Results of surgical management of acute thromboembolic lower extremity ischemia

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Objective: **Acute lower extremity ischemia secondary to arterial thromboembolism is a common problem. Contemporary data regarding this problem are sparse. This report examines a 10-year single-center experience and describes the surgical management and outcomes observed.**

Methods: **Procedural codes were used to identify consecutive patients treated surgically for acute lower extremity embolization from January 2002 to September 2012. Patients presenting >7 days after onset of symptoms, occlusion of grafts/stents, and cases secondary to trauma or iatrogenic injury were excluded. Data collected included demographics, medical comorbidities, presenting clinical characteristics, procedural specifics, and postoperative outcomes. Results were evaluated using descriptive statistics, product-limit survival analysis, and logistic regression multivariable modeling.**

Results: **The study sample included 170 patients (47% female). Mean age was 69.1 ± 16.0 years. Of these, 82 patients (49%) had a previous history of atrial fibrillation, and four (2%) were therapeutically anticoagulated (international normalized ratio ≥2.0) at presentation. Presentation for 83% was >6 hours after symptom onset, and 9% presented with a concurrent acute stroke. Femoral artery exploration with embolectomy was the most common procedural management and was used for aortic, iliac, and infrainguinal occlusion. Ten patients (6%) required bypass for limb salvage during the initial operation. Local instillation of thrombolytic agents as an adjunct to embolectomy was used in 16%, fasciotomies were performed in 39%, and unexpected return to the operating room occurred in 24%. Ninety-day amputation above or below the knee was required during the index hospitalization in 26 patients (15%). In-hospital or 30-day mortality was 18%. Median (interquartile range) length of stay was 8 days (4, 16 days), and 36% of patients were discharged to a nursing facility. Recurrent extremity embolization occurred in 23 patients (14%) at a median interval of 1.6 months. The 5-year amputation freedom and survival estimates were 80% and 41%, respectively. Predictors of 90-day amputation included prior vascular surgery, gangrene, and fasciotomy. Predictors of 30-day mortality included age, history of coronary artery disease, prior vascular surgery, and concurrent stroke.**

Conclusions: **Despite advances in contemporary medical care, lower extremity arterial embolization remains a condition that is associated with significant morbidity and mortality. Furthermore, the condition is resource-intensive to treat and is likely preventable (initially or in recurrence) in a substantial subset of patients. (J Vasc Surg 2014;60:702-7.)**

Thromboembolic disease leading to acute lower extremity ischemia is a common problem associated with significant morbidity and mortality.[1-7] Embolectomy procedures for embolic arterial occlusions of the lower extremities are common, but contemporary data regarding the management and expected outcomes are sparse. This study provides a detailed report from a single center of acute lower extremity thromboembolism describing surgical management and an assessment of outcomes. Considering improvements in critical care, anesthesia, and perioperative risk reduction, we expected that morbidity and mortality had improved relative to prior reports of management for this condition.

METHODS

This study was conducted with approval from the Wake Forest University Baptist Medical Center Institutional Review Board. Patient consent was waived due to the retrospective nature of this study.

Data collection, management, and case selection. Patients undergoing lower extremity embolectomy of the aorta, iliac, or infrainguinal arteries between January 2002 and September 2012 were identified from an operative registry using Current Procedural Terminology (American Medical Association, Chicago, Ill) codes 34201 and 34203 and selected for analysis. Using these codes, 245 patients were identified. Cases due to trauma, iatrogenesis, occlusion of a prior bypass graft or stent, as well as those patients presenting with >7 days of symptoms were excluded from further consideration.

This selection process resulted in a sample of 170 patients for analysis. Demographic, comorbidity, clinical presentation, operative management, postoperative morbidity, and mortality data were abstracted from the electronic medical record. In an effort to elucidate the severity of preexisting peripheral vascular disease, prior vascular surgery

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was defined as a history of any major vascular surgery interventions (including amputations). Rutherford's classification[8] was assigned using abstracted data from the history and physical examination as well as the surgeon's operative note. The patient's limb ischemia was categorized as viable, I; marginally threatened, IIa; immediately threatened, IIb; and irreversible, III.

Surgical treatment. Heparin anticoagulation was generally started upon recognition of acute limb ischemia and continued throughout the operation and postoperative period. The initial revascularization attempt in all patients was femoral or popliteal artery exposure and balloon catheter thromboembolectomy. Our group preference is femoral artery embolectomy as the initial approach in most patients.

Intraoperative angiography was performed as needed from the clinical assessment and at the discretion of the operating surgeon, as was the performance of fasciotomy and adjunct bypass procedures. The dictated results from any intraoperative angiography performed were used to define the presence of significant peripheral arterial disease.

Amputations were recorded as occurring at the time of initial operation, during the index admission, or after discharge, and time to amputation was also recorded. Major amputations were classified as transfemoral or transtibial. Minor amputations were considered any toe or forefoot amputation and were not considered in the analysis of freedom from amputation.

Outcomes. Collected outcome data included 30-day or in-hospital mortality, performance of amputation, postoperative complications, and other adverse events. All such data were obtained from the electronic medical record. Concurrent stroke was identified via the admission or discharge summary and only recorded if the stroke was classified as embolic. Recurrent embolization was defined as a discrete additional embolic event occurring in any limb. Postoperative hemorrhage was defined as a bleeding event requiring surgical evacuation or transfusion of packed red blood cells. Postoperative complications were considered significant if they required additional intervention or prolonged the hospital stay, or both. Acute kidney injury was identified by the discharge summary. Length of stay and discharge disposition (home, return to skilled facility, new assignment to skilled facility) were also recorded.

Statistical analysis. Demographic, medical comorbidity, presentation, operative management, postoperative morbidity, and mortality data were examined using count (%), median (interquartile range [IQR]), or mean ± standard deviation. Freedom from major amputation and in-hospital or 30-day mortality were evaluated using product-limit survival analysis and multivariable logistic regression modeling. Multivariable modeling was conducted using forward model selection ($P = .10$ to enter) with age included in all models. Because of low event rates, a stopping rule of five variables was implemented for model selection.

The candidate covariate list for both outcomes included age, gender, race, hypertension, atrial fibrillation, coronary artery disease, smoking status, diabetes, history of peripheral arterial disease, prior vascular surgery, cancer, history of stroke, history of deep vein thrombosis, chronic obstructive pulmonary disease, end-stage renal disease, prior valvular heart surgery, international normalized ratio ≥2, concurrent stroke, gangrene, days of symptoms, bilateral procedure, and cardiac embolic source. The candidate covariate list for amputation also included popliteal-only cutdown, intraoperative lytics, fasciotomy, concurrent bypass, and arteriogram.

Associations between the Rutherford classification and amputation and mortality outcomes were evaluated using the Fisher exact test because complete evaluations of the Rutherford classification on all patients were not possible. All statistical analyses were conducted using SAS 9.3 software (SAS Institute, Cary, NC).

Table I. Patient demographics and clinical characteristics

Variable	*No.*	*Frequency (%) or mean ± SD*
Age, years	170	69.1 ± 16.0
Female gender	170	80 (47)
Nonwhite race/ethnicity	169	33 (20)
Atrial fibrillation	169	82 (49)
International normalized ratio ≥2	167	4 (2)
Hypertension	169	132 (78)
Smoking		
Current	159	61 (38)
Ever	159	103 (65)
Coronary artery disase	169	63 (37)
Diabetes	169	55 (33)
COPD	169	23 (14)
End-stage renal disease	170	11 (6)
History of		
Peripheral arterial disease	169	47 (28)
Vascular surgery	169	20 (12)
Lower extremity vascular surgery	169	12 (7)
Cancer	169	35 (21)
Stroke	169	30 (18)
Deep vein thrombosis	169	16 (9)
Heart valvular surgery	169	3 (2)

COPD, Chronic obstructive pulmonary disease; *SD*, standard deviation.

RESULTS

Patient and presentation characteristics. We analyzed 170 patients with acute thromboembolic lower extremity ischemia. Table I summarizes patient demographics and clinical characteristics. Mean age was 69.1 ± 16.0 years, and 80 patients (47%) were female. Eighty-two patients (49%) had a known diagnosis of atrial fibrillation, but only four patients at presentation demonstrated a warfarin-associated international normalized ratio ≥2.0. Twenty-three patients (17%) presented with <6 hours of symptoms. The mean duration of symptoms before presentation was 1.7 ± 1.4 days. Thirty-three patients (19%) demonstrated thromboembolic occlusions affecting both lower extremities. During the index admission, 15 patients (9%) experienced a new, concurrent embolic stroke; of which, nine strokes occurred before surgery, and six occurred after

Table II. Patient status according to the Rutherford classification

Rutherford classification	*No. (%) (N = 139)*	*Amputations, No. (%)*	*Mortality, No. (%)*
I	2 (1)	0 (0)	0 (0)
IIa	40 (29)	1 (3)	2 (5)
IIb	72 (52)	8 (11)	13 (19)
III	25 (18)	14 (56)	8 (32)

I, viable; *IIa*, marginally threatened; *IIb*, immediately threatened; and *III*, irreversible.

surgery. Only five (33%) of the concurrent stroke patients survived.

Surgical management. Forty-nine percent of patients were American Society of Anesthesiologists Physical Status Classification class 4 or 5. Common femoral artery exposure for the performance of embolectomy was the initial procedure in 86% of patients, and isolated popliteal fossa exposure for the performance of embolectomy was used in 16 (9%). Combination exposure of the femoral and popliteal vessels to facilitate distal revascularization was required in seven (4%). No direct tibial artery exposure and embolectomy were identified in this series.

Intraoperative angiography was performed in 94 patients (55%), demonstrating concomitant atherosclerotic peripheral arterial disease in 40 patients (43%). Intraoperative thrombolysis was administered in 28 patients (16%) because of incomplete distal arterial revascularization. Fasciotomies were performed in 66 patients (39%), 63 at the time of initial revascularization and three in a delayed fashion. Thirteen patients (8%) required a bypass procedure for persisting limb-threatening ischemia, with four ultimately requiring major amputation. Ten bypass procedures were performed concurrently with the initial thromboembolectomy.

Thromboembolic disease causes. Clinically presumed thromboembolic sources for the study sample were evaluated. The most frequent source, in 88 patients (52%), was cardiac, of which 41% were attributed to documented atrial fibrillation and 4% to other arrhythmias. The presence of multiple potential sources was common, with 23 patients having at least two potential defined sources. No putative etiology was identified in 13 patients.

Rutherford classification. The Rutherford classification for 139 examined patients is summarized in Table II. Two patients heparinized at another institution showed marked improvement in symptoms and signs of ischemia in transit and were classified as I (1%). Fisher exact test analysis showed a statistically significant association between the Rutherford class and amputation ($P < .0001$) and death ($P < .0286$). Of the 25 patients classified as III who did not die or require a known amputation, one patient went to hospice, one patient's family refused amputation, and two were transferred and lost to follow-up.

Morbidity and mortality. Detailed morbidity and mortality outcomes are listed on Table III. Patients required 30 major amputations and three minor amputations; however, amputation within a 90-day interval occurred in 27 patients (16%), with 26 (15%) being major amputations. Median time to amputation was 1 day (IQR, 0-6 days). Freedom from amputation was 80% at 5 years (Fig 1). The 30-day or in-hospital mortality was 18%. Estimated overall survival at 5 years was 41% (Fig 2).

Table III. Morbidity and mortality

Variable	*No.*	*Frequency (%)*
Amputation ≤90 days	170	27 (16)
Amputation type	170	
Major		26 (15)
Minor		1 (1)
Mortality (30-day or in-hospital)	168	31 (18)
Recurrent embolization	168	23 (14)
Wound infection	170	36 (21)
Hemorrhage	170	29 (17)
Return to operating room	170	
None		107 (63)
Planned return only		22 (13)
Any unplanned return		41 (24)
Amputation		10 (6)
Fasciotomy		7 (4)
Hematoma evacuation		13 (8)
Contralateral embolectomy		3 (2)
Incision and drainage or debridement		8 (5)
Other		7 (4)
Post-op infections other than wound	170	31 (18)
Pneumonia		15 (9)
Urinary tract infection		8 (5)
Bacteremia		6 (4)
Central catheter infection		4 (2)
Other		3 (2)
Major noninfectious post-op complications	170	71 (42)
Pulmonary failure		20 (12)
Acute renal failure		13 (8)
Cardiac		10 (6)
Myocardial infarction		11 (6)
Multiorgan system dysfunction		7 (4)
Ischemic bowel		3 (2)
Pulmonary embolism		2 (1)
Other		22 (13)

Additional, discrete embolization events occurred in 23 patients (14%). Median time to recurrent extremity embolization was 1.6 months (IQR, 0.03-10.9 months), and the most common site of recurrence was the contralateral lower extremity in 12 patients. Ten recurrences occurred in the index limb, and one in the upper extremity. Seven of the 23 patients with recurrent embolization underwent major amputations, three of whom underwent bilateral major amputations. Upon recurrent embolization, 11 of the 23 were not therapeutically anticoagulated, and coagulation status was unknown in seven.

Forty-one patients (24%) patients returned to the operating room due to unplanned circumstances, most commonly for hematoma evacuation (bleeding occurred at the femoral exposure site in nine, fasciotomy site in three). Wound complications occurred in 36 patients (21%), and postoperative infections in 31 (18%). Major

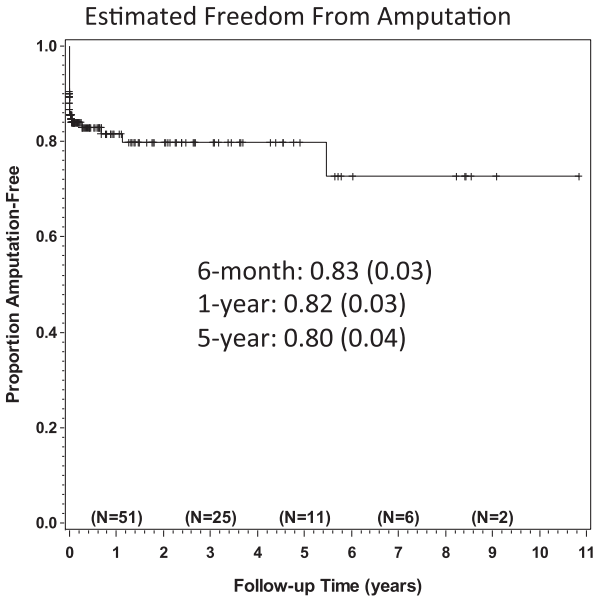

Fig 1. The *y axis* shows the proportion who were free from amputation, and the *x axis* shows the follow-up time in years. The counts shown at the bottom represent the number remaining in the analysis at the given time points.

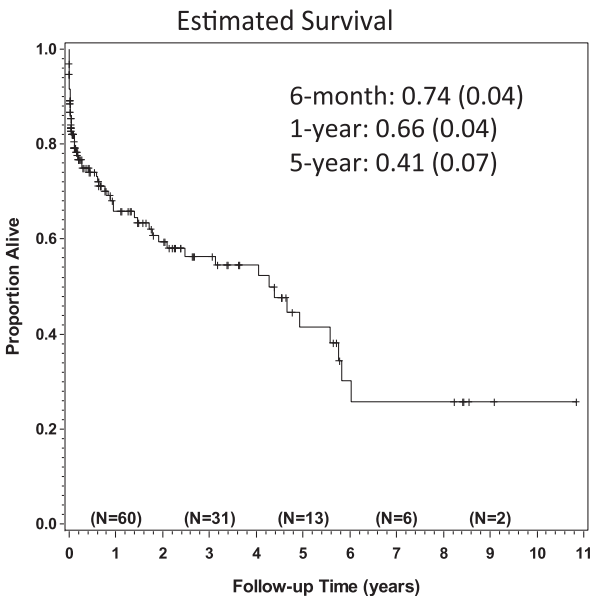

Fig 2. The *y axis* shows the proportion who were alive and the *x axis* shows the follow-up time in years. The counts shown at the bottom represent the number remaining in the analysis at the given time points.

noninfectious complications that prolonged the patient's hospital stay occurred in 71 patients (42%).

Length of stay. The median total length of stay was 8 days (IQR, 4-16 days). Sixty patients (36%) were discharged to a skilled nursing facility. Of these, 10 patients returned to their prior nursing facility and 50 were new dispositions to skilled nursing care.

Multivariable analysis. Results of multivariable logistic regression analyses of mortality and amputation are summarized in Table IV. Statistically significant predictors of amputation included prior vascular surgery, gangrene, and fasciotomy. Predictors of death included age, prior vascular surgery, and concurrent acute stroke.

DISCUSSION

This report details contemporary results of treating acute lower extremity embolization from a single academic medical center. In general, patients with acute lower extremity ischemia secondary to embolization presented in a delayed fashion and were most often treated with balloon catheter embolectomy via an open femoral artery exposure. Despite the relatively minimal physiologic trespass of the procedure, the results demonstrated persistence of significant morbidity and mortality with a high resultant demand for both in-hospital and postacute health care resources.

Published outcomes associated with acute embolic lower extremity ischemia include a 20-year multicenter perspective reported by Tawes et al[1] in 1985, which examined 739 patients (included patients singly treated with anticoagulation). The amputation rate was 5%, mortality was 12%, and wound complications occurred in 19%. The authors' overall recommendation was to treat acute limb ischemia patients aggressively, pursuing secondary operations as needed, and to administer anticoagulation postoperatively—recommendations that represent the current standard of care.

Several additional studies were reported in the 1990s:

- Ljungman et al[2] reported from a Swedish national registry, performing a 19-year review involving 1190 patients and demonstrating a 5-year limb salvage rate of 61% to 81% and a 5-year survival of 33% to 43%.
- Kuukasjärvi et al[3] performed a retrospective, multicenter study of 509 patients, citing a 30-day amputation rate of 16% and 30-day mortality of 13%.
- Davies et al[4] performed the only prospective study, published in 1997, detailing a 30-day amputation rate of 6% and 16% mortality.
- Campbell et al[5] examined records of 474 patients from the United Kingdom and found a 30-day amputation rate in 16% and a mortality rate of 22%.

Eliason et al[6] more recently reported both a thorough single-center study and an analysis of National Inpatient Sample data and demonstrated similar amputation rates of 13% to 14% and mortality rates of 9% to 12%. And finally in 2012, a review of 683 patients by Dag et al[7] from Turkey focused on risk factors for amputation after arterial emboli and found an amputation rate in 14% and an increased risk of amputation with a delay >6 hours from onset and recurrence of embolectomy.

Table IV. Multivariable analysis for in-house or 30-day mortality and 90-day amputation[a]

	30-day or in-hospital mortality		*Major amputation ≤90 days*	
Covariate	*OR (95% CI)*	P	*OR (95% CI)*	P
Age (1-year increment)	1.0 (1.00-1.09)	.0321	1.0 (.93-1.01)	.0941
Prior vascular surgery	9.2 (2.70-31.34)	.0004	18.0 (4.73-68.71)	<.0001
Coronary artery disease	2.3 (.87-5.97)	.0948	…	…
Concurrent stroke	12.4 (2.82-54.15)	.0008	…	…
Current smoker	…	…	0.2 (0.05-0.78)	.0202
Gangrene	…	…	10.4 (1.12-95.96)	.0396
Fasciotomy	…	…	6.0 (1.68-21.31)	.0058

CI, confidence interval; *OR,* odds ratio.
[a]Each model adjusts for all variables shown in the Table (except where noted by "…"). Age was included in each model regardless of significance.

Given the limited recent evidence characterizing outcomes for acute lower extremity arterial ischemia, we believe our results provide a detailed and more contemporary characterization of associated outcomes. Unfortunately, morbidity and adverse event rates associated with this diagnosis remain formidable. Similar to the data summarized previously, our observed 90-day major amputation rate was 15%, and 30-day mortality rate was 18%. The 5-year estimated limb salvage was 80%, and survival was 41%, comparable to those data reported 17 years earlier from the Swedish study by Ljungman et al.[2] A significant rate of other morbidities was also observed, with a prolonged median length of stay of 8 days, postoperative infections in 18%, wound infections in 21%, and any unplanned return to the operating room in 24%.

The features of our patient pool may explain the poor outcomes demonstrated by this study, with 83% presenting with symptoms of >6 hours. Not surprisingly, with this late presentation, 70% of our patients (assessed by the Rutherford classification) had an immediately threatened limb or an irreversible degree of acute limb ischemia. This delay is likely a reflection of our catchment area, with a large proportion of patients coming from neighboring states and from remote distances.

Additional explanations may also account for the lack of significant improvement in outcomes over time associated with acute arterial thromboembolism. Given the absence of major technical changes in the open surgical procedures for arterial embolism, the lack of improvement in outcomes possibly represents a relatively static mode of open surgical management. Conversely, improvements in medical management (including risk factor reduction and critical care) and increases in catheter-based treatment of this disease may offset any potential improvements by corresponding increases in the general level of patient complexity and medical acuity.

In addition to an unyielding morbidity and mortality, this analysis identified a high prevalence of subtherapeutic anticoagulation among patients with a history of dysrhythmia as a likely cause for almost half of the observed cases. No other review has looked specifically at whether patients with an indication for anticoagulation presented with a therapeutic level of anticoagulation. The observation that almost 50% of patients in this series had a known diagnosis of atrial fibrillation, but only four people in the entire study were therapeutically anticoagulated, identifies a major potential target for preventive efforts.

Furthermore, recurrent embolization occurred in 14% of our study sample; Campbell et al[9] showed in 2000 that long-term anticoagulation reduced the risk of recurrent limb ischemia. Although it is impossible to speculate whether anticoagulation of those affected (who represent frail patients at baseline) would have led to a set of hemorrhagic problems eclipsing the severity of issues posed by their ischemia, we do believe that it represents a modifiable risk factor as well as an area for focused prevention efforts.

Short-term and long-term survival for the study sample were both poor. This likely represents arterial thromboembolism as a marker of advanced medical comorbidities and chronic illness that significantly limit survival independently of the acute lower extremity ischemia. Affected patients should be candidates for a comprehensive reassessment of risk and application of primary and secondary preventive efforts aimed at their chronic illnesses as well as being identified as individuals likely to benefit from additional rehabilitation and social support resources. These patients would also likely represent a logical population to engage in a proactive discussion of end-of-life and advanced directive issues, once recovered from their acute illness, to help ensure that those issues are managed in accordance with their wishes when they arise.

Several additional limitations of our study merit specific discussion. The retrospective nature of the review precluded complete data collection for all variables and testing of any a priori hypotheses or management algorithms. Also, the study sample originated from a single center, capturing only a specific group of surgical patients managed by a single specialty group with similar management approaches. Furthermore, owing to the difficulties in identifying patients treated in other fashions, the sample only included those patients whose

treatment started with an embolectomy. Events managed without an embolectomy were not assessed, such as anticoagulation without revascularization, thrombolysis, immediate amputation, bypass, or endovascular revascularization, nor were patients captured who decided to forgo surgery, such as those directed to hospice.

CONCLUSIONS

This report details a large, single academic medical center experience managing acute lower extremity ischemia. The resultant data demonstrated that this problem remains a cause of high mortality, morbidity, and health care resource use that may be preventable in a large number of patients. The reported data also demonstrate that the affected population represents a high-risk population for near-term future death, representing an ideal group for enhanced preventive efforts as health care systems continue to try to reduce the economic and human consequences of repeated admissions for chronic disease conditions.

AUTHOR CONTRIBUTIONS

Conception and design: KK, AI, ME
Analysis and interpretation: KK, JS, MC, ME
Data collection: KK, BS, AM, EL
Writing the article: KK, MC, ME
Critical revision of the article: KK, JS, MC, ME
Final approval of the article: KK, BS, JS, AI, AM, EL, MC, ME
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Overall responsibility: ME

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