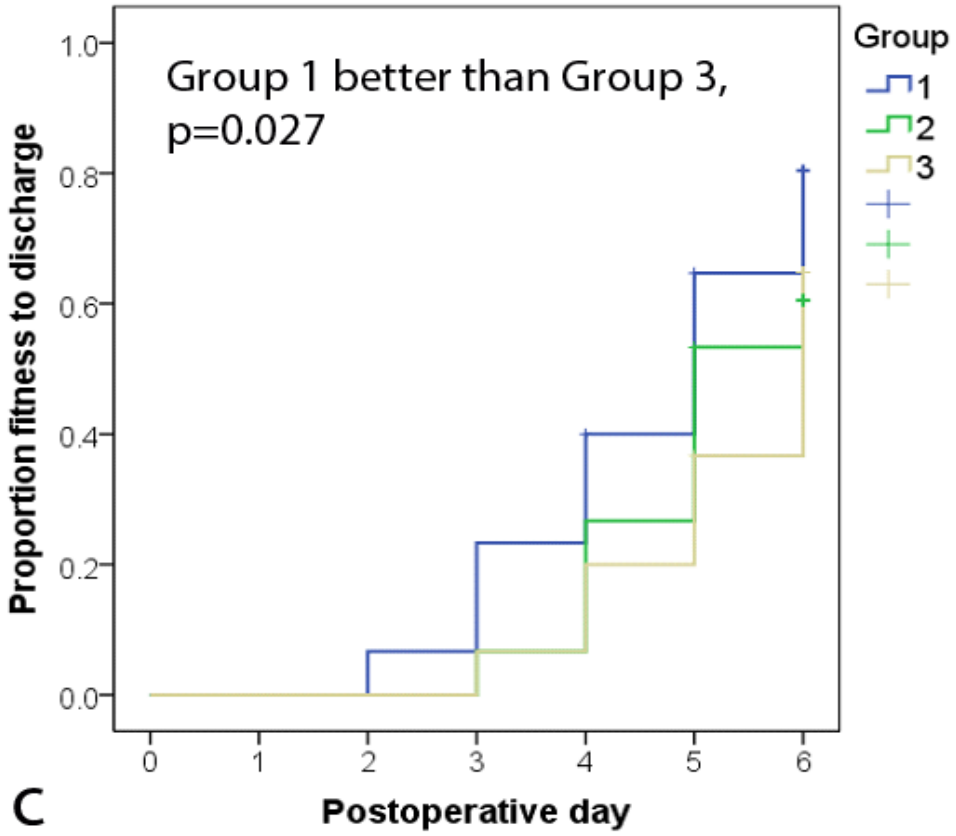
Fig. 2 Estimated blood loss during the perioperative 24 h: estimated blood volume loos in ml (a), ratio of estimated blood volume loos with body weight in ml/kg (b), estimated red cell volume loos in ml (c), and ratio of estimated red cell volume loos with body weight in ml/kg (d). A – calculated by method 1, B – calculated by method 2, C – calculated by method 3, D – calculated by method 4, E – calculated by method 5, F – calculated by method 6, G – calculated by method 7, and H – calculated by method 8.


Group 1 better than Group 3,
p=0.021
Group
1
2
3
Proportion fitness to discharge
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
6
Postoperative day

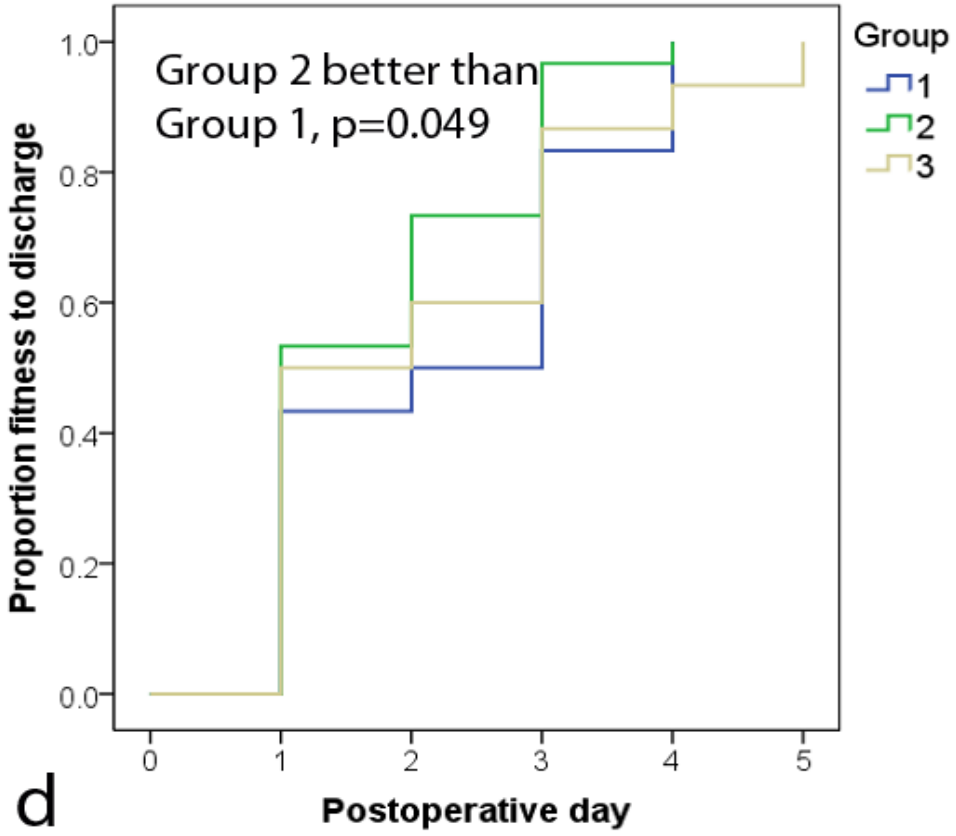
a


Group 1 better
than Group 3,
p=0.048
Group
1
2
3
Proportion fitness to discharge
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
6
Postoperative day

b


Group 1 better than Group 3, p=0.027
Proportion fitness to discharge
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
6
Postoperative day
Group
1
2
3

c


Group 2 better than Group 1, p=0.049
Proportion fitness to discharge
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
Postoperative day
Group
1
2
3

d

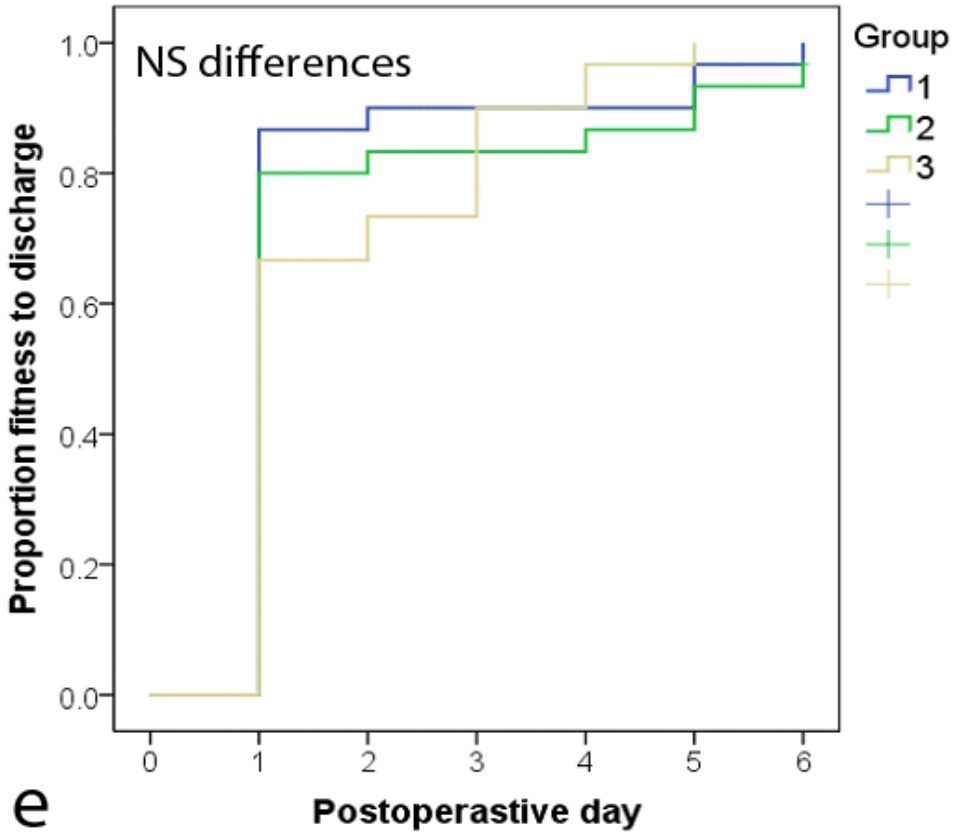


Fig. 3 Kaplan-Meier curves of individual fit-to-discharge criteria during six postoperative days in Group 1, 2 and 3 with different timing of the tourniquet: All criteria taken together (a), Timed up and go test (b), Pain control by oral NSAIDs (c), Normal wound healing (d), Body T < 37.7 °C (e).

Table 10 Comparison of individual fit-to-discharge criteria between Group 1, 2 and 3 during six postoperative days.

Study groups comparing	Fit to discharge criteria				
	Timed up and go test	Pain control by oral NSAIDs	Normal wound healing	Body T < 37.7 °C	Total
1 vs. 2	NS	NS	0.049[a]	NS	NS
1 vs. 3	0.048[b]	0.027[c]	NS	NS	0.021[c]
2 vs. 3	NS	NS	NS	NS	NS
1, 2 and 3	NS	NS	NS	NS	0.044[d]

[a] Group 2 better than Group 1 (log-rank test)

[b] Group 1 better than Group 3 (log-rank test)

[C] Group 1 better than Group 3 (Breslow test)

[d] Breslow test

.

Table 11 The lower limb swelling. Values are presented as a ratio between post- and pre-operative circumferences, where the post-operative variable is the means of measurements on days 4-6.

Leg	Measure place	Group 1	Group 2	Group 3	p- value *1 vs 2*	p- value *1 vs 3*	p- value *2 vs 3*
Operated	At the level of the superior pole of the patella	0.958 [0.928 to 1.000]	0.952 [0.928 to 0.977]	0.927 [0.912 to 0958]	0.342	0.007	0.025
Operated	10 cm above the patella	0.945 [0.825 to 0.987]	0.946 [0.904 to 0.978]	0.938 [0.911 to 0.955]	0.455	0.130	0.529
Non operated	At the level of the superior pole of the patella	1.023 [1.006 to 1.050]	1.019 [1.000 to 1.050]	1.019 [1.000 to 1.036]	0.646	0.359	0.569
Non operated	10 cm above the patella	1.024 [1.014 to 1.052]	1.037 [1.000 to 1.046]	1.025 [0.993 to 1.051]	0.821	0.796	0.889

Values are median (25^{th} - 75^{th} percentiles), p is the result from the Mann-Whitney-Wilcoxon test.

4.2. Comparison of revGDT with conventional fluid therapy (Group 1 and Group 4)

4.2.1. Perioperative fluid therapy administration

Group 1 received a higher volume of acetated Ringer solution with no difference in the volume of normal saline, and the total volume of crystalloids was higher than in Group 4, but 24-h fluid balance did not differ between the groups (Table 12). Each subject in both groups received the same volume of colloids, so they were not included in the comparison of the fluid balance. There was no difference in the blood volume in the surgical suction device and the volume in the drainage container when the drain was removed.

Table 12 The 24-h fluid balance.

	Group		*P* - value[a]
	Intervention	**Control**	
Total crystalloids (ml)	4000 (3500 - 4575)	3000 (3000 - 3150)	0.000
Ringer‘s acetate (ml)	2000 (1500 – 2500)	1000 (1.000 – 2000)	0.000
NaCl 0,9% (ml)	2000 (1475 – 2725)	2000 (1000 – 2000)	0.093
Diuresis (ml)	2075 (1300 – 3276)	1500 (1025 – 2625)	0.058
Balance (ml)	1940 (458 – 2913)	1750 (525 – 2750)	0.335

Values are median (25^{th} - 75^{th} percentiles), [a] Mann-Whitney-Wilcoxon test.

4.2.2. Fitness-to-discharge

Fitness-to-discharge was met earlier in Group 1 than in Group 4 (Breslow test, P = 0.039, Table 13; Kaplan-Meier graph, Fig. 4), but there was no difference between the time of switching to pain control by oral NSAIDs, TUG test, and other criteria serving as components for the evaluation of fitness-to-discharge as a whole (table 13).

Table 13 Comparison of individual fit-to-discharge criteria between the groups during six postoperative days.

	Fit to discharge criteria				
	Pain control by oral NSAIDs	Timed up and go test	Normal wound healing	Body T < 37.7 °C	Total
p-value[a]	NS	NS	NS	NS	0.039

[a] Breslow test.

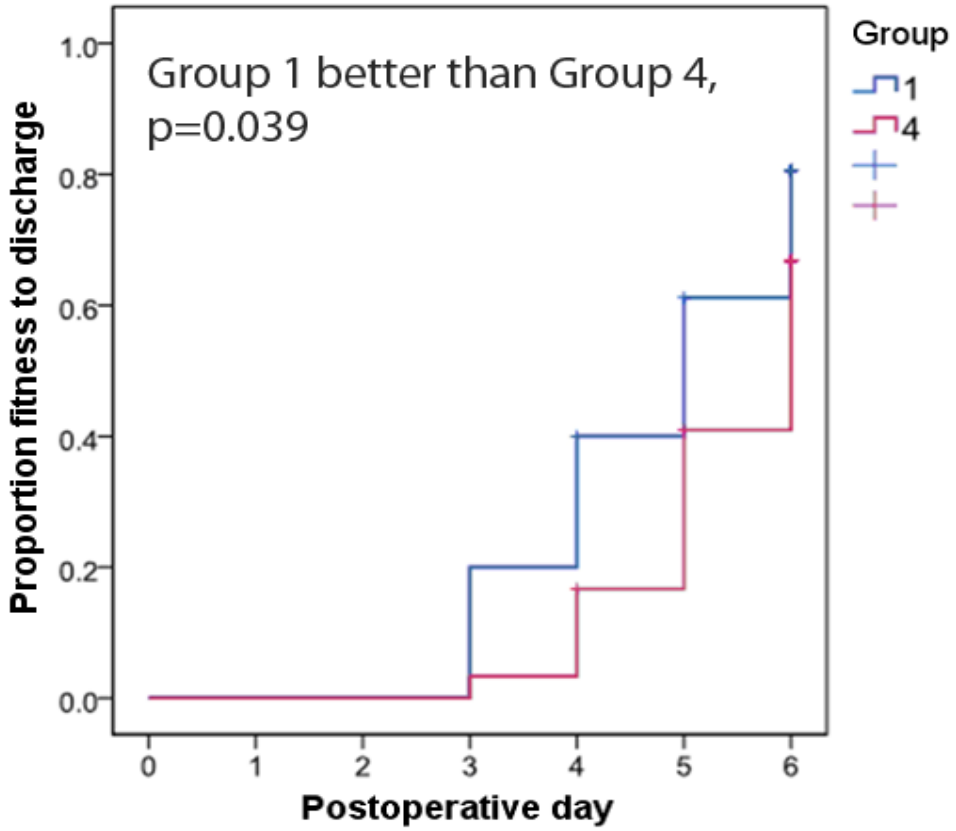


Fig. 4 Kaplan-Meier curves of all fit-to-discharge criteria together during six postoperative days.

4.2.3. Swelling of legs

The ratio between the post- and preoperative circumferences 10 cm above the patella (site 2) of both legs as well as at the superior pole of the patella (site 1) of the operated leg was lower in Group 1 than in Group 4 (P = 0.006, 0.033, and 0.001, respectively; Table 14).

Table 14 The lower limb swelling. Values are presented as a ratio between post- and pre-operative circumferences, where the post-operative variable is the means of measurements on days 4-6.

Leg	Measure place	Group 1	Group 4	p- value
Operated	At the level of the superior pole of the patella	0.958 [0.928 to 1.000]	0.952 [0.928 to 0.977]	0.342
Operated	10 cm above the patella	0.945 [0.825 to 0.987]	0.946 [0.904 to 0.978]	0.455
Non operated	At the level of the superior pole of the patella	1.023 [1.006 to 1.050]	1.019 [1.000 to 1.050]	0.646
Non operated	10 cm above the patella	1.024 [1.014 to 1.052]	1.037 [1.000 to 1.046]	0.821

Values are median (25^{th} - 75^{th} percentiles), [a] Mann-Whitney-Wilcoxon test.

Table 15 Comparison of complications between the groups during six postoperative days.

Complications	Group 1	Group 2	Group 3	Group 4	p-value[a]
Not related to tourniquet use:					0,079
Transient ischemic attack	1				
Arrhythmia	1	2	1		
Dizziness	1				
Urinary tract infection	1				
Wrist haematoma	1				
Related to tourniquet use:					1,000
Peripheral neuropathy	1	1	1		
Blisters	1			2	
Large haematoma			1		
Total	7	3	3	2	0,295

[a] Fisher's test

4.3. Complications

Fifteen patients experienced complications (12.5%; Table 15). Seven of them were related to the tourniquet (5.8%). All of them were short in duration. Only one patient had two days prolonged hospitalization because of dizziness and exacerbation of bronchitis. All peripheral nerve damages were mild transient loss of sensitive function. All symptoms of nerve injury disappeared during the hospital stay. There were no significant differences between groups.

5. CONCLUSIONS

1. Estimated blood loss was lower with longer tourniquet application lasting at least between skin incision and hardening of the cement.
2. .The blood transfusion rate was similar in all groups. The transfusions are rare in primary TKA.
3. The hospital stay according to discharge criteria was longer for the patients operated with tourniquet inflated during the whole surgery than for those who were operated with tourniquet inflated before incision and deflated after hardening of cement.
4. Blood volume loss differences between the study groups were more significant than the estimated red cell loss.
5. Perioperative revGDT reduced fit-to-discharge time after TKA.
6. The complication rate was similar in patients with different timing of the tourniquet.

6. PRACTICAL RECOMMENDATIONS

Inflation of an automatic pneumatic lower limb tourniquet before skin incision and its deflation after hardening of cement optimises outcomes in TKA patients. The estimated blood loss is highest when the tourniquet is inflated just before cement application and deflated after its hardening. The application of tourniquet during the whole TKA (about 1 hour) could prolong the hospital stay.

The individualised fluid therapy by using revGDT may reduce hospital stay.

7. LIST OF PUBLICATIONS ON THE TOPIC OF THE DISSERTATION

1. Andrijauskas A, Sakavičiūtė I, Ivaškevičius J, Porvaneckas N, Kvederas G, Činčikas D, Mažunaitis J, Marmaitė U, Sakalaitė L, Andrijauskas P, Sakalauskaitė Perioperative fluid therapy: old problems, new solutions. Lithuanian Surger, 2012, 10(1–2):7–20.
2. Andrijauskas A, Svensen CH, Ivaskevicius J, Porvaneckas N, Kvedaras G, Marmaite U. Goal Directed Fluid Therapy Revised: Indirect Monitoring of Interstitial Fluid Accumulation During Mini Fluid Challenges with Crystalloids. The Open Conference Proceedings Journal, 2012, 3, 42-51.
3. Kvederas G, Porvaneckas N, Andrijauskas A, Svensen CH, Ivaskevicius J, Mazunaitis J, Marmaite U, Andrijauskas P. A randomized double-blind clinical trial of tourniquet application strategies for total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 2013, 21: 2790-9.
4. Markevičius V, Andrijauskas A, Navikas D, Svensen C, Porvaneckas N, Andriukaitis D, Kvederas G, Cincikas D**,** Andrijauskas P.Statistically Biased Calibration Method for the Real-time Adjustment of Noninvasive Haemoglobin Measurements in Semiautomated Infusion System. Electronics and Electrical Engineering, 2013, 19(7): 1392-1215.
5. Andrijauskas A, Sakavičiūtė I, Ivaškevičius J, Porvaneckas N, Činčikas D, , Kvederas G. Crystalloids and colloids: aspects of their co-administration in perioperative fluid therapy. Lithuanian Surgery. 2013, 12 (–2):13–19.
6. Andrijauskas A, Svensen CH, Porvaneckas N, Kvederas G, Cincikas D, Svediene S. Mini volume loading test (mVLT) for the evaluation of hydration status: initial validation in patients. Archive Euromedica. 2014, 4 (1):4-14.
7. Andrijauskas A, Markevicius V, Navikas D, Porvaneckas N, Andriukaitis D, Stankevicius E, Uvarovas V, Sipylaite J, Kvederas G, Gelzinis G. In Vivo Testing of the Semi-Closed Loop Infusion System: the Preliminary Observations. Electronics and Electrical Engineering. 2015;21(1):28-32.
8. Andrijauskas A, Ivaškevičius J, Porvaneckas N, Stankevičius E, Svensen CH, Uvarovas V, Švedienė S, Kvederas G. A mini volume loading test for indication of preoperative dehydration in surgical patients. Medicina. 2015; 51(2): 81-91.

8. LIST OF PRESENTATIONS ON THE TOPIC OF THE DISSERTATION

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10. APPENDIX

Estimated blood loss: loss of blood volume and red cell mass

Estimated loss of blood volume

The six methods used to estimate blood loss were the following:

1. 'Classic' formula (version 1):

$$BVL = BV \bullet (Hb_i \bullet Hb_f^{-1}) - BV \quad [1]$$

where BV is the normal BV calculated by Nadler's formula (ref Nadler).

2. 'Classic' formula (version 2):

$$BVL = BV \bullet (Hb_i \bullet Hb_f^{-1}) - BV \quad [2]$$

where BV is the normal BV calculated by the formula recommended by the International Council for Standardization in Haematology.

3. Modified Gross formula (version 1):

$$BVL = BV \bullet (Hct_i - Hct_f) \bullet Hct_m^{-1} \quad [3]$$

where BV is the normal BV calculated by Nadler's formula.

4. Modified Gross formula (version 2):

$$BVL = BV \bullet (Hct_i - Hct_f) \bullet Hct_m^{-1} \quad [4]$$

where BV is the normal BV calculated by the formula recommended by the International Council for Standardization in Haematology.

5. Shander's modification of the Gross formula (version 1):

$$BVL = BV \bullet (Hct_i - Hct_f) \bullet (3 - Hct_m) \quad [5]$$

where BV is the normal BV calculated by Nadler's formula.

6. Shander's modification of the Gross formula (version 2):

$$BVL = BV \bullet (Hct_i - Hct_f) \bullet (3 - Hct_m) \quad [6]$$

where BV is the normal BV calculated by the formula recommended by the International Council for Standardization in Haematology.

Hb_i = initial Hb; Hb_f = final Hb; Hct_i = initial Hct; Hct_f = final Hct; Hct_m = mean Hct.

Estimated normal blood volume

1. Nadler's formula:

$$BV = k1 \times \text{height (m)}^3 + k2 \times \text{weight (kg)} + k3 \quad [7]$$

where BV is the normal blood volume, kl = 0.3669, k2 = 0.03219, k3 = 0.6041 for men, and kl = 0.3561, k2 = 0.03308, k3 = 0.1833 for women.

Thus, BV for males is calculated as follows:

$BV_{male} = 0.3669 \bullet H\ (m)^3 + 0.03219 \bullet W\ (kg) + 0.6041$ [7a]

and BV for females is calculated as follows:

$BV_{female} = 0.3561 \bullet H\ (m)^3 + 0.03308 \bullet W\ (kg) + 0.1833$ [7b]

2. Formula recommended by the International Council for Standardization in Haematology:

$BV = PV + RCV$ [8]

Formula for normal blood volume in males:

$BV = PV + RCV = (W^{0.425} \times H^{0.725}) \times 0.007184 \times 3064\ (ml/m^2) - 825$ [8a]

$PV = BSA \times 1578$

$RCV = BSA \times 1486 - 825$

where BV is the normal blood volume, PV is the normal plasma volume, RCV is the normal red cell volume, BSA is the body surface area in m^2, W is the body weight in kilograms, and H is the body height in centimetres.

Formula for normal blood volume in females:

$BV = PV + RCV = (W^{0.425} \times H^{0.725}) \times 0.007184 \times 2217 + age\ (yrs) \times 1.06$ [8b]

$PV = BSA \times 1395$

$RCV = BSA \times 822 + age\ (yrs) \times 1.06$

Formula for calculating body surface area (BSA) in both genders:

$BSA = (W^{0.425} \times H^{0.725}) \times 0.007184$

where BSA is the body surface area in m^2, W is the body weight in kilograms and H is the body height in centimetres.

Estimated loss of red cell mass (volume)

The six methods used to estimate red cell mass loss were the following:

$RCL = BVL \bullet (Hct_i + Hct_f^{-1}) \bullet 0.5$ [9]

where RCL is the estimated loss of red blood cells, BVL is blood volume loss calculated by any formula for estimated normal blood volume loss (formulas 1, 2 3, 4, 5 and 6).

7. **The homeostatic red cell loss(version 1)**

$RCL = RCV_1 - RCV_2$ [10]

where RCL is the estimated loss of red blood cell, RCV_1 is the red cell volume before surgery, and RCV_2 is the red cell volume after surgery.

$$RCV_n = C_n \cdot (BV + 0.6 \cdot BV \cdot (1 - tHct_n)^{-1})) \cdot Hct_n \quad [11]$$

where RCM_n - red cell mass inherent to target state at target Hct value n, Cn- coefficient inherent to target Hct value n, BV- normal blood volume calculated by Nadler‘s formula, IPV- ideal plasma volume and tHct- target hematocrit value n.

Coefficient inherent to target Hct value n is calculated as follows:

$$C_n = ((BV + IPV) \cdot (2 - Hct_n)^{-1}) \div (BV + IPT \cdot (1 - Hct_n)^{-1}) =$$
$$= ((BV + 0.6 \cdot BV) \cdot (2 - Hct_n)^{-1}) \div (BV + 0.6 \cdot BV \cdot (1 - Hct_n)^{-1}) \quad [12]$$

where C_n - coefficient inherent to target Hct value n, RCL - estimated loss of red blood cells, BV - normal blood volumecalculated by Nadler’s formula, IPV - ideal plasma volume, Hct_n hematocrit value n.

8. **The homeostatic red cell loss(version 2)**

$$RCL = RCV_1 - RCV_2 \quad [13]$$

where RCL is the estimated loss of red blood cell, RCV_1 is the red cell volume before surgery, and RCV_2 is the red cell volume after surgery.

$$RCV_n = C_n \cdot (BV + 0.6 \cdot BV \cdot (1 - tHct_n)^{-1})) \cdot Hct_n \quad [14]$$

where RCM_n - red cell mass inherent to target state at target Hct value n, Cn- coefficient inherent to target Hct value n, BV- normal blood volume calculated by the formula recommended by the International Council for Standardization in Haematology, IPV- ideal plasma volume and tHct- target hematocrit value n.

Coefficient inherent to target Hct value n is calculated as follows:

$$C_n = ((BV + IPV) \cdot (2 - Hct_n)^{-1}) \div (BV + IPT \cdot (1 - Hct_n)^{-1}) =$$
$$= ((BV + 0.6 \cdot BV) \cdot (2 - Hct_n)^{-1}) \div (BV + 0.6 \cdot BV \cdot (1 - Hct_n)^{-1}) \quad [15]$$

where C_n - coefficient inherent to target Hct value n, RCL - estimated loss of red blood cells, BV - normal blood volumecalculated by the formula recommended by the International Council for Standardization in Haematology, IPV - ideal plasma volume, Hct_n hematocrit value n.

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12. RESUME IN LITHUANIAN

Įvadas. Optimalus manžetės naudojimas pirminio kelio sąnario endoprotezavimo metu (KE) yra diskutuotinas. Daugelio tyrimų, o taip pat ir metaanalizių duomenys yra prieštaringi. Prospektyvinio atsitiktinės imties dvigubai aklo tyrimo tikslas – palyginti KE metu naudojamas tris skirtingos trukmės manžetės naudojimo taktikas.

Ligoniai ir tyrimo metodika. 133 ligoniai, kuriems buvo atlikta pirminė KE operacija, buvo atsitiktinai įtraukti į 4 grupes. 120 ligonių baigė tyrimą. 1 grupės ligoniams KE metu manžetė pripūsta prieš pjūvį ir atspausta sustingus kauliniam cementui. 2 grupės ligoniams manžetė laikyta užspausta tik cementavimo metu. 3 grupės ligoniams manžetė užspausta prieš pjūvį, o atleista susiuvus žaizdą. Siekiant standartizuoti ligonių hidratacinę būklę prieš ir po operacijos taikytas į tikslą nukreiptas skysčių skyrimo (TST) algoritmas bei mažasis infuzinis plazmos atskiedimo (mIPA) mėginys. Papildomai į tyrimą įtraukta 4 kontrolinė grupė, kuriai taikytas standartinis intraveninių skysčių skyrimas, siekiant nustatyti TST ir mIPA galimą įtaką artimosioms pooperacinėms išeitims. Į kiekvieną grupę įtraukta po 30 ligonių. Kraujo netekimas skaičiuotas lyginant kraujo tyrimo duomenis prieš operaciją bei po 24val. Naudoti 6 absoliutaus ir 6 santykinio kraujo tūrio bei 8 absoliutaus ir 8 santykinio eritrocitų masės tūrio skaičiavimo metodai. Lygintas eritrocitų masės transfuzijų dažnis. Pooperaciniu periodu registruota, kada ligonis atitinka išrašymo kriterijus, vertintas abiejų kojų tinimas, lyginant šlaunies apimties santykį prieš ir po operacijos ties girnelės viršutiniu poliumi bei 10cm aukščiau virš girnelės. Komplikacijos registruotos iki 6 parų po operacijos.

Rezultatai. Kraujo netekimas 1 grupėje buvo mažesnis negu 2 (27 iš 28 kraujo netekimo skaičiavimo metodų), taip pat 3 grupėje mažesnis negu 2 (21 iš 28). Nenustatyta patikimo kraujo netekimo skirtumo tarp 1 ir 3 grupių. Kraujo transfuzijų dažnis grupėse nesiskyrė. 1 grupės ligoniai anksčiau negu 3 atsisakė narkotinių analgetikų, greičiau įvykdė dozuoto fizinio krūvio mėginį bei anksčiau atitiko visus išrašymo kriterijus. 2 grupės ligoniai anksčiau atitiko žaizdos gijimo kriterijus negu 1. 1 grupės ligoniai anksčiau atitiko visus išrašymo kriterijus negu 4. 3 grupės ligonių operuotos kojos santykinė apimtis ties girnelės viršūne buvo didesnė negu 1 ar 2 grupių. 4 grupės ligonių

abiejų kojų santykinė apimtis buvo patikimai didesnė negu 1 grupės. Komplikacijų dažnis grupėse nesiskyrė.

Išvados. Pirminio kelio sąnario endoprotezavimo metu optimalus kraujotakos sustabdymas manžete yra nuo pjūvio iki cemento sustingimo. Manžetės naudojimas tik kelio sąnario cementavimo metu didina kraujo netekimą. Kraujotakos stabdymas visos operacijos metu ir užsitęsęs apie 1 val. gali sulėtinti funkcinį ligonio atsistatymą ir yra sietinas su ilgesne pooperacine hospitalizacija. Perioperacinė individuali skysčių terapija ligoniams, kuriems atliekamas pirminis kelio sąnario endoprotezavimas, gali sutrumpinti hospitalizacijos laikotarpį.

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