Total Blood Loss After Transfemoral Amputations Is Twice the Intraoperative Loss: An Observational Cohort Study of 81 Nontraumatic Amputations

Christian Wied, MD[1], Peter T. Tengberg, MD, PhD[1],
Morten T. Kristensen, PT, PhD[1,2], Gitte Holm[1], Thomas Kallemose, MSc[1,3],
Anders Troelsen, MD, PhD, DMSc[1], and Nicolai B. Foss, MD, DMSc[4]

Abstract

Introduction: Underestimation of the actual blood loss in patients undergoing nontraumatic transfemoral amputation (TFA) can impact negatively on outcome in these often frail patients, with very limited physiological reserves. The primary aim of this study is to estimate the total blood loss (TBL) after TFA, and second, to evaluate the impact of blood loss on 30-day mortality and medical complications. **Methods:** A single-center retrospective cohort study conducted from 2013 to 2015. The TBL was calculated on the fourth postoperative day. It was based on the hemoglobin levels, transfusions, and the estimated blood volume. **Results:** Eighty-one patients undergoing TFA were included for final analysis. The median TBL was 964 mL (interquartile range [IQR]: 443-1558). The intraoperative blood loss (OBL) was 400 mL (IQR: 200-500). The median difference between TBL and OBL was 688 mL (IQR: 124-1075). The patient received red blood cell (RBC) transfusion of a median amount of 2 units. Higher number of transfusions (>2) did not impact the outcome. From multivariable analysis, it was evident that the TBL increased significantly in patients with renal disease prior to surgery, (P = .034). The TBL itself was not independently associated with increased 30-day mortality or medical complications. **Conclusion:** The TBL after TFAs is significantly greater than the volume estimated intraoperatively and increases significantly in the presence of renal disease prior to surgery. An increased TBL and requirement for RBC transfusion is not directly associated with 30-day mortality or medical complications. A high vigilance for anemia seems advisable when planning for TFA surgery. Research on optimum blood conservation and transfusion strategies during TFA is warranted.

Keywords

transfemoral amputation, total blood loss, lower extremity amputation, intraoperative blood loss, transfusion strategy

Introduction

Patients requiring transfemoral amputation (TFA) on the basis of atherosclerosis or diabetes mellitus are often fragile, old, and with several comorbidities.[1,2] They pose a challenge to all medical staff involved in the treatment due to their limited physiological reserves. The total blood loss (TBL) associated with TFA surgery has, to our knowledge, never been investigated. Due to their limited physiological reserves, these patients are at increased risk of reduced organ perfusion and subsequent ischemia, organ failure, and death as a consequence of anemia.[1]

The primary aim of this study is to quantify the TBL in the perioperative period until the fourth postoperative day and the

[1] Department of Orthopaedic Surgery, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark
[2] Physical Medicine and Rehabilitation Research–Copenhagen (PMR-C), Department of Physiotherapy, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark
[3] Clinical Research Centre, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark
[4] Department of Anesthesiology and Intensive Care, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark

Corresponding Author:
Christian Wied, Department of Orthopaedic Surgery, Copenhagen University Hospital Hvidovre, Kettegaard Alle 30, 2650 Hvidovre, Denmark.
Email: chr.wied@gmail.com

potential related predictors. Second, since medical complications and 30-day mortality are high during the early phase after TFA, the TBL and the red blood cell (RBC) transfusion amount are to be investigated as potential contributors.

Patients and Methods

Study Population

Between January 2013 and March 2015, a total of 150 consecutive TFA procedures were studied. Through a systematic search of our institutional surgical database, we extracted the demographic baseline and postoperative parameters of interest. Patients were included if the indication for surgery was severe atherosclerosis with pain or diabetes-related complications. Only patients with a primary TFA were included. We excluded patients who had undergone bilateral procedures, in whom intramedullary nails were removed as part of the procedure, who previously underwent lower extremity amputation surgery on ipsilateral or contralateral extremity, who had clinical signs of gastrointestinal bleeding (melena or hematemesis), who used pneumatic tourniquet, and with missing data, including patients who died before final Hgb at day 4. The study was approved by the local ethics committee and registered at the regional data protection agency (December 04, 2012; j. no. 01975 HVH-2012-053).

Procedure

The patients were treated in a dedicated amputation unit within the department, regardless of their preoperative status. The amputation unit uses a multimodal treatment and rehabilitation program.[3] This includes consultation with the department of vascular surgery and the supplementary measurement of skin perfusion pressure to determine the level of amputation. The patients received general or neuroaxial anesthesia and antibiotics preoperatively and low-molecular-weight heparin after surgery as prophylaxis against thromboembolism. The procedure was performed approximately 10 cm above the knee joint and with anterior and posterior skin flaps. Trained residents or senior consultants performed the surgical procedures. Standardized fluid and transfusion procedures were followed. Blood loss was replaced with isotonic saline at a rate of 1:1 until the level of hemoglobin fell below 9.67 g/dL (6 mmol/L), at which point RBC transfusion was initiated. Postoperative fluid therapy and intravenous fluids were only administered if the patient's oral intake was less than 2000 mL daily or if they were hypovolemic. The level of hemoglobin was measured on admission, prior to operation (less than 1 day before surgery), and every morning until the fifth postoperative day. If a patient received transfusions prior to surgery, a new hemoglobin measurement was done hours afterward. The final hemoglobin value was defined as the last sample obtained on the fourth postoperative day. In the event of transfusion on day 4, the hemoglobin value on day 5 was used instead.

Collection of Data

The variables of interest were collected retrospectively, along with the 30-day mortality and medical complications. The patients included were not weighed on a conventional scale until the first postoperative day. The anesthesiologists estimated patient weight prior to surgery supported by the patient's own information. The regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid in any dose, as well as the regular use of clopidogrel or vitamin K antagonists before the amputation, was recorded. The use of vasopressor drugs during surgery was also recorded. Medical complications were defined as the occurrence of any of the following: acute renal failure (RIFLE consensus definitions),[4,5] deep venous thrombosis, myocardial infarction, pneumonia, pulmonary embolism, sepsis, and stroke.

Blood Loss

The TBL was calculated using the Nadler approach,[6,7] based on the difference between the preoperative and fourth postoperative day Hgb, the number of RBC transfusions, and the estimated blood loss (OBL) was evaluated by the weight difference in surgical swabs and the measured suction loss. The blood volume was determined according to body mass, height, and gender. The following formulas were used for calculation:

$$\text{Blood volume(l)} = \text{height(m)}^3 \times 0.356 + \text{weight(kg)} \times 0.033 + 0.183 \text{ for women;}$$

$$\text{Blood volume(l)} = \text{height(m)}^3 \times 0.367 + \text{weight(kg)} \times 0.032 + 0.604 \text{ for men.}$$

The formula used was as follows:

$$\text{Hgb}_{loss} = \text{blood volume} \times (\text{Hgb}_{adm} - \text{Hgb}_{fin}) + \text{Hgb transfusion,}$$

where Hgb_{loss} is the calculated total Hgb loss (g), Hgb_{adm} is the Hgb value on admission, Hgb_{fin} is the final recorded Hgb value on day 4, and Hgb_{trans} is the total amount of Hgb (g) in the transfused RBCs before the measurement of Hgb_{fin}. The blood loss was estimated using the following formula:

$$\text{Blood loss in mL} = (\text{Hgb}_{loss}/\text{Hgb}_{adm}) \times 1000.$$

Statistical Analysis

Continuous data are presented as median values with interquartile range (IQR) or mean values with standard deviations. Categorical data are presented as numbers and percentages. Preoperative data, with known influence on the TBL in other orthopedic subspecialties,[7,8] are analyzed in a multivariable linear regression analysis. The medical complications and 30-day mortality in relation to TBL and transfusion requirements are analyzed by multivariable logistic regression. The level of

Table 1. Details on the Transfemoral Amputations.[a]

Sex (female/male)	42/39
Age, years, mean (SD)	76.8 (11.2)
Body mass index, mean (SD)	24.0 (7.5)
Cause of amputation	
Diabetes/atherosclerosis/other	22/52/7
ASA groups, 1-2/3-4	10/71
Poor preamputation functional level (new mobility score 0-5)	78%
Preamputation nursing home residence/other hospital department	23%/17%
Duration of surgery, minutes (SD)	78.2 (16.7)
NSAIDs or acetylsalicylic acid (yes)	44
Clopidogrel (yes)	22
Cardiovascular disease	14
Renal disease	20
Diabetes	29
Patients with >2 units of RBC transfusion	27
Patients with Hgb <9.67 g/dL prior to surgery	16
Delta Hgb ≥20% (presurgery to day 4 postsurgery)	15

Abbreviations: ASA, American Society of Anesthesiologists; HGB, hemoglobin; NSAIDs, nonsteroidal anti-inflammatory drugs; RBC, red blood cell; SD, standard deviation.
[a]n = 81.

significance is set at $P < .05$. All analyses were performed using IBM SPSS Statistics version 22.

Results

Of the 150 consecutive amputations accessible for inclusion, 81 patients met the inclusion criteria and were included in the final analysis. In total, 69 TFAs were excluded due to reamputation (36), bilateral procedure (12), use of pneumatic tourniquet (11), gastrointestinal bleeding prior to surgery (5), lack of data due to death before day 4 (4), and amputation in relation to removal of an intramedullary nails (1). The preoperative demographics are presented in Table 1. The patients were weighed on a conventional scale the day after amputation. This was possible in 50% of the cases. The average difference in weight compared to the estimated weight before surgery was −8.0 kg. The daily Hgb measurements were at no point below 10 g/dL on average.

The median TBL was 964 mL (IQR: 443-1558) and the OBL 400 mL (IQR: 200-500). The median delta value between TBL and OBL was 688 mL (IQR: 124-1075). In total, a median of 2.0 (IQR: 1-3) units of RBC transfusion were administered per patient from surgery until the fourth postoperative day. Preamputation treatment with NSAID or acetylsalicylic acid, duration of surgery, and cardiovascular or renal comorbidities were all associated with an increased TBL in univariable analysis (Table 2). When a multivariable analysis was performed, only the variable renal disease ($P = .034$) was associated with an increased TBL (Table 2).

Total blood loss per 100 mL and RBC transfusion amount exceeding 2 units (n = 27) showed no statistically significant influence on medical complications or perioperative mortality (Table 3). In all, 7 of the 15 patients who died had registered

Table 2. Univariable and Multivariable Linear Regression of Predictors of Increased Total Blood Loss.

	Estimate (mL)	95% CI	P Value
Univariable linear regression			
Age, per year older	15	−0.9 to 29.3	.064
Sex, male	223	124 to 569	.205
Body mass index, per 1 unit	3.5	−20 to 27	.969
Charge of surgeon, senior consultant	−40	−433 to 353	.840
Duration of surgery, per minute	15	5 to 25	.005
NSAID/magnyl, yes	473	126 to 819	.008
Clopidogrel, yes	−43	−473 to 387	.842
Cardiovascular comorbidity, yes	521	73 to 969	.023
Diabetes, yes	102	−263 to 466	.580
Renal disease, yes	564	169 to 958	.006
Multivariable linear regression			
Age, per year older	12	−6 to 29	.190
Sex, male	200	−152 to 552	.260
Body mass index, per 1 unit	−1	−25 to 24	.954
Charge of surgeon, senior consultant	−121	−513 to 271	.540
Duration of surgery, per minute	11	−1 to 23	.075
NSAID/magnyl, yes	401	−6 to 808	.053
Clopidogrel, yes	62	−449 to 573	.809
Cardiovascular comorbidity, yes	209	−272 to 691	.388
Diabetes, yes	−169	−612 to 274	.449
Renal disease, yes	489	38 to 940	.034

Abbreviation: NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 3. Medical Complication or 30-Day Mortality in Relation to TBL per 100 mL and RBC Transfusions >2 Units.

Multivariable Logistic Regression

Variable	Estimate	95% CI	P Value
TBL, per 100 mL	0.979	0.893-1.075	.660
>2 Units of RBC transfusion (yes)	1.774	0.367-8.569	.476
Preoperative anemia, (yes)	4.525	0.882-23.213	.070
Age, per year	0.959	0.906-1.015	.146
Sex, male	3.512	1.065-11.583	.039
Duration of surgery, per minute	1.039	0.995-1.085	.081
Charge of surgeon, senior consultant	0.773	0.212-2.821	.697
Thrombocyte inhibitors, (yes)	0.588	0.165-2.097	.413
Renal disease, (yes)	1.109	0.290-4.247	.880

Abbreviations: RBC, red blood cell; TBL, total blood loss.

medical complications prior to their death; 3 of them received more than 2 units of RBC transfusion.

In total, 22 patients were amputated due to diabetes-related complications. Nine of them had postoperative complications (41%). In total, 52 patients were amputated due to atherosclerotic complications and 16 had postoperative complications (31%). We expect some overlap between the group with

diabetes-related complications and the patients in the group with atherosclerosis. The following results are only indicative. There were no significant difference between the 2 subgroups regarding TBL ($P = .841$), the OBL ($P = .748$), or complication rates ($P = .431$).

Discussion

From this study, it seems warranted to conclude that the TBL in relation to TFA is significantly higher than the amount recorded by the operating surgeon. One should expect a higher TBL when the patient presents with renal comorbidity. In this study, an increased TBL and RBC transfusion rate above 2 units did not have a statistically significant impact on the 30-day mortality or medical complications.

The TFA patients are, most likely, the patients with the highest 30-day mortality, within orthopaedic surgery. In this study, 88% of the patients were coded with American Society of Anesthesiologists (ASA) score 3 to 4, and 30-day mortality was 18.5%. In comparison to patients with Danish hip fracture, which we consider the best match for the TFA population, only 58% of the patients with hip fracture were coded with (ASA score, 3-4) and with a perioperative mortality of 13%.[7] This clearly underlines the vulnerability of these patients and serves to remind us of how the continuous optimization of treatment protocols is important.

The calculated TBL is an alternative way to approach the bleeding in relation to surgery. From the study of patients with hip fracture and using a similar approach, it was understood that "the total blood loss is much greater than that observed intraoperatively and frequent postoperative measurements of hemoglobin are necessary to avoid anemia."[7(p1053)] In regard to the TFA procedure, there still remains a lack of knowledge regarding the actual scope of the blood loss. The results of this study showed TBL is approximately twice the amount of blood loss recorded just after the surgical procedure. The most obvious reasons for this difference are diffuse hematomas occurring postoperatively and an underestimation of the OBL by the operating surgeons. This underestimation is described in other orthopedic subspecialties, and it also seems to be a potential factor in TFA surgery.[9] The postoperative bleeding into the soft tissues could be a result of insufficient hemostatic control of minor vessels, in combination with seepage from the femur canal after the femur is divided. Based on univariate analysis, there was an association between increased TBL and the duration of surgery, renal or cardiovascular disease, and the treatment with NSAIDs/acetylsalicylic acid. The most pronounced impact is when a patient has renal disease prior to surgery, and this remains the only statistically significant variable according to multivariable regression analysis (Table 2). These patients (n = 20) have a TBL of 1288 mL (IQR: 791-2303). Little is known about perioperative management of platelet dysfunction associated with renal disease, but the finding of increased blood loss is consistent with other studies.[7,10,11]

Anticoagulation therapy with low-molecular-weight heparin was standard for all TFAs, and therefore, we cannot comment on the impact on the TBL. However, the TBL in this study is of such magnitude that it may be warranted to evaluate different anticoagulant regimes.

The TBL had no direct association with perioperative medical complications and the 30-day mortality. This study illuminates how often the patients receive RBC transfusions which is a potential proxy for the deleterious effects of anemia.[12,13] Other departments may have other experiences regarding this amount since it depends on the chosen transfusion trigger. It is acknowledged that patients benefit from a liberal perioperative transfusion strategy,[12] especially when patients have some degree of cardiovascular disease prior to surgery.[14] A liberal transfusion trigger of 9.67 g/dL (6 mmol/L) was therefore used to standardize transfusion therapy and to minimize the potential effects of anemia on the postoperative outcome. We did not find a transfusion rate above the median 2 units to be associated with an increased 30-day mortality or medical complications, which could be due to a reduced impact of blood loss within a setting of high anemia vigilance and a liberal transfusion policy.

Limitations

The change in blood volume over time when an extremity is removed is considered a challenge in this study. This could affect the calculated TBL, which depends entirely upon the accuracy of the presurgery Hgb, the final Hgb values, and the estimated blood volume. In order to assess the impact of a reduced weight and thereby blood volume after amputation, the patient's weight after amputation was measured on a conventional scale on the first postoperative day. As noted in the results section, the average weight difference before and after surgery was 8 kg. Since the weight difference is relatively small, by taking into account the removal of the amputated limb, it seems that the weight issue has a limited influence on the results. We find it acceptable not to attempt to integrate the weight change into the formula. The potential dehydration when blood work is performed is also a source of biased results; however, the patients included in this study followed a strict fluid therapy protocol, and we believe the influence is minimal. We did exclude a large number of patients in an effort to obtain the most accurate estimation of blood loss during TFA. It did not make sense to us to include patients with secondary bleeding disorders or a procedure that deviates from the standard operation protocol. However, we do acknowledge that this approach could potentially lead to selection bias. A future prospective study with a larger number of patients should be performed to understand the real influence of TBL on mortality and also to ensure that complications are not overlooked.

In conclusion, TBL calculated on day 4 after TFA surgery is up to twice the amount of that observed during a surgical procedure. Patients having renal disease prior to amputation are more likely to have an increase in TBL. The TBL did not significantly influence the 30-day mortality or medical complications, nor did an RBC transfusion amount >2 units. Therefore, a high anemia vigilance is recommended when planning

for TFA surgery. Further knowledge of the coagulation deficit, platelet dysfunction, and possible treatment mechanisms in patients with renal failure presenting for surgery is warranted together with research on optimum blood saving and transfusions strategies in TFA.

Declaration of Conflicting Interests

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