

Mortality and Reoperations following Lower Limb Amputations

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ABSTRACT: **Background:** Above-the-knee amputations (AKA) and below-the-knee amputations (BKA) are commonly indicated in patients with ischemia, extensive tissue loss, or infection. AKA were previously reported to have better wound-healing rates but poorer rehabilitation rates than BKA.

Objectives: To compare the outcomes of AKA and BKA and to identify risk factors for poor outcome following leg amputation.

Methods: This retrospective cohort study comprised 188 consecutive patients (mean age 72 years, range 25–103, 71% males) who underwent 198 amputations (91 AKA, 107 BKA, 10 bilateral procedures) between February 2007 and May 2010. Included were male and female adults who underwent amputations for ischemic, infected or gangrenotic foot. Excluded were patients whose surgery was performed for other indications (trauma, tumors). Mortality and reoperations (wound debridement or need for conversion to a higher level of amputation) were evaluated as outcomes. Patient- and surgery-related risk factors were studied in relation to these primary outcomes.

Results: The risk factors for mortality were dementia [hazard ratio (HR) 2.769], non-ambulatory status preoperatively (HR 2.281), heart failure (HR 2.013) and renal failure (HR 1.87). Resistant bacterial infection (HR 3.083) emerged as a risk factor for reoperation. Neither AKA nor BKA was found to be an independent predictor of mortality or reoperation.

Conclusions: Both AKA and BKA are associated with very high mortality rates. Mortality is most probably related to serious comorbidities (renal and heart disease) and to reduced functional status and dementia. Resistant bacterial infections are associated with high rates of reoperation. The risk factors identified can aid surgeons and patients to better anticipate and possibly prevent severe complications.

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KEY WORDS: below-knee amputation (BKA), above-knee amputation (AKA), reoperation, infection, gangrene, ischemia

ing revascularization efforts, or those with extensive tissue loss or infection [1]. Despite the development and more widespread availability of new diagnostic procedures and peripheral vascular interventions, the rates of amputation and subsequent survival have remained relatively unchanged over the last few decades [2]. Various studies have shown that the main risk factors for lower limb amputations include peripheral vascular disease and diabetes mellitus [3], and that these operations were associated with high rates of postoperative mortality (7%–23%) and morbidity (15%–40%) [4–6].

Wound healing complicates major lower limb amputations and affects the patient's functional outcome and postoperative course. AKA generally have better healing rates and lower reoperation rates compared to BKA [5–8]. On the other hand, several studies have demonstrated that the higher the level of amputation, the lower the chances of the patient to successfully undergo rehabilitation [9–11]. Choosing the optimal level of amputation for each patient is therefore of major importance, and correct decisions can potentially obviate untoward sequelae such as unnecessary procedures and complications. This study was designed to identify the risk factors for mortality and major complications following lower limb amputations, and to compare them between AKA and BKA.

PATIENTS AND METHODS

Following institutional review board approval for the study, a list of 289 patients who underwent AKA or BKA in our institution between February 2007 and May 2010 was generated from our medical center's database. Inclusion criteria were adults of both genders who underwent amputations for ischemic, infected or gangrenotic foot. Exclusion criteria were patients whose surgery was performed for other indications (such as trauma and tumors).

The level of primary amputation was decided by the surgeon after consulting with the patient. AKA was performed when tissue ischemia or infection proximal to the BKA level was evident and in those patients with severe knee flexion contracture who were non-ambulatory. BKA was also performed in some patients who refused to undergo AKA against

AKA = above-knee amputations
BKA = below-knee amputations

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Above-knee amputations and below-knee amputations are usually performed in patients with failed attempts at revascularization, comorbidities or anatomic factors preclud-

the surgeon's advice. Data on reoperations were collected from medical charts, and data on mortality were retrieved from the national registry. The collected demographic and medical data of patients included age, gender, smoking habits, diabetes mellitus (treated orally or by insulin, or leading to organ failure), PVD (mild, severe, or after vascular intervention), ischemic heart disease (mild, severe, or post-cardiac intervention), congestive heart failure, chronic renal failure (mild, severe, or end-stage renal disease) dementia, ambulatory status (ambulatory, chair-bound or bedridden), infectious status (no evidence of infection, simple bacteria or resistant bacteria), and previous amputation (same or contralateral leg). The recorded surgery-related data included the side and level of amputation, the surgeon's seniority, and selected laboratory results (white blood cell count, blood hemoglobin concentration, albumin, C-reactive protein, creatinine) during the immediate preoperative period.

The outcomes chosen for analysis were mortality at 30 days and at 1 year, reoperation within 60 days (either debridement or re-amputation), as well as any postoperative complications including wound discharge, infection (urinary, pulmonary, or wound), renal failure, or cardiovascular complications.

STATISTICAL ANALYSIS

Patients undergoing AKA and BKA amputations were compared using the χ^2 analysis for categorical variables and the two-sample *t*-test for continuous variables. The mixed model was used for continuous parameters and GLIM for binary variables when comparing surgery-related outcomes to enable the inclusion of more than one surgery per patient. Multivariate linear logistic regression was used to model the probability for reoperation and mortality. Three model-building methods were used: forced entry, forward selection, and backward elimination. The following parameters were included in the 60 day revision analysis: type of surgery, gender, age, smoking, DM, PVD, IHD, CHF, CRF, dementia, resistant bacterial infection, preoperative WBC data count, lymphocyte count $< 1500 \times 10^3/\text{ml}$, time from admission to surgery, surgeon seniority, and main indication for surgery. The following parameters were included in the 30 day mortality analysis: type of surgery, gender, age, smoking, DM, PVD, IHD, CHF, CRF, dementia, resistant bacterial infection, preoperative WBC count, lymphocyte count, preoperative hemoglobin count, time from admission to surgery, main indication for surgery, and preoperative ambulatory status. The Kaplan-Meier method was used to estimate the survival and time to revision for each study group, and the log-rank test was performed to compare between the two. Survival analysis

PVD = peripheral vascular disease
DM = diabetes mellitus
IHD = ischemic heart disease
CHF = congestive heart failure
CRF = chronic renal failure
WBC = white blood cell count

using the Cox proportional hazards model was employed to study the independent effect of the different parameters on the risk for mortality and need for revision surgery. Data for the last surgery only were included in the analysis of patients who underwent more than one amputation. All statistical analyses were performed by SAS for Windows 9.2. A result with a value of $P \leq 0.05$ was considered statistically significant.

RESULTS

A total of 198 amputations (91 AKA, 107 BKA, 10 bilateral) were performed in 188 patients (mean age 72 years, range 25–103, 71% males). The mean follow-up period was 27.2 months (range 8–46 months). The two patient groups differed in a number of parameters. Patients in the AKA group were older than those in the BKA group (77 years compared to 69 years, $P = 0.039$), they were more often demented (29.7% vs. 17.8%, $P = 0.03$), more were females (36.1% vs. 23.8%, $P = 0.049$), fewer had DM (16.8% vs. 51.8%, $P < 0.0001$), they had lower baseline creatinine levels (1.73 vs. 2.17, $P = 0.036$), fewer had previous amputations (18.1% vs. 32.7%, $P = 0.0004$), and more were non-ambulatory (53% vs. 34%, $P = 0.02$), respectively. Table 1 presents a summary of the main demographic and preoperative factors.

Mortality was significantly higher at 1 year among patients who underwent AKA compared to BKA (58% vs. 33%, $P = 0.0006$), but not at 30 days (21.7% for AKA vs. 14.9% for BKA, $P = 0.26$). Reoperation rates at 60 days were marginally higher among BKA patients (26.7% vs. 16.9% for AKA patients, $P = 0.114$). A higher level of amputation was more often required for BKA patients (15.8% vs. 3.6% for AKA patients, $P = 0.018$). An AKA was found to be associated with a higher postoperative cardiovascular complication rate (33.7% after AKA vs. 18.8% after BKA, $P = 0.038$) [Table 2].

The univariate analysis was repeated for diabetic patients only, including 46 AKA and 89 BKA patients with a mean age of 71 years. For this patient population, mortality was significantly higher among AKA patients at 1 year but not at 30 days (57% vs. 36%, $P = 0.02$ at 1 year and 20% vs. 14.6% at 30 days). The reoperation rate (60 days), on the other hand, was greater among BKA patients (24.7% vs. 11%, $P = 0.05$).

The risk factors for mortality identified by our findings included dementia (hazards ratio 2.769, $P = 0.0002$ by Cox analysis and odds ratio 3.52, $P = 0.009$ by logistic regression), non-ambulatory status preoperatively (HR 2.281, $P = 0.0025$ by Cox analysis and OR 4.467, $P = 0.0023$ by logistic regression), CHF (HR 2.013, $P = 0.0174$ by Cox analysis and OR 3.95, $P = 0.015$ by logistic regression), and CRF (HR 1.87, $P = 0.0154$ by Cox analysis and OR 4.029, $P = 0.005$ by logistic regression). DM was not identified as an independent risk factor for mortality.

HR = hazards ratio
OR = odds ratio

Table 1. Demographics and comorbidities of above-knee amputation and below-knee amputation patients

	AKA (n=81)*	BKA (n=97)*	P value
Age (yr) (range)	76.9 (40–103)	69.2 (25–91)	0.039
Male gender (%)	63.8	76.2	0.049
Ambulatory status (%)			
Ambulatory	47	66	0.02
Chair-bound	17	12	
Bedridden	36	22	
Dementia (%)	29.7	17.8	0.03
Diabetes mellitus (%)			
Oral treatment	18.1	15.8	<0.0001
Insulin treatment	9.6	11.9	
End-organ failure	20.5	55.5	
Peripheral vascular disease (%)			
Mild	3.6	3	0.31
Severe	35	22.8	
Post-intervention	28.9	36.6	
Cerebrovascular accident (%)	31.3	28.7	0.7
Renal failure (%)			
Mild	13.2	11.9	0.67
Severe	19.3	15.9	
End-stage renal disease	10.8	16.8	
Ischemic heart disease (%)			
Mild	3.6	5	0.52
Post-myocardial infarction	10.8	5.9	
Post-intervention	38.6	45.6	
Smoking (%)	27.7	21.8	0.35
WBC count (x 10 ³ /ml) Mean (range)	16,924 (3900–76,100)	15,179 (4900–30,600)	0.13
Hemoglobin (g/dl) Mean (range)	10.5 (7.5–17.1)	10.43 (6.9–16.4)	0.71
Albumin (g/dl) Mean (range)	28.81 (20–38)	30.14 (18–43)	0.15
C-reactive protein (mg/L) Mean (range)	155.71 (13–380)	153.68 (9–436)	0.9

*Excluding patients with bilateral amputations

Among the AKA patients, 46 were diabetic compared to 45 who were not. The 60 day revision rate (20% in non-diabetics vs. 12% in diabetics) and mortality rates (20% at 30 days and 55% at 1 year in non-diabetic vs. 21% at 30 days and 60% at 1 year) did not differ significantly between diabetic and non-diabetic patients.

Among BKA patients, 89 were diabetic compared to only 18 who were not. The 60 day revision rate (22% in non-diabetics vs. 24% in diabetics) and mortality rates (12.5% at 30 days and 50% at 1 year in non-diabetics vs. 15% at 30 days and 37% at 1 year in diabetics) did not differ significantly between diabetic and non-diabetic patients.

Resistant bacterial infection (HR 3.083, $P = 0.0013$ by Cox analysis and OR 3.186, $P = 0.0047$ by logistic regression), male gender (HR 2.137, $P = 0.03$ by Cox analysis and OR 2.25, $P = 0.06$ by logistic regression) and younger age (HR 1.04, P

Table 2. Reoperation mortality and complications following above-knee amputation and below-knee amputation

	AKA (n=91)	BKA (n=107)	P value
Mortality			
≤ 30 days	21.7	14.9	0.26
1 year	58	33	0.0006
Reoperation at 60 days			
Debridement	12.1	10.3	0.114
Higher level of amputation	3.6	15.8	0.018
Postoperative complications			
Cardiovascular	31.8	17.8	0.038
Renal	8.8	10.3	0.74
Pneumonia	16.5	13	0.425
Urinary tract infection	7.7	10.3	0.58
Wound	28.6	38.3	0.18
Gastrointestinal	19.8	9.4	0.032

All results are given as % of total procedures in that group

Mortality in patients with bilateral amputations is attributed to the first of the two amputations (AKA or BKA)

= 0.018 by Cox analysis and OR 1.026, $P = 0.09$ by logistic regression) were found to be risk factors for revision surgery. The level of amputation was not found to be an independent predictor of either outcome. The Kaplan-Meier and log-rank function showed that BKA patients had better survival ($P < 0.0001$), but there were no significant group differences in the need for revisions ($P = 0.2$) [Figures 1 and 2]. DM was not identified as an independent risk factor for reoperation.

DISCUSSION

Lower extremity amputations are performed in large numbers worldwide. While some studies report a decrease in the number of amputations due to ischemic prevention by vascular interventions [12,13], others claim that lower extremity amputation rates have remained relatively unchanged during the past two decades [14-16].

The 30 day and 1 year mortality rates following lower limb amputations in this study were 16.7% and 44%, respectively. Lim and Angel [17] reported 10% mortality at 30 days that rose to 43% at 1 year following AKA and BKA. Other authors reported an overall survival after BKA and AKA of 83–95% at 30 days, 69–78% at 1 year, and 33% at 5 years [5,18,19]. The overall mortality rates in our study are similar to those of Lim and Angel and higher than other reports. We speculate that these high mortality rates can be partially explained by the fact that this analysis included a subgroup of critically ill patients as well as patients with multiple risk factors. While we found higher mortality rates among AKA patients at 1 year (58% compared to 33% for BKA patients, $P = 0.0006$), the analysis of short-term mortality (30 days) yielded no significant differences between the two patient groups. Nelson and colleagues [5] reported increased mortality rates (12.8% vs. 6.5%) following AKA compared to BKA, but they did not

Figure 1. Mortality following above-knee (blue line) and below-knee (red line) amputation (Kaplan-Meier plot)

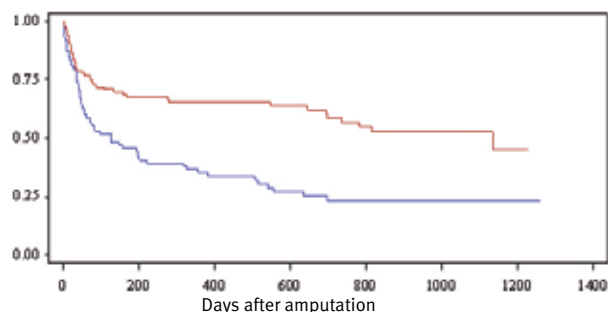
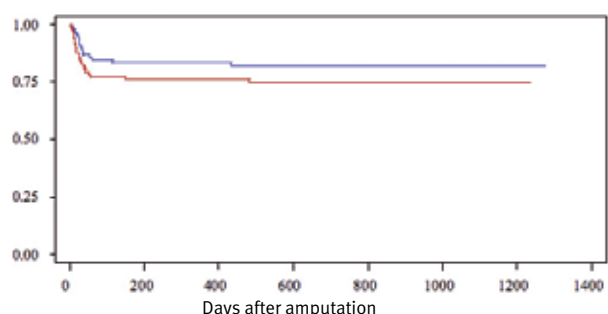


Figure 2. Rate of reoperation following above-knee (blue line) and below-knee (red line) amputation (Kaplan-Meier plot)



perform an analysis to determine if the level of amputation is an independent factor affecting mortality.

We suggest that a short-term analysis showing no significant differences between the two procedures may be more directly connected to the surgical intervention than to the patient's comorbidities, which differed significantly between the two groups [Table 1]. Furthermore, the level of amputation was not found to be a significant factor according to a multivariate analysis model, suggesting that the higher mortality rate among AKA patients was related to confounders and not to the level of limb surgery that had been performed.

The analysis in this study pointed to four risk factors for mortality: dementia (HR 2.8), preoperative non-ambulatory status (HR 2.2), congestive heart failure (HR 2), and chronic renal failure (HR 1.8). These results are in agreement with those of Nehler et al. [19], Mayfiel et al. [20], Belmont et al. [4] and Nelson et al. [5], who also found renal disease, cardiac disease and non-ambulatory status prior to surgery to be risk factors for short-term mortality following amputation. These authors also reported proximal levels of amputation, pulmonary disease, cardiovascular disease, older age, sepsis, use of steroids, thrombocytopenia, and increased international normalized ratio as risk factors for early mortality, but those factors did not significantly contribute to mortality in our cohort.

Previous studies found that BKA are preferable to AKA in terms of improved postoperative rehabilitation, function, and a higher degree of independence in daily living [9,21,22]. Lim and Angel [17] observed that 60% of BKA patients were rehabilitated using a prosthesis as compared to only 29% of AKA patients. They also found no correlation between the initial level of amputation and the risk of developing infection. However, while none of their patients who initially underwent AKA had later required a higher level of amputation, 17.6% of their BKA patients subsequently required an AKA [17]. Our results showed that reoperation rates are marginally higher after BKA compared to AKA (15.7% for AKA vs. 26.1% for BKA, $P = 0.088$). The level of amputation was not a significant contributor to the need for revision, while resistant bacterial infection was and possibly male gender as well. Other studies showed that an AKA heals better than a BKA. Dormandy et al. [8] reported that 70% of AKA heal primarily, compared to 30–92% of BKA. Enroth and Persson [23] reviewed several studies in which primary amputation at more proximal levels was associated with lower rates of morbidity and mortality. Hasanadka et al. [6] and Coulston et al. [7] reported significantly higher rates of wound complications and infections after BKA. Recently, Nelson et al. [5] reported 22.7% reoperations after BKA compared to only 11.7% after AKA in a large cohort of 9368 patients.

Our data analysis revealed that resistant bacterial infection was a significant contributor to reoperation. Resistant bacterial strains are difficult to eradicate and can cause prolonged and persistent infection. In combination with poor tissue perfusion, this condition often requires surgical debridement. We found no previous reports on an association linking gender and type of bacteria with reoperations. Interestingly, Sadat and collaborators [24] reported that a 5 day prophylactic postoperative course of wide-spectrum antibiotic treatment was associated with lower rates of infection, reoperations and hospital stay. Their study included 80 patients and was retrospective. We found that male gender was a significant risk factor for reoperation (Cox analysis) and marginally significant for 60 day revision surgery (logistic regression). We are unable to provide an explanation for these findings. Other factors were previously reported to contribute to wound infection and reoperation, including younger age, smoking, increased body mass index and increased INR [6] as well as the use of suction drains and skin clips [7].

A significantly higher rate of cardiovascular complications after AKA was also found (31% compared to 18% after BKA). These differences could not be explained by the preoperative cardiac state, which was similar for both our groups. Lee and co-authors [25] found six independent predictors of cardiac complications: high risk surgery, history of coronary artery

INR = international normalized ratio

disease, history of CHF, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative creatinine of ≥ 2.0 mg/dl. It is possible that the more extensive tissue loss and blood loss in AKA compared to BKA may be responsible for the increased rates of cardiovascular complication.

Finally, the analysis of diabetic patients alone suggested that AKA are associated with higher mortality (as was demonstrated for the entire cohort) and lower rates of reoperation. These results should be considered with caution, since diabetes mellitus was not proven to be an independent risk factor in our multivariate analysis or in large studies such as those of Nelson et al. [5] and Hasanadka et al. [6].

The present analysis has some limitations. This is a retrospective study and therefore the data are subject to bias. A direct comparison of AKA and BKA patients is not valid since they differ in many aspects. We could not comment on the functional and ambulatory outcomes of the patients but only on major complications and mortality. Even so, since a prospective controlled study to compare AKA and BKA would probably be unethical if not impossible to perform, the results of this analysis can contribute to making better decisions regarding the level of lower limb amputation and the expected outcome.

CONCLUSIONS

Both above-knee and below-knee amputations are associated with very high mortality rates. Mortality can be expected in both the early and the late postoperative periods and is most probably related to serious comorbidities, such as renal and heart disease, as well as reduced functional status and dementia, rather than the level of amputation. Resistant bacterial infections are associated with high rates of reoperation following surgery at both levels. Wound complications are commonly seen after below-knee amputations.

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“Memoir is not an act of history but an act of memory, which is innately corrupt”

Mary Karr (b. 1955), American poet, essayist and memoirist