Ann Vasc Dis Vol. 10, No. 3; 2017; pp 217–222
©2017 Annals of Vascular Diseases
Online August 21, 2017
doi: 10.3400/avd.oa.17-00046

Original Article

A Series of 210 Peripheral Arterial Disease Below-Knee Amputations and Predictors for Subsequent Above-Knee Amputations

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Objective: To review patient characteristics and outcomes after peripheral arterial disease (PAD)-related below-knee amputation (BKA), and identify risk factors predicting subsequent above-knee amputation (AKA).
Materials and Methods: A retrospective study of 210 BKAs between May 2008 and December 2015.
Results: The mean age of the study population was 66 years. Most of the patients had cardiovascular comorbidities, and 33% had end-stage renal failure (ESRF); 89% were American Society of Anesthesiologists 3 or 4. Previous ipsilateral lower-limb minor amputation was present in 49% and previous contralateral lower-limb major amputation was present in 20% patients. Limb salvage revascularization via angioplasty prior to BKA was performed in 73%, while 27% had extensive tissue loss that was not suitable for limb salvage. Postoperatively, 20% had BKA wound infection, with 3% requiring further surgical debridement, and 9% (19 patients) required subsequent AKA within 1 month. Overall survival analysis at 1–5 years was 75%, 66%, 64%, 59%, and 58%, respectively. Multivariate analysis showed ESRF (Odds Ratio [OR]=3.85; p=0.01) and preoperative non-ambulatory status (OR=5.58; p=0.01) to be independent risk factors in predicting for subsequent AKA.
Conclusion: Patients with underlying ESRF or preoperative non-ambulatory status may benefit from direct AKA if major amputation is required.

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Received: May 14, 2017; Accepted: June 28, 2017
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Keywords: below-knee amputation, above-knee amputation, peripheral arterial disease, end-stage renal failure, diabetic foot ulcer

Introduction

Despite current aggressive revascularization and limb salvage management, peripheral arterial disease (PAD) contributes to more than half of all amputations, with trauma as the second leading cause.[1)] The second Trans-Atlantic Inter-Society Consensus Working Group (TASC II) reported an incidence of major amputation as a result of PAD of 12 to 50 per 100,000 individuals a year,[2)] with numbers expected to rise by at least 50% in the next 15 years due to the aging population.[1)]

With diabetes mellitus (DM) being a major risk factor for PAD, and with the prevalence of diabetes steadily increasing worldwide (108 million in 1980 to 422 million in 2014),[3)] major lower-limb amputations are expected to increase correspondingly. This is of concern as such major interventions are often poorly tolerated, particularly in this subgroup of patients with multiple comorbidities.[4)]

Below-knee amputation (BKA) is associated with better rehabilitative success compared with above-knee amputation (AKA) because of preservation of the knee joint.[2)] However, BKA generally has poorer healing rates and higher reoperative rates than AKA. Failure of BKA often necessitates subsequent revision or even AKA.[5–7)] Therefore, it is imperative to determine the optimal level of amputation in each individual patient to avoid unnecessary additional salvage operations as well as associated complications.[8)]

This study aimed to review patient characteristics and outcomes after PAD-related BKA within an Asian population, and identify risk factors predicting subsequent AKA.

Methodology

We conducted a single-institutional retrospective study of 210 patients who underwent BKA for PAD-related tissue loss or sepsis between May 2008 and December 2015 at a tertiary university hospital. Patients whose surgery was performed for other reasons, such as trauma or malignancy, were excluded.

In accordance with internationally accepted clinical guidelines,[9] "major" lower-limb amputation was defined as amputation proximal to the ankle—namely, BKA (also known as trans-tibial amputation) or AKA (also known as trans-femur amputation)—and "minor" lower-limb amputation as amputation distal to the ankle, such as Ray amputation or trans-metatarsal amputation.

Preoperatively, an amputee multidisciplinary meeting comprising vascular surgeons, rehabilitation physicians, physiotherapists, occupational therapists, and prosthetists was conducted to collaboratively decide on the rehabilitation potential of the patient and optimal amputation level. As all the patients had underlying infected foot ulcers, perioperative antibiotics were culture-directed, and ceased on the third postoperative day if the wound was clean with no signs of systemic infection.

All BKAs were performed under regional or general anesthesia using the Burgess posterior-flap technique.[10] Routinely, a size 10 Redivac drain was inserted and removed by the third postoperative day if there was minimal output. There was no routine insertion of nerve sheath catheters. Wound closure was performed in layers with a vertical mattress technique using nonabsorbable sutures, which were routinely removed on postoperative day 14 if there was no surgical site infection.

Early mobilization from the first postoperative day was ensured primarily by the physiotherapists and rehabilitation physicians from the multidisciplinary team. Indication for subsequent conversion to AKA was based on either deep infection at the BKA stump or exposed bone at the BKA stump.

Risk factors investigated to predict subsequent AKA conversion (**Table 1**) included patient demographics, comorbidities, preoperative clinical examination findings, preoperative investigation findings, angioplasty revascularization results, and intraoperative factors.

The primary outcome was the need for subsequent AKA (indicating BKA failure), while secondary outcomes included the need for further surgical debridement, wound infection rates, mean length of hospital stay, and postoperative complications (acute myocardial infarction, cerebrovascular accident, and nosocomial infection), as well as 30-day unplanned readmission and 30-day mortality (**Table 2**).

Table 1 Patient characteristics

	Below-knee amputation (n=210)
Demographics	
Male/Female	134 (64%)/76 (36%)
Chinese/Malay/Indian	152 (72%)/37 (18%)/18 (9%)
Mean age (range)	66 (41–97)
Right/Left leg	120 (57%)/91 (43%)
Comorbidities	
Preoperative non-ambulatory status	46 (22%)
Preoperative ambulatory status	164 (78%)
ASA 2	24 (11%)
ASA 3	157 (75%)
ASA 4	29 (14%)
Smoker	77 (37%)
T2DM	206 (98%)
Good T2DM control (HbA1c <7%)	57 (27%)
Hypertension	190 (90%)
Hyperlipidemia	188 (90%)
Ischemic heart disease	131 (62%)
Previous stroke	56 (27%)
End-stage renal failure	70 (33%)
Previous ipsilateral minor amputation	103 (49%)
Previous contralateral major amputation	42 (20%)
On examination	
Septic shock	9 (4%)
Absent popliteal pulse	107 (51%)
Ulceration	153 (73%)
Wet gangrene	97 (46%)
Investigations	
Raised white cell count ($>10\times10^9$/L)	185 (88%)
Anemia ($<12\times10^{12}$/L)	188 (90%)
Low serum albumin (<35 g/L)	206 (98%)
Radiographic osteomyelitis	53 (25%)
Arterial duplex TASC A	0 (0%)
Arterial duplex TASC B	21 (10%)
Arterial duplex TASC C	109 (52%)
Arterial duplex TASC D	80 (38%)
Toe pressure <50 mmHg	206 (98%)
Angioplasty revascularization	**153/210 (73%)**
Patent iliac artery post-angioplasty	153/153 (100%)
Patent superficial femoral artery	152/153 (99%)
Patent popliteal artery	147/153 (96%)
Patent anterior tibial artery	83/153 (54%)
Patent peroneal artery	110/153 (72%)
Patent posterior tibial artery	78/153 (51%)
Surgery	
GA: RA	59 (28%): 147 (70%)
Mean operative time in minutes (range)	95 (45–195)

ASA: American Society of Anesthesiologists; GA: general anesthesia; RA: regional anesthesia; T2DM: type 2 diabetes mellitus; TASC: Trans-Atlantic Inter-Society Consensus

Investigated factors were analyzed using descriptive statistics. Percentages were used for categorical data and means with standard deviations (SD) for continuous data. Univariate analysis was performed using the two-tailed Fisher's exact test (bivariate analysis) for categorical variables and Student's t-test for continuous variables to identify risk factors associated with BKA failure. Factors achieving a p-value ≤ 0.05 were considered of statistical significance. Factors achieving a p-value ≤ 0.10 were then subsequently selected for multiple logistic regression analysis to identify independent risk factors associated with BKA failure. Odds ratios (ORs) and their 95% confidence

Table 2 Outcomes after below-knee amputation

	Below-knee amputation (n=210)
Further surgery	
Surgical debridement	7 (3%)
Above-knee amputation	19 (9%)
Postoperative complications	
Wound infection	43 (20%)
Mean length of stay (days)	52 (6–303)
Acute myocardial infarction	25 (12%)
Stroke	3 (1%)
Nosocomial infection	42 (20%)
30-day unplanned readmission	42 (20%)
30-day mortality	11 (5%)

intervals (CIs) were calculated. A p-value ≤0.05 was considered statistically significant in the multivariate analysis. Comparison between Kaplan–Meier survival analysis was evaluated with a log-rank test. All data analysis was performed using IBM SPSS Statistics for Windows, Version 21.0 (Armonk, NY, USA).

Results

Two hundred ten BKAs were performed between May 2008 and December 2015 (**Table 1**). Within the study population, 64% were male, mean age was 66 years, and 57% of patients underwent BKA of the right leg. The ethnic composition of the study population was 72% Chinese, 18% Malay, and 9% Indian, similar to that of the general Singapore population.

Most of the patients had cardiovascular comorbidities, with 98% having underlying type 2 diabetes mellitus (T2DM) and only 27% having good diabetic control with HbA1c <7%. Additionally, hypertension was present in 90% of patients, hyperlipidemia in 90%, end-stage renal failure (ESRF) in 33%, and ischemic heart disease in 62%; and 37% were chronic smokers. The majority (89%) of patients were either ASA 3 (75%) or ASA 4 (14%), reflecting the high operative risk of the study population. Previous ipsilateral lower-limb minor amputation was present in 49% and previous contralateral major amputation was present in 20% patients.

On presentation, 51% of patients had clinically absent popliteal pulse. BKA was performed in the presence of septic shock in 4%. Most of the BKAs (73%) were performed in the setting of ulceration and 46% in the presence of wet gangrene. Tissue loss extending beyond the midfoot that precluded any reasonable limb salvage attempts was present in 27%.

Laboratory investigation findings revealed ongoing infection in the majority of patients, with 88% having a raised white cell count of $>10\times10^9$/L, 99% having elevated C-reactive protein of >5 mg/L, and 100% having elevated procalcitonin of >0.05 ng/mL. Anemia with hemoglobin levels of less than 12 and 11 g/dL in male and female patients, respectively, was present in 90%, and a toe pressure of <50 mmHg was present in 98% of patients. Radiographically proven osteomyelitis within the phalanges, metatarsals, or tarsal bones was present in 25%. Preoperative arterial investigations revealed 52% of patients with TASC C and 38% with TASC D PAD patterns.

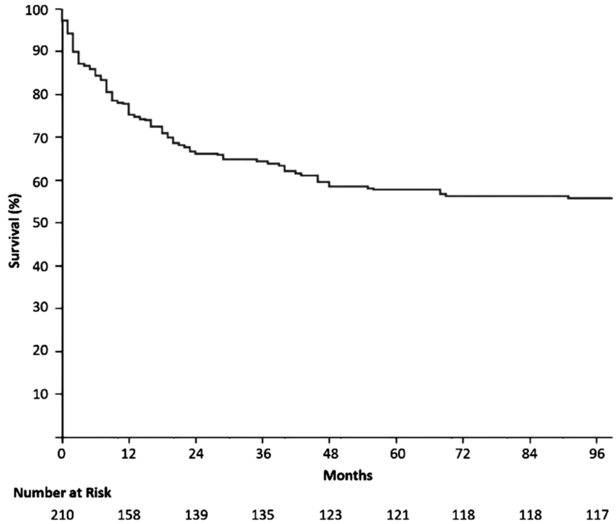

Fig. 1 Overall survival analysis of patients post-BKA.

Limb salvage with revascularization via percutaneous transluminal angioplasty was attempted in 73% of patients. Of those who underwent angioplasty, 99% had a patent superficial femoral artery and 96% had a patent popliteal artery after revascularization.

BKA was performed under regional anesthesia in 70% of cases, with a mean operative duration of 95 min. Postoperatively, 43 patients (20%) had BKA wound infection with 7 (3%) requiring further surgical debridement and 19 (9%) requiring subsequent AKA (**Table 2**). The mean length of hospital stay varied widely with a mean of 52 days (6 to 303 days). The 30-day unplanned readmission rate was 20%, and the 30-day mortality was 5%. Overall survival analysis at 1 to 5 years was 75%, 66%, 64%, 59%, and 58%, respectively (**Fig. 1**).

Univariate analysis between patients with BKA and those who needed subsequent AKA showed that factors that predict for BKA failure included ESRF (p=0.008) and preoperative non-ambulatory status (p=0.001) (**Table 3**). Relevant negatives included age (p=0.527), diabetic control (p=0.173), presence of popliteal pulse clinically (p=0.102), toe pressure <50 mmHg (p=1.000), and post-angiogram patent popliteal pulse (p=0.406). Multivariate analysis revealed ESRF (OR=5.58; p=0.01) and preoperative non-ambulatory status (OR=3.85; p=0.01) to be independent predictors for BKA failure.

Table 3 Univariate and multivariate analyses of risk factors predicting BKA failure

	BKA failure (n=19, 9%)	BKA success (n=191, 91%)	Univariate analysis (Fisher's p-value)	Multivariate analysis (odds ratio; p-value)
Demographics				
Male	9 (47%)	125 (65%)	0.137	—
Mean age	65	67	0.527*	—
Comorbidities				
Smoker	6 (32%)	71 (37%)	0.804	—
Preoperative non-ambulatory status	11 (58%)	35 (18%)	**0.001**	**OR=5.58; p=0.01**
Type 2 diabetes mellitus	19 (100%)	187 (98%)	1.000	—
Good T2DM control (HbA1c <7%)	8 (42%)	49 (26%)	0.173	—
Ischemic heart disease	13 (68%)	118 (62%)	0.627	—
End-stage renal failure	12 (63%)	58 (30%)	**0.001**	**OR=3.85; p=0.01**
Previous ipsilateral minor amputation	11 (58%)	92 (48%)	0.336	—
Previous contralateral major amputation	5 (26%)	37 (19%)	0.546	—
On examination				
Septic shock	2 (11%)	7 (4%)	0.190	—
Absent popliteal pulse	14 (73%)	94 (59%)	0.102	—
Wet gangrene	8 (42%)	89 (47%)	0.811	—
Investigations				
Anemia	17 (89%)	171 (90%)	1.000	—
Hypoalbuminemia	19 (100%)	187 (98%)	1.000	—
Radiographic osteomyelitis	3 (16%)	50 (26%)	0.414	—
Toe pressure <50 mmHg	19 (100%)	185 (97%)	1.000	—
Angioplasty revascularization				
Patent iliac post-angioplasty	12/12 (100%)	135/135 (100%)	1.000	—
Patent superficial femoral artery	11/12 (92%)	133/135 (99%)	0.227	—
Patent popliteal artery	11/12 (92%)	130/135 (96%)	0.406	—
Surgery				
General anesthesia	6 (32%)	53 (28%)	0.598	—
Mean operative time in minutes	84	96	0.129*	—

* Student's t-test

Subgroup survival analyses of ESRF patients and non-ESRF patients showed that those with ESRF had higher mortality rates compared with those without ($p=0.0371$) (**Fig. 2**). Survival analysis at 1 to 5 years was 60%, 49%, 49%, 44%, and 43%, respectively, in ESRF patients compared with 79%, 71%, 68%, 61%, and 61%, respectively, in non-ESRF patients.

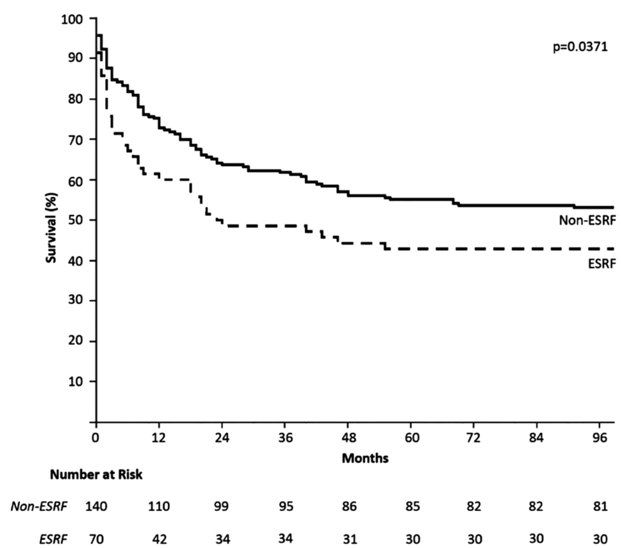

Fig. 2 Survival analysis of patients with ESRF and without ESRF.

Discussion

This is the largest single-center series of BKA from an Asian institution. Almost all (98%) our study population had underlying diabetes and 73% had poor glycemic control defined as elevated HbA1c of >7%. Poor diabetic control with high HbA1c has been shown to be a risk factor for PAD[11] and major limb amputation.[12] The percentage of BKA patients with diabetes in our study is higher than that reported in Western countries, which ranges from 63% to 83%.[13–17] Similar rates are however observed in other Asian institutions, with the proportion of diabetic patients being 94%.[18] This is expected as diabetes is a disease more prevalent in Asians.[19]

Our BKA failure rate of 9% is similar to that reported in the literature, which ranges from 9% to 16%.[2,8,13,14,17,20,21] In a large retrospective analysis of 8878 patients within the American NSQIP registry, O'Brien et al. identified emergency operations, transmetatarsal amputations, sepsis and septic shock, ESRF, systemic inflammatory response syndrome, intraoperative surgical trainee participation, obesity, and smoking as risk factors for early failure of surgical amputations.[16] Within our study cohort, multivariate analysis revealed preoperative non-ambulatory status and ESRF to be independent predictors for BKA failure. A retrospective cohort study conducted by Rosen et al. revealed similar risk factors for mortality: preoperative non-ambulatory status, chronic renal failure, congestive heart failure, and dementia.[8] These results are further substantiated by other studies that report similar risk factors.[5,17,22]

ESRF is a well-known risk factor for limb salvage failure, and revascularization is commonly avoided in ESRF patients with extensive tissue loss.[23,24] This is attributed to the high rates of perioperative complications and early amputation despite a patent revascularization attempt.[23] Poor tissue healing in spite of sufficient blood supply in ESRF patients may be a result of various associated conditions including malnutrition and uremia, which are associated with poor granulation tissue formation in wounds, and immune deficiency, which predisposes to infections.[25]

ESRF patients with PAD also commonly suffer from multiple comorbidities such as DM and cardiovascular diseases,[26] which render them high-risk surgical candidates and place them at higher risk of perioperative mortality and morbidity. Despite the general consensus that BKA provides better rehabilitative potential than does AKA, the poorer healing potential of BKA in combination with the generally poorer constitution of ESRF patients results in a high risk of BKA failure and need for revision to AKA.[8,13,16] This exposure to multiple operations further worsens their prognosis.

Within our study population, subgroup survival analysis of ESRF patients versus non-ESRF patients showed that those with ESRF had higher mortality rates compared with those without ESRF. This correlates well with other studies on the effects of renal failure and lower-extremity amputations.[14] AKA as the primary form of lower extremity amputation, compared with BKA may allow for better wound healing and reduce the need for further multiple surgeries.[5–7] In light of this, a single operation via a primary AKA may offer better functional outcome in ESRF patients with multiple comorbidities and poor rehabilitative potential.

In addition, our study showed that preoperative non-ambulatory status is an independent risk factor for BKA failure. The BKA stump is more prone to contracture and pressure-related ulceration, particularly in non-ambulatory patients.[27] Furthermore, BKA in patients with poor baseline mobility status may result in falls and fractures during rehabilitation.[15] As such, AKA should be considered the primary modality of choice in non-ambulatory patients with extensive tissue loss.

Traditionally, the presence of a palpable popliteal pulse is a strong predictor for good healing rates in BKA.[28] However, the absence of one does not preclude BKA because it is not a reliable predictor for BKA success.[29] It has been recommended that a "minimal knee stump" BKA approach be employed in patients without popliteal pulse.[30] Within our study, neither the presence of a palpable popliteal pulse nor post-revascularization presence of popliteal flow was predictive of BKA success. Other factors such as good diabetes control and osteomyelitis on presentation were not significant determinants of BKA success rate (**Table 3**).

Limitations of our study include its retrospective design, with associated selection and information biases. In addition, we did not obtain information regarding patient weight and intraoperative blood loss.

Conclusion

In this Asian single-institutional review of 210 BKAs, most of our patient population had DM with poor control. The overall BKA failure rate with subsequent need for AKA was 9%, and the overall 1-year survival and 5-year survival was 75% and 58%, respectively. Multivariate analysis revealed ESRF and preoperative non-ambulatory status to be independent predictors for BKA failure. Patients with underlying ESRF and preoperative non-ambulatory status may benefit from direct AKA if major amputation is required.

Disclosure Statement

All authors have no conflict of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions

Study conception: ZJL, WW
Data collection: JTW, MW, WW
Analysis: JTW, MW, ZJL
Investigation: JTW, MW
Writing: JTW, MW, ZJL
Funding acquisition: NIL
Critical review and revision: all authors

Final approval of the article: all authors
Accountability for all aspects of the work: all authors

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