



Published in final edited form as:

Ann Vasc Surg. 2016 February ; 31: 124–133. doi:10.1016/j.avsg.2015.08.017.

Pre-operative predictors of 30-day mortality and prolonged length of stay after above-knee amputation

Eric S. Wise, MD^{1,*}, William G McMaster Jr, MD¹, Kelly Williamson, MS², Justine E Wergin, BS², Kyle M Hocking, PhD^{1,3}, and Colleen M Brophy, MD^{4,1}

¹Department of Surgery, Vanderbilt University Medical Center, Nashville, Tennessee, USA

²Vanderbilt University School of Medicine, Nashville, Tennessee, USA

³Department of Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, USA

⁴VA Tennessee Valley Healthcare System, Nashville, Tennessee, USA

Abstract

Background—The above-knee amputation (AKA) is an operation of last resort with high post-operative morbidity and mortality. This study identifies pre-operative risk factors predictive of both 30-day mortality and extended length of stay (LOS) in AKA patients.

Materials and Methods—Two hundred and ninety-five AKA patients from 2004-2013 from a single institution were retrospectively reviewed using a de-identified electronic medical record. Rationally selected factors potentially influencing 30-day mortality and LOS were chosen, including demographics, etiologies, vascular surgical history, lifestyle factors, comorbidities and laboratory values. Variables trending with one of the endpoints on bivariate analysis ($P < .10$) were entered into multivariate forward stepwise regression models to determine independence as a risk factor ($P < .05$). Subgroup analysis of AKA patients without a traumatic, burn or malignant etiology was similarly conducted.

Results—Within the 295 patient cohort, 60% of patients were male, 18% were African-American, mean age was 58 years old and mean body-mass index was 28 kg/m². The 30-day mortality rate was 9%, and mean post-operative LOS of discharged patients was 9.3 days. Upon logistic regression, thrombocytopenia (platelet count $< 250 \times 10^6$ /mL; $P < .001$, odds ratio 6.1) and pre-operative septic shock ($P = .02$, odds ratio 5.1) were identified as independent risk factors for 30-day mortality. Upon linear regression, burn etiology ($P < .001$, B = 15.8 days), leukocytosis (white blood cell count $< 12 \times 10^6$ /mL; $P < .001$, B = 6.2 days) and guillotine amputation ($P < .001$, B = 7.6 days) were independently associated with prolonged LOS. Excluding patients with AKAs due to trauma, burn or malignancy, only thrombocytopenia (platelet count $< 250 \times 10^6$ /mL;

* Corresponding author: Eric S. Wise, M.D., Department of Surgery, Vanderbilt University Medical Center, 1161 21st Ave S, MCN T2121, Nashville, TN 37232-2730. (eric.s.wise@vanderbilt.edu).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

CONFLICTS OF INTEREST

None

$P < .001$, odds ratio 10.2) and leukocytosis (white blood cell count $> 12 \times 10^6/\text{mL}$; $P = .01$, $B = 5.2$ days) were independent risk factors for in-hospital mortality and prolonged LOS, respectively.

Conclusions—Pre-operative septic shock and thrombocytopenia are independent risk factors for 30-day mortality after AKA, while burn etiology, leukocytosis and guillotine amputation contribute to prolonged LOS. Awareness of these risk factors may help enhance both pre-operative decision-making and expectations of the hospital admission.

Keywords

outcomes; amputation; above-knee amputation; peripheral arterial disease; diabetic neuropathy; mortality; length of stay

INTRODUCTION

Over 100,000 major lower extremity amputations, including below-knee amputations (BKA) and above-knee amputations (AKA), are performed annually in the United States.^{1, 2} The one-year survival rate for these patients is estimated to be 69-78%, lower in the cohort requiring AKA.^{3, 4} Relative to BKA patients, AKA patients are less likely to regain mobility and functional independence post-operatively due to loss of the knee joint.⁵ AKA recipients are frequently poor surgical candidates.⁵ The care of these patients extends well beyond their inpatient stay, as they require aggressive rehabilitation, assessment for prosthesis, nutritional optimization and significant social work needs. The care of these patients is extremely costly, and a post-operative course wrought with complications and a poor quality of life is not uncommon.^{1, 4-7} In cases of chronic ischemia, a contributor to the etiology of the majority of AKA operations, even revascularization attempts with a low chance of success are recommended for limb salvage therapy antecedent to AKA.⁸

Identification of patients who are at risk for perioperative mortality or prone to extended hospitalizations presents a challenge. In 2012 and 2013, the American College of Surgeons National Surgical Quality Improvement Program database was retrospectively examined, finding that not only was the 30-day mortality rate of AKA patients double that of the BKA (12.8% vs. 6.5%), but mortalities could be partially predicted on the basis of a panel of pre-operative variables.^{9, 10} Hospital length of stay (LOS) is another important outcome measure. Among diabetic inpatients with peripheral arterial disease, those who required a major amputation experienced a far more costly clinical course than those who required other interventions including bypass, percutaneous transluminal angioplasty, minor amputation or debridement.¹¹ This finding was chiefly attributed to the profoundly long hospital stays these patients often require.¹¹ The purpose of our study was to examine and evaluate simple, rationally selected pre-operative variables that may portend the important outcome measures of 30-day mortality or prolonged LOS among our patient population, using our institutional cohort of AKA patients.

MATERIALS AND METHODS

This was a single-institution, retrospective analysis of risk factors for 30-day mortality and prolonged LOS after AKA from 2004-2013. Patients who underwent AKA were determined

via the Vanderbilt University Synthetic Derivative, a database that mirrors the electronic medical record after removal of all patient identifiers.¹² As there was no identifying information available, this study was approved by the Vanderbilt University Institutional Review Board with waiving of informed consent. Using a search algorithm for patients with an associated *Current Procedural Terminology* code for AKA (27590, 27591 or 27592), 514 patients who underwent AKA were found. Patients were excluded if they did not have their operation between 2004-2013 (182 patients) or did not have sufficient data available in the medical record (37 patients). Ultimately, 295 patients were included for analysis.

Included patients were reviewed for demographics and rationally selected patient characteristics. Body-mass index (BMI) and laboratory values were taken as the last documented value before surgery, though laboratory values > 7 days prior to surgery were excluded. Comorbidities were attributed by the presence of an associated ICD.9 code pre-operatively,¹³ with chart review confirmation.¹⁴ For simplicity, only the presence or absence of a comorbidity was considered. Selected variables are reported in **Table I**. All continuous patient variables were dichotomized prior to statistical analysis, using clinical sense and prior reports to approximate a useful and appropriate cut-off value (e.g. white blood cell [WBC] count cut-off at $12 \times 10^6/\text{mL}$). Primary endpoints were 30-day mortality and LOS, defined as the difference from the day of the index operation to discharge (home, rehabilitation or assisted living facility). All data was managed using the Vanderbilt Research Electronic Data Capture (REDCap) platform.¹⁵ Subgroup analysis was also performed on 206 patients, excluding those with etiologies related to trauma, burn or malignancy.¹³

Bivariate analysis of all variables was conducted to screen for those factors associated with 30-day mortality (via Pearson chi-squared test) and LOS (via bivariate linear regression analysis). Factors that trended with 30-day mortality or LOS ($P < .10$) were included in logistic and linear multivariate stepwise regression models, respectively. Variables significant upon multivariate analysis were deemed independent predictors of the endpoints, at a level of statistical significance of $P \leq .05$. As all variables included in multivariate analyses had a variance inflation factor < 1.8, collinearity was not statistically considered. Albumin level was excluded from multivariate models due to a prohibitively large number of missing values. Measures of central tendency were reported as mean \pm standard deviation. Statistical analysis was performed with JMP Pro 11 (Cary, NC) and GraphPad Prism (La Jolla, CA).

RESULTS

The cohort included 295 patients who underwent AKA from 2004-2013. Patient demographics and clinical characteristics for these patients are presented in **Table I**. Sixty percent (176/295) of the patients were male, 18% (52/295) were African-American, the mean age at operation was 58 ± 18 years and the mean body-mass index (BMI) was 28 ± 9 kg/m². Thirty-one percent (90/292) of the patients had a prior revascularization attempt on the amputated extremity. Consistent with reported estimates,^{4, 5} 9% of patients were 30-day mortalities (26/295), and the mean LOS, considered only for the 269 patients who survived to discharge, was 9.3 ± 12.9 days.

Bivariate Pearson chi-squared analysis was conducted for those factors which exhibited a trend towards increased risk of mortality, at a level of evidence $P \leq .10$. The results of this analysis are presented in **Table II**. Gender, race, age and BMI were not associated with 30-day mortality. Traumatic etiology ($P = .06$; odds ratio [OR] 2.4) and malignant etiology ($P = .06$; OR 0.13) trended toward an increased and decreased risk of 30-day mortality, respectively. Prior vascular surgical history was not associated with 30-day mortality. Several lifestyle factors did demonstrate a trend, including current smoker ($P = .02$, OR 0.28), fully independent functional status ($P = .08$, OR 2.5) and partially dependent functional status ($P = .07$; OR 0.19). Among comorbidities, congestive heart failure ($P = .09$; OR 2.0) and septic shock trended with 30-day mortality ($P = .001$; OR 6.8). Laboratory measurements associated with 30-day mortality included thrombocytopenia (platelets $< 250 \times 10^6/\text{mL}$, $P < .001$; OR 6.4), elevated international normalized ratio (INR; $\text{INR} > 1.3$, $P = .006$; OR 3.4) and hypoalbuminemia (albumin < 2.2 , $P = .005$; OR 4.5). Guillotine amputation ($P = .004$; OR 3.4) and pre-operative steroid use ($P = .03$; OR 3.6) were also associated with 30-day mortality.

Bivariate linear regression analysis was used to determine those variables that demonstrated a trend ($P \leq .10$) with LOS. The results of this analysis are presented in **Table III**. Three etiologies trended with LOS, including trauma ($P = .05$; B = 4.5 days), burn ($P < .001$; B = 19.4 days) and malignancy ($P = .02$; B = -5.7 days). Fully independent ($P = .007$; B = 4.6 days) and partially dependent ($P = .03$; B = -4.4 days) functional statuses were the only correlated lifestyle factors. Additional factors associated with LOS included leukocytosis ($\text{WBC} > 12 \times 10^6/\text{mL}$, $P < .001$; B = 7.7 days) and guillotine amputation ($P < .001$; B = 10 days).

Results of the stepwise multivariate regression analyses are presented in **Table IV**. Independent predictors of 30-day mortality were thrombocytopenia (platelet count $< 250 \times 10^6/\text{mL}$; $P < .001$, OR 6.1) and pre-operative septic shock ($P = .02$, OR 5.1). Pre-operative predictors of prolonged LOS were burn etiology ($P < .001$, B = 15.8 days), leukocytosis ($\text{WBC} > 12 \times 10^6/\text{mL}$; $P < .001$, B = 6.2 days) and guillotine amputation ($P < .001$, B = 7.6 days). Traumatic and malignant etiologies, and strata of functional status lost significance.

A brief contrast between the subgroup and the excluded cohort of patients amputated due to trauma, burn or malignancy is reported in **Table V**. Notably, the patients within the subgroup had a greater percentage of African-Americans (22% vs. 8%, $P = .004$), were older (61.9 ± 14.9 years vs. 49.8 ± 20.6 years, $P < .001$) and had a shorter LOS (8.2 ± 11.9 days vs. 11.8 ± 15.0 days, $P = .04$). No differences in gender, BMI and mortality rate were noted.

Results of the subgroup bivariate screen for both 30-day mortality and LOS are reported in **Table VI**. Pre-operative variables trending with 30-day mortality in this cohort included previous smoker ($P = .09$, OR 2.4), current smoker ($P = .052$, OR 0.30), fully independent ($P = .04$, OR 3.3) and partially independent ($P = .10$, OR 0.21) functional statuses, septic shock ($P < .001$, OR 8.7), thrombocytopenia (platelet count $< 250 \times 10^6/\text{mL}$; $P < .001$, OR 10.3), elevated INR ($\text{INR} > 1.3$; $P = .04$, OR 3.0), hypoalbuminemia (albumin < 2.2 g/dL; $P = .01$, OR 4.5), low packed cell volume (packed cell volume $< 31\%$, $P = .04$, OR 2.8) and guillotine amputation ($P = .052$, OR 3.2). Those that trended with LOS included African-

American race ($P = .02$, $B = 4.9$ days), fully independent functional status ($P = .07$, $B = 3.3$ days), diabetes mellitus ($P = .08$, $B = 3.0$ days) and leukocytosis ($WBC > 12 \times 10^6/mL$; $P < .001$, $B = 5.2$ days). Reported in **Table VII**, only thrombocytopenia (platelet count $< 250 \times 10^6/mL$; $P < .001$, odds ratio 10.2) and leukocytosis ($WBC > 12 \times 10^6/mL$; $P = .01$, $B = 5.2$ days) remained significant risk factors for 30-day mortality and LOS, respectively, on subgroup multivariate analysis.

DISCUSSION

Patients undergoing an AKA have a high 30-day mortality, which has been reported between 9% and 31%.^{4, 7, 9, 10, 16-18} Patients who are unlikely to survive past thirty days would benefit from non-operative management rather than undergo the AKA, which is often associated with significant deleterious psychological and physical sequelae.^{5, 6, 9, 10} Moreover, even if patients with a poor prognosis pre-operatively do survive to discharge, they are unlikely to have a successful functional outcome.⁶ Conversely, patients who have a low risk for 30-day mortality are more likely to have a meaningful and more independent functional status.^{19, 20}

Independent risk factors for 30-day mortality among all patients included thrombocytopenia and pre-operative septic shock, providing the first validation of the novel findings of Nelson and colleagues; only thrombocytopenia after exclusion of patients with traumatic, burn and malignant etiologies.⁹ Thrombocytopenia is a risk marker of infection and septic shock. Its development is thought to be multifactorial, due to decreased platelet production, increased platelet consumption and platelet sequestration in severely ill patients.^{21, 22} Among patients in the intensive care setting for all causes, thrombocytopenia (or a dramatic drop in platelet count) is also validated independent marker for mortality.²² In septic shock patients, the AKA operation is ostensibly required for source control. To this effect, the concurrent bivariate association of guillotine amputations with 30-day mortality was found as well; unlike thrombocytopenia, guillotine amputation was not sufficiently distinct from septic shock to maintain independent association, however. Our data confirms the association of septic shock with 30-day mortality, though these patients are also at risk for early amputation failure, wound complications and non-wound complications during the remainder of their inpatient stay.²³

Our bivariate analysis suggested additional potential risk factors, though we lacked power to detect independent association on multivariate analysis. Bivariate analysis revealed that being an active smoker was protective toward 30-day mortality, a seemingly counterintuitive result but consistent with findings from both the Veterans Administration population and the private sector.^{10, 24} Karam *et al.* postulated this was due to the notion that active smoking status may indicate the patient is still healthy enough to do so.¹⁰ Additionally, albumin level as a surrogate for poor nutritional status was a strong risk factor for 30-day mortality ($P = .005$; OR 4.5) on bivariate analysis. Though excluded from multivariate models due to an abundance of missing values, the serum albumin level as a surrogate for poor nutritional status is regarded as a strong predictor of post-operative mortality following myriad operations.²⁵

Though our data did demonstrate the association of two pre-operative variables with 30-day mortality, there were several notable negative findings. As an example, it was anticipated that patients with poor functional status pre-operatively would have a greater 30-day mortality rate.¹⁸ Patients with a poor functional status, as quantified by the Activities of Daily Living Long Form Score,²⁶ have a poor post-operative trajectory, with a very slow recovery to their baseline functional status. However, full independence was associated with increased risk of 30-day mortality on bivariate analysis, possibly due to association with etiologies carrying a high mortality, though this trend was lost upon multivariate analysis.

Along with 30-day mortality, we identified pre-operative risk factors for prolonged LOS following AKA. LOS was determined for patients who were not 30-day mortalities. As an endpoint, LOS is important due to its association with increased costs, morbidities as well risk of nosocomial sequelae including infection and delirium, complications exacerbated in AKA patients.^{27, 28} Median post-operative LOS for AKA patients has been reported at 5 days, similar to patients who undergo BKA or transmetatarsal amputation.²³ Our median LOS was 6 days, with a mean of 9.3 days. Upon multivariate analysis, our study had the power to detect the association of burn etiology with LOS. Expectedly, while burn patients survive to discharge, they experience a prolonged post-operative inpatient stay for wound management, debridement and skin grafting procedures as well as suitable recovery of function prior to discharge to rehabilitation. An AKA for burn also represents an unplanned, urgent procedure. Non-elective AKAs are established independent risk factors for death, amputation failure and readmission; our data infers it may also be a risk factor for prolonged LOS.^{10, 23, 29} In contrast, patients with a planned AKA due to malignancy likely had infrastructure in place to facilitate prompt discharge.

We further report the association between leukocytosis and guillotine amputation with prolonged LOS, only the former, however, in the subgroup. Leukocytosis is a proxy for concomitant infection or sepsis, while the need for guillotine amputation represents a more acute, urgent pre-operative disease requiring wound care and eventual formal closure. Fully independent functional status was also associated with prolonged post-operative stay, though only upon bivariate analysis. We postulate this is due to the needed time necessary to facilitate an appropriate disposition, requiring the *ab initio* establishment of appropriate rehabilitation and assisted living resources, though this may reflect a degree of collinearity with burn patients who were previously fully functional.

The failure to exclude patients with traumatic, burn and malignant etiologies represents a legitimate criticism of existing outcomes data, as analysis of this cohort together with amputees due to chronic ischemic disease or complications thereof may be faulty or impractical.^{9, 10} Other studies selectively excluded this cohort to provide an emphasis on those patients with primarily vascular disease and diabetic neuropathy.^{5, 7, 13, 16} In our study, we report both a procedure-level analysis considering all patients who underwent AKA, and a dedicated subgroup analysis with selective exclusion to allow our data an adequate comparison with existing literature.

In summary, our study affirmed the reported independent association of septic shock and thrombocytopenia with 30-day mortality after AKA and reported three novel risk factors,

burn etiology, leukocytosis and guillotine amputation, contributing to prolonged LOS. We were not able to detect a significant association with other reported risk factors, including age, race and select comorbidities and laboratory values, among others.^{7, 9, 10, 17} Inability to detect these associations may be partially a function of sample size, one of the primary limitations of our study. Our 295 patient cohort is commensurate with multiple other studies of patients with major lower extremity amputation, however, our 30-day mortality rate of 9% limits the ability to detect differences among the survivors and the mortalities. Additionally, the study data was retrospectively collected from a prospectively maintained database, leading to the selection bias and potential loss of accuracy inherent in this approach. Data collection required a small degree of subjectivity, particularly in etiologic classifications and attribution of comorbidities. While our 30-day mortality data provides selective validation to previously reported data in both the private and Veterans Administration sector, identified risk factors for prolonged LOS require externally validation, as the generalizability of our cohort may be limited.²⁶ Finally, endpoints such as wound complications, major adverse cardiac events and other major morbidities were not considered in this analysis, and these factors may be of paramount importance in both assessing the potential futility of an AKA or providing appropriate prognostic information to patients and families. Furthermore, it would be valuable to extend our mortality rates to one, two or five years out, with a concomitant validated measure of functional status or quality of life as well.

Suggestion of non-operative management due to a high risk of mortality is difficult, and guided primarily by the clinician's judgment. Understanding the aspects of the clinical profile of a pre-operative patient unlikely to survive to discharge provides an evidence-based adjunct to assist the surgeon in providing the patient and family the appropriate context to make the best clinical decision. Additionally, our findings may optimize prognostic guidance in providing realistic expectations about the time until discharge, particularly with respect to burn patients who required an AKA.

CONCLUSIONS

The AKA is a highly morbid procedure, one in which outcomes data severely lacks in contrast to other common vascular operations. In this study, we validated several important risk factors for 30-day mortality after AKA, and provided new insight into risk factors portending a prolonged LOS as well. Despite limitations, these data allow for the improved pre-operative stratification of AKA patients, and subsequently may allow for more informed decision making and improved anticipation of a pending post-operative course.

Acknowledgments

FUNDING

Grant Support Acknowledgement:

Vanderbilt RedCAP: CTSA Award UL1 TR000445 from NCATS/NIH

REFERENCES

1. Sandnes DK, Sobel M, Flum DR. Survival after lower-extremity amputation. *J Am Coll Surg.* 2004; 199(3):394–402. [PubMed: 15325609]
2. Dillingham TR, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. *South Med J.* 2002; 95(8):875–83. [PubMed: 12190225]
3. Nehler MR, Hiatt WR, Taylor LM Jr. Is revascularization and limb salvage always the best treatment for critical limb ischemia? *J Vasc Surg.* 2003; 37(3):704–8. [PubMed: 12618724]
4. Ploeg AJ, Lardenoye JW, Vrancken Peeters MP, et al. Contemporary series of morbidity and mortality after lower limb amputation. *Eur J Vasc Endovasc Surg.* 2005; 29(6):633–7. [PubMed: 15878543]
5. Nehler MR, Coll JR, Hiatt WR, et al. Functional outcome in a contemporary series of major lower extremity amputations. *J Vasc Surg.* 2003; 38(1):7–14. [PubMed: 12844082]
6. Suckow BD, Goodney PP, Cambria RA, et al. Predicting functional status following amputation after lower extremity bypass. *Ann Vasc Surg.* 2012; 26(1):67–78. [PubMed: 22176876]
7. Cruz CP, Eidt JF, Capps C, et al. Major lower extremity amputations at a Veterans Affairs hospital. *Am J Surg.* 2003; 186(5):449–54. [PubMed: 14599605]
8. Faglia E, Clerici G, Caminiti M, et al. Mortality after major amputation in diabetic patients with critical limb ischemia who did and did not undergo previous peripheral revascularization Data of a cohort study of 564 consecutive diabetic patients. *J Diabetes Complications.* 2010; 24(4):265–9. [PubMed: 19328013]
9. Nelson MT, Greenblatt DY, Soma G, et al. Preoperative factors predict mortality after major lower-extremity amputation. *Surgery.* 2012; 152(4):685–94. discussion 694–6. [PubMed: 23021137]
10. Karam J, Shepard A, Rubinfeld I. Predictors of operative mortality following major lower extremity amputations using the National Surgical Quality Improvement Program public use data. *J Vasc Surg.* 2013; 58(5):1276–82. [PubMed: 23830311]
11. Malone M, Lau NS, White J, et al. The effect of diabetes mellitus on costs and length of stay in patients with peripheral arterial disease undergoing vascular surgery. *Eur J Vasc Endovasc Surg.* 2014; 48(4):447–51. [PubMed: 25116276]
12. Roden DM, Pulley JM, Basford MA, et al. Development of a large-scale de-identified DNA biobank to enable personalized medicine. *Clin Pharmacol Ther.* 2008; 84(3):362–9. [PubMed: 18500243]
13. Zayed M, Bech F, Hernandez-Boussard T. National review of factors influencing disparities and types of major lower extremity amputations. *Ann Vasc Surg.* 2014; 28(5):1157–65. [PubMed: 24365081]
14. Wise ES, Ladner TR, Song J, et al. Race as a predictor of delay from diagnosis to endarterectomy in clinically significant carotid stenosis. *Journal of Vascular Surgery.* 2015:61. In Press.
15. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009; 42(2):377–81. [PubMed: 18929686]
16. Fortington LV, Geertzen JH, van Netten JJ, et al. Short and long term mortality rates after a lower limb amputation. *Eur J Vasc Endovasc Surg.* 2013; 46(1):124–31. [PubMed: 23628328]
17. Stone PA, Flaherty SK, Aburahma AF, et al. Factors affecting perioperative mortality and wound-related complications following major lower extremity amputations. *Ann Vasc Surg.* 2006; 20(2): 209–16. [PubMed: 16586027]
18. Rosen N, Gigi R, Haim A, et al. Mortality and reoperations following lower limb amputations. *Isr Med Assoc J.* 2014; 16(2):83–7. [PubMed: 24645225]
19. Reed AB, Delvecchio C, Giglia JS. Major lower extremity amputation after multiple revascularizations: was it worth it? *Ann Vasc Surg.* 2008; 22(3):335–40. [PubMed: 18466814]
20. Brewer P, Riddell Z, Grimer RJ, et al. Perioperative mortality following above-knee amputations indicated for bone and soft tissue tumours. *Eur J Surg Oncol.* 2012; 38(8):706–10. [PubMed: 22465587]

21. Levi M, Opal SM. Coagulation abnormalities in critically ill patients. *Crit Care*. 2006; 10(4):222. [PubMed: 16879728]
22. Vanderschueren S, De Weerd A, Malbrain M, et al. Thrombocytopenia and prognosis in intensive care. *Crit Care Med*. 2000; 28(6):1871–6. [PubMed: 10890635]
23. O'Brien PJ, Cox MW, Shortell CK, et al. Risk factors for early failure of surgical amputations: an analysis of 8,878 isolated lower extremity amputation procedures. *J Am Coll Surg*. 2013; 216(4): 836–42. discussion 842–4. [PubMed: 23521969]
24. Feinglass J, Pearce WH, Martin GJ, et al. Postoperative and late survival outcomes after major amputation: findings from the Department of Veterans Affairs National Surgical Quality Improvement Program. *Surgery*. 2001; 130(1):21–9. [PubMed: 11436008]
25. Mullen JL, Gertner MH, Buzby GP, et al. Implications of malnutrition in the surgical patient. *Arch Surg*. 1979; 114(2):121–5. [PubMed: 106804]
26. Vogel TR, Petroski GF, Kruse RL. Impact of amputation level and comorbidities on functional status of nursing home residents after lower extremity amputation. *J Vasc Surg*. 2014; 59(5):1323–30. e1. [PubMed: 24406089]
27. Ambler GK, Brooks DE, Al Zuhir N, et al. Effect of frailty on short- and mid-term outcomes in vascular surgical patients. *Br J Surg*. 2015
28. Visser L, Prent A, van der Laan MJ, et al. Predicting postoperative delirium after vascular surgical procedures. *J Vasc Surg*. 2015
29. Curran T, Zhang JQ, Lo RC, et al. Risk factors and indications for readmission after lower extremity amputation in the American College of Surgeons National Surgical Quality Improvement Program. *J Vasc Surg*. 2014; 60(5):1315–24. [PubMed: 24985536]

Table I

AKA recipient baseline characteristics, all patients

Pre-operative Variable	<i>n</i>	Number (%), or Mean ± Standard Deviation
Demographics:		
Male Gender	295	176 (60)
African-American	295	52 (18)
Age (yrs)	291	58 ± 18
Body-Mass Index (kg/m ²)	199	28 ± 9
Etiology:		
Trauma	295	43 (15)
Burn	295	13 (4)
Malignancy	295	33 (11)
Vascular History:		
Prior Revascularization Attempt	292	90 (31)
Prior Amputation (any), AKA side	293	83 (28)
Prior BKA-Level Amputation, AKA side	293	61 (21)
Prior Amputation (any level), contralateral side	295	35 (12)
Prior Contralateral BKA/AKA	295	29 (10)
Lifestyle Factors:		
Smoking Status:		
Previous Smoker	277	71 (26)
Current Smoker	277	103 (37)
Functional Status:		
Fully Independent	274	163 (59)
Partially Dependent	274	52 (19)
Dependent	274	59 (22)
Residence:		
Assisted Living	275	38 (14)
Non-Assisted Living	275	237 (86)
Comorbidities:		
Ischemic Heart Disease	295	106 (36)
Congestive Heart Failure	295	73 (25)
Chronic Pulmonary Disease	295	40 (14)
Diabetes Mellitus	295	109 (37)
Peripheral Arterial Disease	295	117 (40)
Septic Shock	295	11 (4)
Dialysis Use or Dependence	295	30 (10)
Laboratory Values:		
Blood Urea Nitrogen (mg/dL)	213	21 ± 14
Platelets (10 ⁶ /mL)	260	286 ± 141
International Normalized Ratio	249	1.3 ± 0.6

Pre-operative Variable	<i>n</i>	Number (%), or Mean ± Standard Deviation
White Blood Cells (10 ⁶ /mL)	255	12.1 ± 6.7
Albumin (g/dL)	128	2.9 ± 0.8
Packed Cell Volume (%)	276	31.8 ± 6.0
<i>Other Factors:</i>		
Guillotine Amputation	288	53 (18)
Steroid Use	295	17 (6)
<i>Outcome Measures:</i>		
30-day Mortality	295	26 (9)
LOS, Discharged Patients (days)	269	9.3 ± 12.9

n- number of patients considered in analysis; *AKA*- above-knee amputation; *BKA*- below-knee amputation; *LOS*, length of stay

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table II

Bivariate analysis of pre-operative factors associated with 30-day mortality, all patients

Pre-operative Variable*	Mortality Rate (with variable)	Mortality Rate (without variable)	P	OR (95% CI)
Demographics:				
Male Gender	16/176	10/119	.84	1.1 (0.48, 2.5)
African-American	3/52	23/243	.39	0.59 (0.17, 2.0)
Age > 60 yrs	16/147	10/144	.24	1.6 (0.72, 3.7)
Body-Mass Index > 27.5 kg/m ²	7/85	9/114	.93	1.0 (0.37, 2.9)
Etiology:				
Trauma	7/43	19/252	.06	2.4 (0.94, 6.1)
Burn	1/13	25/282	.88	0.86 (0.11, 6.9)
Malignancy	0/33	26/262	.06	0.13 (0.008, 2.2)
Vascular History:				
Prior Revascularization Attempt	8/90	18/202	.99	1.0 (0.42, 2.4)
Prior Amputation (any), AKA side	6/83	19/210	.92	0.78 (0.30, 2.0)
Prior BKA-Level Amputation, AKA side	4/61	21/232	.53	0.71 (0.23, 2.1)
Prior Amputation (any level), contralateral side	5/35	21/260	.22	1.9 (0.67, 5.4)
Prior Contralateral BKA/AKA	4/29	22/266	.32	1.8 (0.56, 5.6)
Lifestyle Factors:				
Smoking Status:				
Previous Smoker	9/71	17/206	.27	1.6 (0.68, 3.8)
Current Smoker	4/103	22/174	.02	0.28 (0.09, 0.83)
Functional Status:				
Fully Independent	17/163	5/111	.08	2.5 (0.88, 6.9)
Partially Dependent	1/52	21/222	.07	0.19 (0.03, 1.4)
Dependent	4/59	18/215	.69	0.80 (0.26, 2.5)
Residence:				
Assisted Living	1/38	19/237	.24	0.31 (0.04, 2.4)
Non-Assisted Living	19/237	1/38	.24	3.2 (0.42, 24.8)
Comorbidities:				
Ischemic Heart Disease	10/106	16/189	.78	1.1 (0.49, 2.6)
Congestive Heart Failure	10/73	16/222	.09	2.0 (0.88, 4.7)
Chronic Pulmonary Disease	3/40	23/255	.75	0.82 (0.23, 2.9)
Diabetes Mellitus	8/109	18/186	.49	0.74 (0.31, 1.8)
Peripheral Arterial Disease	10/117	16/178	.90	0.95 (0.41, 2.2)
Septic Shock	4/11	22/284	.001	6.8 (1.8, 25.1)
Dialysis Use or Dependence	4/30	22/265	.36	1.7 (.54, 5.3)
Laboratory Values:				

Pre-operative Variable *	Mortality Rate (with variable)	Mortality Rate (without variable)	<i>P</i>	OR (95% CI)
Blood Urea Nitrogen > 30 mg/dL	7/52	15/161	.39	1.5 (0.58, 3.9)
Platelets < 250 ×10 ⁶ /mL	20/110	5/150	<.001	6.4 (2.3, 17.8)
International Normalized Ratio > 1.3	17/111	7/139	.006	3.4 (1.4, 8.6)
White Blood Cells >12 ×10 ⁶ /mL	12/93	13/162	.21	1.7 (0.75, 3.9)
Albumin < 2.2 g/dL	8/31	7/97	.005	4.5 (1.5, 13.6)
Packed Cell Volume < 31%	14/115	11/161	.12	1.9 (0.82, 4.3)
Other Factors:				
Guillotine Amputation	10/53	15/235	.004	3.4 (1.4, 8.1)
Steroid Use	4/17	22/278	.03	3.6 (1.1, 11.9)

n, number of patients considered in analysis; *OR*, odds ratio; *CI*, confidence interval

* Continuous variables have been dichotomized

Table III

Bivariate analysis of factors associated with post-operative length of stay, all patients

Pre-operative Variable*	n	P	B (days)	95% CI (days)
Demographics:				
Male Gender	269	.93	0.13	-3.0, 3.3
African-American	269	.21	2.6	-1.4, 6.6
Age > 60 yrs	265	.12	-2.5	-5.6, 0.64
Body-Mass Index > 27.5 kg/m ²	183	.93	-0.20	-4.5, 4.1
Contribution to Etiology:				
Trauma	269	.05	4.5	0.04, 9.0
Burn	269	<.001	19.4	12.3, 26.5
Malignancy	269	.02	-5.7	-10.3, -0.99
Vascular History:				
Prior Revascularization Attempt	266	.61	-0.88	-4.3, 2.5
Prior Amputation (any), AKA side	268	.46	1.3	-2.1, 4.7
Prior BKA-Level Amputation, AKA side	268	.27	2.1	-1.6, 5.9
Prior Amputation (any level), contralateral side	269	.82	2.3	-2.6, 7.2
Prior Contralateral BKA/AKA	269	.22	3.3	-2.0, 8.6
Lifestyle Factors:				
Smoking Status:				
Previous Smoker	257	.60	1.0	-2.7, 4.7
Current Smoker	257	.91	-0.20	-3.5, 3.1
Functional Status:				
Fully Independent	252	.007	4.6	1.3, 7.9
Partially Dependent	252	.03	-4.4	-8.4, -0.34
Dependent	252	.24	-2.4	-6.4, 1.6
Residence:				
Assisted Living	255	.11	-3.8	-8.3, 0.84
Non-Assisted Living	255	.11	3.8	-0.84, 8.3
Comorbidities:				
Ischemic Heart Disease	269	.22	-2.0	-5.3, 1.2
Congestive Heart Failure	295	.20	-2.4	-6.0, 1.2
Chronic Pulmonary Disease	269	.76	-0.71	-5.2, 3.8
Diabetes Mellitus	269	.34	1.5	-1.6, 4.7
Peripheral Arterial Disease	269	.27	-1.8	-4.9, 1.4
Septic Shock	269	.68	2.0	-7.6, 11.8
Dialysis Use or	269	.74	0.87	04.4, 6.1

Pre-operative Variable*	<i>n</i>	<i>P</i>	B (days)	95% CI (days)
Dependence				
Laboratory Values:				
Blood Urea Nitrogen > 30 mg/dL	191	.38	1.9	-2.4, 6.2
Platelets < 250 ×10 ⁶ /mL	235	.48	1.3	-2.3, 4.9
International Normalized Ratio > 1.3	225	.18	2.1	-0.92, 5.0
White Blood Cells >12 ×10 ⁶ /mL	230	<.001	7.7	4.1, 11.3
Albumin < 2.2 g/dL	113	.13	4.0	-1.2, 9.1
Packed Cell Volume < 31%	276	.16	2.1	-0.82, 5.0
Other Factors:				
Guillotine Amputation	263	<.001	10.0	5.9, 14.1
Steroid Use	269	.96	0.18	-7.0, 7.4

n, number of patients considered in analysis; *CI*, confidence interval

* Continuous variables have been dichotomized

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table IV

Multivariate analysis for independent association with 30-day mortality and length of stay, all patients

Pre-operative Variable*	30-day mortality [†]		Length of Stay [‡]	
	P	OR (95% CI)	P	B (95% CI)(days)
Traumatic Etiology	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
Burn Etiology	–	–	<.001	15.8 (8.4, 23.2)
Malignant Etiology	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
Current Smoker	<i>ns</i>	<i>ns</i>	–	–
Fully Independent	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
Partially Dependent	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
Congestive Heart Failure	<i>ns</i>	<i>ns</i>	–	–
Septic Shock	.02	5.1 (1.2, 20.2)	–	–
Platelets < 250 ×10 ⁶ /mL	<.001	6.1 (2.3, 19)	–	–
INR > 1.3	<i>ns</i>	<i>ns</i>	–	–
WBC > 12 ×10 ⁶ /mL	–	–	<.001	6.2 (2.7, 9.7)
Guillotine Amputation	<i>ns</i>	<i>ns</i>	<.001	7.6 (3.3, 12)
Steroid Use	<i>ns</i>	<i>ns</i>	–	–

INR, international normalized ratio; WBC, white blood cells; OR, odds ratio; CI, confidence interval; *ns*, not significant

* Continuous variables have been dichotomized;

[†] n = 260, multivariate stepwise logistic regression; constant = 3.5, Chi-square = 21.1, $r^2 = .13$, $P < .001$;

[‡] n = 225 patients, multivariate stepwise linear regression; constant = 5.6 days, $r^2 = 0.19$, $F = 17.7$, $P < .001$

Table V

Comparison of AKA patient demographics, by class of etiology

Pre-operative Variable *	<i>Non-Trauma/Burn/ Malignant subgroup</i>	<i>Trauma/Burn/ Malignant Etiologies</i>	<i>P *</i>
Male Gender	56% (116/206)	67% (60/89)	.07
African-American	22% (45/206)	8% (7/89)	.004
Age	61.9 ± 14.9	49.8 ± 20.6	<.001
Body-Mass Index (kg/m ²)	28 ± 8	28 ± 10	.70
30-day Mortality	9% (18/206)	9% (8/89)	.94
LOS, Discharged Patients (days)	8.2 ± 11.9	11.8 ± 15.0	.04

LOS, length of stay

* Categorical variables, expressed as percentages (fractions), were analyzed via Pearson chi-squared test; continuous variables, expressed as mean ± standard deviation, were analyzed using unpaired Student *t*-test

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table VI

Bivariate analysis of preoperative factors associated with 30-day mortality and length of stay, subgroup

Pre-operative Variable *	30-day Mortality			Length of Stay		
	<i>n</i>	<i>P</i>	OR (95% CI)	<i>n</i>	<i>P</i>	B (95% CI)(days)
Demographics:						
Male Gender	206	.57	0.76 (0.29, 2.0)	188	.91	-0.2 (-3.6, 3.2)
African-American	206	.25	0.42 (0.09, 1.9)	188	.02	4.9 (0.92, 8.8)
Age > 60 yrs	206	.18	2.1 (0.70, 6.0)	188	.64	-0.81 (-4.2, 2.6)
Body-Mass Index > 27.5 kg/m ²	206	.61	0.74 (0.24, 2.3)	138	.83	0.50 (-3.9, 4.9)
Vascular History:						
Prior Revascularization Attempt	204	.97	0.99 (0.37, 2.7)	186	.72	0.65 (-2.8, 4.1)
Prior Amputation (any), AKA side	204	.50	0.68 (0.26, 1.8)	187	.27	2.1 (-1.6, 5.7)
Prior BKA-Level Amputation, AKA side	204	.33	0.48 (0.10, 2.2)	187	.14	3.1 (-0.95, 7.2)
Prior Amputation (any level), contralateral side	206	.34	1.8 (0.54, 5.8)	188	.64	1.2 (-3.7, 6.0)
Prior Contralateral BKA/AKA	206	.49	1.6 (0.42, 6.0)	188	.49	1.9 (-3.5, 7.2)
Lifestyle Factors:						
Smoking Status:						
Previous Smoker	199	.09	2.4 (0.86, 6.4)	182	.27	2.2 (-1.7, 6.1)
Current Smoker	199	.052	0.30 (0.08, 1.1)	182	.12	-2.8 (-6.3, 0.71)
Functional Status:						
Fully Independent	193	.04	3.3 (1.0, 10.7)	177	.07	3.3 (-0.3, 6.8)
Partially Dependent	193	.10	0.21 (0.03, 1.6)	177	.12	-3.3 (-7.4, 0.84)
Dependent	193	.42	0.59 (0.16, 2.1)	177	.62	-1.0 (-5.0, 3.0)
Residence:						
Assisted Living	195	.17	0.26 (0.03, 2.1)	179	.23	-2.7 (-7.1, 1.7)
Non-Assisted Living	195	.17	3.8 (0.48, 29.6)	179	.23	2.7 (-1.7, 7.1)
Comorbidities:						
Ischemic Heart Disease	206	.88	1.1 (0.41, 2.9)	188	.96	-0.08 (-3.5, 3.3)
Congestive Heart Failure	206	.12	2.1 (0.81, 5.6)	188	.45	-1.4 (-5.0, 2.2)
Chronic Pulmonary Disease	206	.84	1.1 (0.31, 4.2)	188	.97	-0.09 (-4.8, 4.6)
Diabetes Mellitus	206	.52	0.72 (0.27, 1.9)	188	.08	3.0 (-0.37, 6.3)
Peripheral Arterial Disease	206	.82	1.1 (0.42, 2.9)	188	.85	0.31 (-3.1, 3.7)
Septic Shock	206	<.001	8.7 (2.2, 34.4)	188	.56	2.9 (-6.7, 12.4)
Dialysis Use or Dependence	206	.88	1.2 (0.34, 4.6)	188	.39	2.2 (-2.7, 7.0)
Laboratory Values:						

Pre-operative Variable*	30-day Mortality			Length of Stay		
	<i>n</i>	<i>P</i>	OR (95% CI)	<i>n</i>	<i>P</i>	B (95% CI)(days)
Blood Urea Nitrogen > 30 mg/dL	160	.73	1.2 (0.40, 3.7)	144	.38	2.2 (-2.7, 7.0)
Platelets < 250 ×10 ⁶ /mL	180	<.001	10.3 (2.8, 37.6)	163	.51	-1.4 (-5.5, 2.7)
International Normalized Ratio > 1.3	185	.04	3.0 (1.0, 8.7)	167	.24	2.2 (-1.4, 5.7)
White Blood Cells >12 ×10 ⁶ /mL	176	.29	1.7 (0.63, 4.7)	159	<.001	5.2 (1.1, 9.2)
Albumin < 2.2 g/dL	94	.01	4.5 (1.3, 15.8)	82	.96	0.18 (-6.8, 7.1)
Packed Cell Volume < 31%	202	.04	2.8 (1.0, 7.6)	184	.53	1.1 (-2.4, 4.7)
Other Factors:						
Guillotine Amputation	200	.052	3.2 (0.94, 11.0)	183	.14	4.6 (-1.5, 10.7)
Steroid Use	206	.11	2.9 (0.74, 11.6)	188	.68	1.5 (-5.4, 8.3)

n, number of patients considered in analysis; *OR*, odds ratio; *CI*, confidence interval; *AKA*, above-knee amputation; *BKA*, below-knee amputation

* Continuous variables have been dichotomized

Table VII

Multivariate analysis for independent association with 30-day mortality and length of stay, subgroup

Pre-operative Variable*	30-day mortality [†]		Length of Stay [‡]	
	P	OR (95% CI)	P	(95% CI)(days)
African-American race	-	-	ns	ns
Previous Smoker	ns	ns	-	-
Current Smoker	ns	ns	-	-
Fully Independent	ns	ns	ns	ns
Partially Dependent	ns	ns	-	-
Diabetes Mellitus	-	-	ns	ns
Septic Shock	ns	ns	-	-
Platelets < 250 ×10 ⁶ /mL	<.001	10.2 (2.9, 45.9)	-	-
INR > 1.3	ns	ns	-	-
WBC > 12 ×10 ⁶ /mL	-	-	.01	5.2 (1.1, 9.3)
PCV < 31%	ns	ns	-	-
Guillotine amputation	ns	ns	-	-

INR, international normalized ratio; WBC, white blood cells; PCV, packed cell volume; OR, odds ratio; CI, confidence interval; ns, not significant

* Continuous variables have been dichotomized;

[†] n = 180, multivariate stepwise logistic regression; constant = 3.6, Chi-square = 17.0, R² = .10, P < .001;

[‡] n = 159 patients, multivariate stepwise linear regression; constant = 5.6 days, R² = 0.04, F = 6.2, P = .01