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Safety of transfer, type of procedure, and factors predictive of limb salvage in a modern series of acute limb ischemia

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ABSTRACT

Objective: The primary objective was to evaluate the safety of transfer, type of procedure, and factors associated with limb salvage in patients with acute limb ischemia (ALI) treated at a quaternary referral center.

Methods: A retrospective review of all patients with ALI secondary to thrombotic or embolic occlusion at a quaternary referral hospital from 2013 to 2016 was conducted. Patients were transferred from throughout Washington and Alaska by ambulance, helicopter, or fixed-wing modes of transportation. Demographics, transport and operative timing, Rutherford classification, level of occlusion, procedural information, and fasciotomy characteristics were reviewed. Outcomes measured included limb salvage rates, discharge disposition, and mortality.

Results: One hundred twelve patients with ALI were identified, with 82% due to thrombosis and 18% due to arterial embolization. Fifty-seven percent of patients were transferred from a referring hospital with low mean transfer times (1.9 hours for embolic, 2.7 hours for thrombotic). Although the initial operative strategy varied according to the etiology, with 50% of thrombotic occlusions treated with endovascular therapies and 80% of embolic occlusions treated with open thrombectomy, the rates of limb salvage did not vary based on operative approach (92% endovascular first, 90% open first). Further, limb salvage rates were identical between transferred and nontransferred patients (77%). Limb salvage was successful in 91% of patients with Rutherford class 1 and 2 disease, but only 8% in patients with Rutherford class 3 disease. In-hospital and 30-day mortality rates were not different based on ischemic etiology (5%), although patients with Rutherford class 3 disease had significantly higher mortality rates (15%) compared with patients with class 1 (6%), class 2a (6%), and class 2b (2%) disease. Fasciotomy was performed in 29% of patients, with 59% of fasciotomy wounds closed primarily. Predictors of amputation include multiple attempts at limb salvage, higher Rutherford class, multilevel occlusion, more proximal levels of occlusion, and nonviable muscle seen after fasciotomy, with ischemic times trending toward higher amputation rates without statistical significance. There was no difference in discharge disposition based on ischemic etiology.

Conclusions: The modern treatment of patients with ALI is effective, with high rates of limb salvage and low mortality regardless of transfer status, etiology, or initial operation performed. In situations where compartment syndrome is unclear, fasciotomy should not be withheld because it provides valuable predictive information regarding limb salvage. (J Vasc Surg 2019;69:1174-9.)

Keywords: Limb salvage; Ischemia; Thrombosis; Embolism

Acute limb ischemia (ALI) due to in situ thrombosis, arterial embolization, or bypass graft thrombosis remains challenging to treat effectively with historically high rates of limb loss (12%-50%) and mortality (20%-40%).[1-6] On initial presentation, the severity of ALI is categorized according to the Rutherford classification, which defines a limb as not immediately threatened (Rutherford class 1), marginally threatened (Rutherford class 2a), immediately threatened (Rutherford class 2b), or irreversibly threatened or nonviable (Rutherford class 3). Previous studies have confirmed the usefulness of the Rutherford classification as a risk stratification tool, with higher classes being associated with higher rates of limb loss.[7] Additional factors associated with amputation include advancing age and preoperative ischemic times.[8-11]

Previous studies have examined the natural history and treatment outcomes of ALI, whether treated by open surgical bypass or with endovascular techniques; however, only two studies have included any discussion of transfer times,[12,13] with only one analyzing the impact of transfer times on outcomes.[13] This study was limited by its small

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subset of patients, spread over a large study period, during which practice patterns and the standard of care may have changed. Given the fact that muscle necrosis increases without revascularization in an expeditious fashion, knowledge of outcomes of patients transferred to a quaternary referral center may assist referring providers in deciding whether to transfer a patient for a revascularization attempt. Furthermore, although ischemic time, age, certain comorbidities, and severity of symptoms on presentation have all been correlated with poorer rates of limb salvage, the role of prophylactic fasciotomy, performed at the time of revascularization, for both the prevention of compartment syndrome and the prediction of limb loss, is unclear.

The primary aim of this contemporary, retrospective, single-center review was to analyze the rates of limb salvage and death among patients presenting with ALI to a quaternary referral center serving a wide geographical distribution. Specifically, this modern series examines the association between limb salvage and transfer status, etiology, ischemia severity, and initial revascularization procedure attempted. Additional objectives included determining those factors most predictive of limb salvage and further defining the usefulness of prophylactic fasciotomy.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of single center cohort data
- **Key Findings:** Treatment for acute limb ischemia in 112 patients demonstrated that transfer of patients with acute limb ischemia is safe and that predictors of amputation included multiple attempts at limb salvage, higher Rutherford class, multilevel occlusion, more proximal levels of occlusion, and nonviable muscle seen after fasciotomy.
- **Take Home Message:** Transfer of patients with acute limb ischemia is safe. Clinical factors predictive of amputation in patients with acute limb ischemia include multiple attempts at limb salvage, higher Rutherford class, multilevel occlusion, more proximal occlusions, and nonviable leg muscles.

METHODS

A review of all patients primarily diagnosed with ALI at Harborview Medical Center in Seattle between February 2013 and December 2016 was performed. Acting as the only quaternary referral center serving the states of Washington, Wyoming, Alaska, Montana, and Idaho, Harborview Medical Center receives transfers from 27% of the land mass of the United States. The majority of transfers to our facility occur via ambulance, helicopter, or fixed-wing modes of transportation. All patients undergoing endovascular, open, or hybrid procedures for treatment of acute lower extremity ischemia were included in this study. Patients with upper extremity ALI and those with ALI owing to traumatic injury were excluded from the study. No patients with the primary diagnosis of ALI were managed palliatively. Before transfer, all patients were placed on an intravenous heparin infusion. The indications for transfer most often were unavailability of local vascular surgeons and the determination that the patient's illness exceeded the capabilities of the referring hospital.

Using a direct review of the electronic medical record, we extracted the following data for each patient: time and date of arrival and transfer from referral hospital (if any), method of transfer, time and date of arrival to Harborview Medical Center, time and date of each procedure performed, procedural details of each procedure performed, Rutherford classification, procedural complications, mechanism of ischemia (embolic or thrombotic), presence and type of preoperative imaging (computed tomography vs ultrasound), and level of arterial occlusion. In addition, ischemic time included the transfer time of the patient and time from arrival to the operating room (OR). Basic demographic and clinical details of hospitalization were obtained from our electronic medical record. Data abstraction was performed by two independent reviewers and compared for consistency. The study was carried out with University of Washington Institutional Review Board approval and patient consent was waived for this study.

The primary outcome was the success of limb salvage during the index hospitalization for ALI. Secondary outcomes included length of hospitalization, total number of procedures performed, discharge disposition, in-hospital mortality, and 30-day mortality.

Continuous variables were expressed in terms of median and interquartile range (IQR) and categorical variables were expressed in percentages. Multivariate logistic and linear regression analyses were performed to correlate variables with primary and secondary outcomes as listed above after correcting for patient age and sex. All statistical analyses were performed using JMP 12.0 software (SAS International Inc., Cary, NC), and a P value of less than .05 was considered statistically significant.

RESULTS

One hundred twelve patients with ALI of the lower extremity were identified and separated into two groups based on etiology. Ninety-two patients (82%) presented with ischemia secondary to thrombosis and 20 patients (18%) presented with ischemia secondary to embolization from a proximal source. The Table describes the background patient demographics, transfer information, disease severity on presentation, procedural data, and outcomes for each group. The majority of patients were male (75% and 50% in the thrombotic and embolic

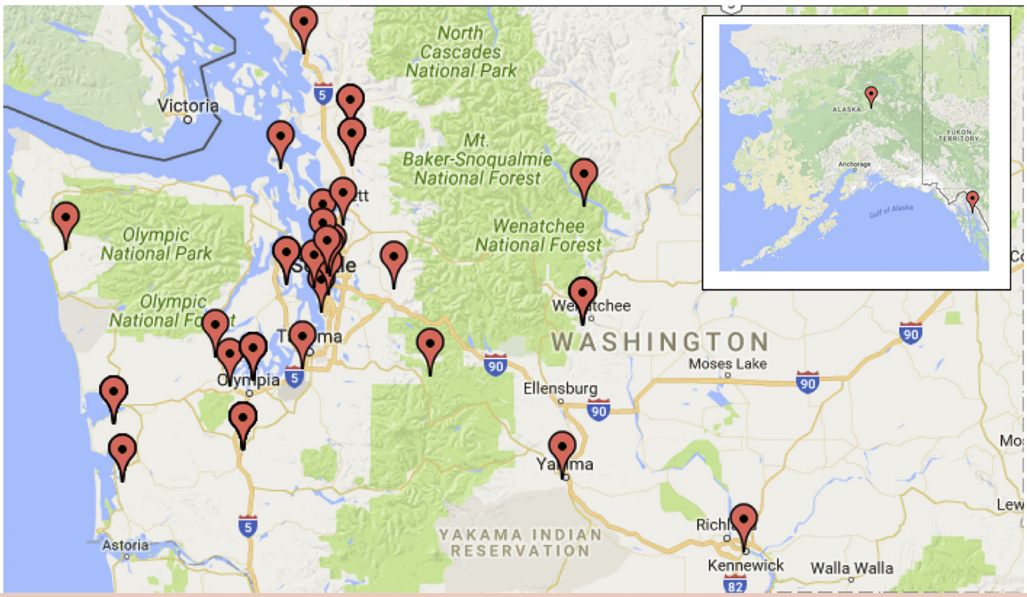

Fig 1. Transfer locations. The locations of transferring hospitals. Sixty-two patients were transferred from within Washington State and two were transferred from Alaska.

groups, respectively). Cardiac sources accounted for 75% of embolic causes of ALI (15 patients), with 10% (2 patients) embolizing from an aortic thrombus and 15% (3 patients) having no identified embolic source. Of those with a cardiac source, all 15 carried a previous diagnosis of atrial fibrillation, and 11 of these 15 patients (73%) had a subtherapeutic international normalized ratio on presentation.

Regarding the origin of the patient, 57% of patients were transferred from a referral hospital (50% of the thrombotic group, 70% of the embolic group), with mean transfer times of 2.7 hours and 1.9 hours in the thrombotic and embolic groups, respectively. Fig 1 shows the locations of referring hospitals.

Despite the wide geographical range of referrals, the transfer time alone cannot explain the prolonged ischemic time of the patient, as evidenced by the longer average times from admission to the OR seen in both groups (8.7 hours and 3.0 hours in the thrombotic and embolic groups, respectively). In addition, a lack of correlation between transfer time and time to OR ($R^2 = .02$) was identified. Patients in both groups had a highly variable ischemic time, as shown by the high IQRs for median time from admission to the OR (an IQR of 2.4-35.0 hours in the thrombotic group, and an IQR of 2.2-17.0 hours in the embolic group). The median time from presentation to operation is further dependent on transfer status, as transferred patients showed a statistically significant longer ischemic time (15.83 hours; IQR, 7.03-34.79 hours) compared with nontransferred patients (4.85 hours; IQR, 2.28-13.55 hours). No differences were observed in ischemic time based on Rutherford classification.

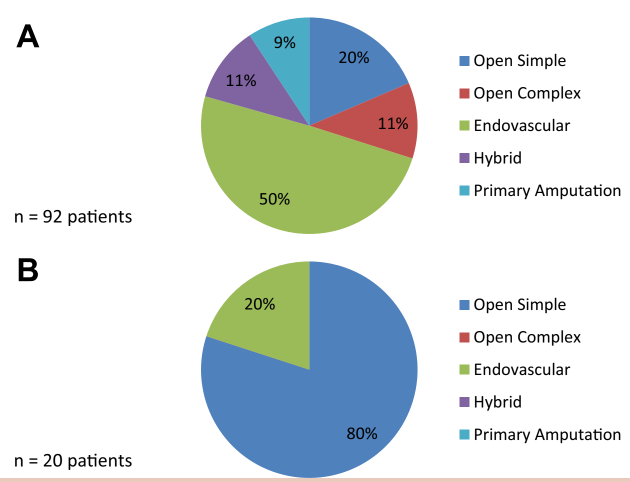

Fig 2. Initial procedure type for patients presenting with ALI owing to thrombotic (n = 92) **(A)** or embolic (n = 20) **(B)** occlusion. For thrombotic patients, endovascular methods comprised one-half of the initial procedures, whereas 80% of embolic patients underwent open simple approaches as an initial therapy.

Upon arrival in the OR, thrombotic and embolic patients differed in the approach taken for initial revascularization (Fig 2). In those patients with thrombotic occlusion, an endovascular-first approach via arteriograms with thrombolysis, mechanical thrombectomy, balloon angioplasty, and stenting was attempted in 50% of patients. No covered stents or atherectomies were used. The remainder of the thrombotic group was treated in the following manner: 20% of patients underwent open thrombectomy (open simple operation), 11% of patients underwent an open complex procedure, 11% of patients underwent a hybrid procedure, and 9% of patients underwent a primary amputation. The hybrid approach consisted of a first attempt at endovascular intervention, with thrombolysis or mechanical thrombectomy, and ultimately a patch angioplasty or bypass when endovascular options were no longer available. Polytetrafluoroethylene was the most common conduit for bypass grafts placed in patients who underwent both the open complex and hybrid procedures. In contrast, the majority of patients with embolic occlusion (80%) were treated first with an open thrombectomy, whereas only 20% were treated using an endovascular approach. No patients with embolic occlusion required primary amputation.

Further examination of operative characteristics in Table I reveals a fasciotomy rate of 29% in the cohort, with 24% of patients with thrombotic origin and 50% of patients with embolic origin undergoing fasciotomy. Eighteen patients (56%) underwent fasciotomy during the primary procedure. Twenty-five patients (78%) underwent a four-compartment fasciotomy, 3 patients (9%) underwent a two-compartment fasciotomy (anterior and lateral compartment), and 4 patients (13%) underwent a single compartment fasciotomy (anterior compartment). The different number of compartments opened during fasciotomy was based on the operating surgeon's discretion and the appearance or absence of tense compartments intraoperatively. Fasciotomy incisions in 19 patients (59%) were able to be closed in a delayed primary fashion, whereas only 4 patients (13%) required skin grafting. The remaining 10 patient's fasciotomy wounds (31%) were never closed, with 1 patient dying, 7 patients undergoing amputation before closure, and 2 patients being discharged before closure. All fasciotomies closed primarily were done so within 4 days.

Overall, amputation occurred in only 9% of patients in Rutherford class 1, 2a, and 2b, but 92% of patients in Rutherford class 3 (Table I). Transferred and nontransferred patients showed cumulatively identical limb salvage rates (77%), with no statistically significant differences ($P = .95$) seen between the two groups (Fig 3). Furthermore, limb salvage rates were similar regardless of the initial approach taken (92% for the endovascular-first patients vs 90% for the open approach). Primary amputation occurred only in thrombotic patients with Rutherford class 3 ischemia, and of all patients in Rutherford class 3, only one survived without undergoing an amputation. This patient initially presented clinically with Rutherford class 3 ischemia in both lower extremities owing to occlusion of the distal aorta and both common iliac arteries; however, viable muscle was found bilaterally on fasciotomy. All seven patients with dead muscle seen at the time of fasciotomy required amputation, compared with only 19% of patients with viable muscle ($P < .05$).

Table. Demographics and outcomes

	Thrombotic (n = 92)	Embolic (n = 20)
Median age, years	64 (61-74)	58 (51-83)
Male (%)	69 (75)	10 (50)
Transferred from outside hospital	50 (54)	14 (70)
Median transfer time, hours	2.7 (2.0-3.9)	1.9 (1.7-3.3)
Median time from admit to OR, hours	8.7 (2.4-35.0)	3.0 (2.2-17.0)
Preoperative computed tomography	31 (34)	5 (25)
Rutherford classification		
1	15 (16)	1 (5)
2a	29 (32)	6 (30)
2b	37 (40)	11 (55)
3	11 (12)	2 (10)
Level of occlusion (%[a])		
Multilevel	14 (15)	8 (40)
Aortoiliac	8 (9)	2 (10)
Femoral-popliteal	36 (39)	9 (45)
Tibial	4 (4)	1 (5)
Suprainguinal graft	4 (4)	0
Infrainguinal graft	26 (28)	0
Initial procedure type (%[a])		
Open simple	18 (20)	16 (80)
Open complex	10 (11)	0
Endovascular	46 (50)	4 (20)
Hybrid	10 (11)	0
Amputation	8 (9)	0
Mean no. of procedures		
Open simple	1.9 ± 1.1	1.7 ± 0.7
Open complex	1.8 ± 0.8	n/a
Endovascular	2.5 ± 1.1	3.3 ± 2.3
Hybrid	2.8 ± 1.2	n/a
Amputation	1.4 ± 0.7	n/a
Fasciotomy at initial operation	10 (11)	8 (40)
Fasciotomy at subsequent operation	12 (13)	2 (10)
Median length of total stay, days	8 (5-13)	8 (6-18)
Median length of ICU stay, days	2 (1-4)	3 (1-4)
Limb salvage, total	69 (75)	17 (85)
Rutherford class		
1	14 (93)	1 (100)
2a	26 (90)	6 (100)
2b	28 (76)	10 (91)
3	1 (9)	0 (0)
Discharge to SNF	29 (32)	7 (35)
Death	5 (5)	1 (5)

ICU, Intensive care unit; *SNF,* skilled nursing facility.
Values are median (interquartile range [IQR]), n (%), or mean ± standard deviation.
[a]Percentages do not equal 100% as a result of rounding.

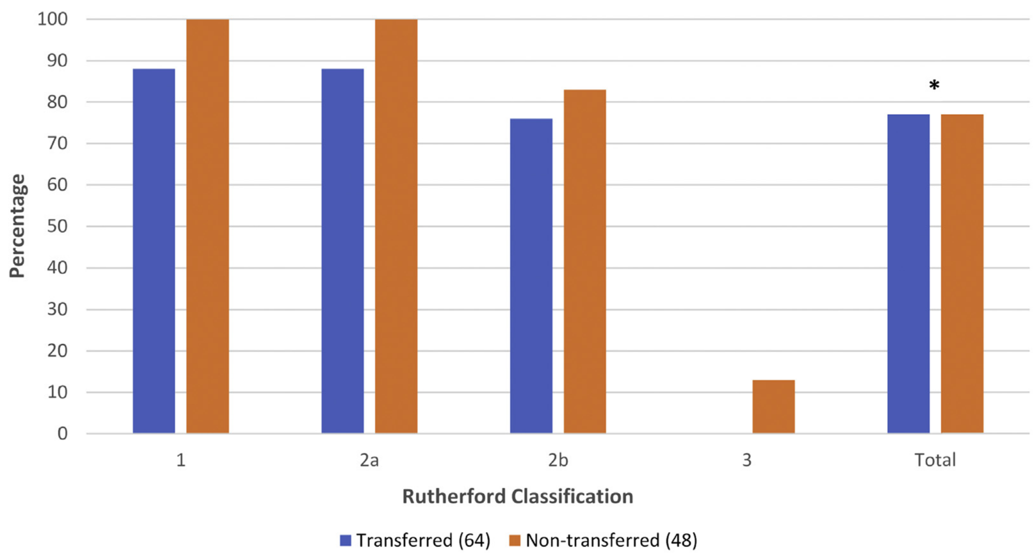

Fig 3. Limb salvage rates for transferred and nontransferred patients based on the Rutherford classification. There is no statistically significant difference in limb salvage rates between transferred and non-transferred patients (*$P = .95$).

Factors predictive of limb loss include multiple attempts at limb salvage, a higher Rutherford classification on presentation, nonviable muscle found during fasciotomy performed at the initial operation, and multilevel or aortoiliac levels of occlusion ($P < .05$). Although longer transfer times were associated with higher rates of amputation, these trends were not statistically significant.

At the time of discharge, 63% of patients were discharged home and 32% of patients were discharged to a skilled nursing facility. There was no difference in the proportion of patients discharging to home vs a skilled nursing facility based on ischemic etiology. Of those patients with Rutherford class 1 ischemia, 81% were discharged home, with 13% being discharged to a skilled nursing facility. The proportion of patients discharging to home vs a skilled nursing facility with Rutherford class 2a, 2b, and 3 ischemia were 57% vs 37%, 67% vs 31%, and 39% vs 46%, respectively.

The overall mortality rate, a composite of 30-day and in-hospital mortality, was 5% for both the thrombotic and embolic groups. The mortality rate for patients with Rutherford class 3 ischemia was significantly higher, at 15%, as compared with 6% for patients in class 1, 6% for patients in class 2a, and 2% for patients in class 2b ($P < .05$).

DISCUSSION

Excellent limb salvage rates have been previously demonstrated through both the endovascular and open surgical treatment of ALI[14,15]; however, little is known regarding the outcomes of these patients after transfer. In addition, few studies have examined the morbidity and predictive function of fasciotomy in these cases. This retrospective study of a contemporary series of 112 patients with nontraumatic ALI, the majority of whom were transferred from another hospital within a multistate geographical area between February 2013 and December 2016, demonstrated identical limb salvage among transferred and nontransferred patients. As expected, successful limb salvage was seen in 91% of patients with Rutherford class 1 and 2 disease, with predictors of amputation including multiple attempts at limb salvage, higher Rutherford class, multilevel occlusion, and a more proximal levels of occlusion. Although longer ischemic times showed trends toward higher amputation rates, the association was not statistically significant; furthermore, there was no correlation between transfer time and time to operation.

Although no clear guidelines exist regarding the decision to perform fasciotomy after revascularization, this series suggests that fasciotomy provides valuable information regarding the possibility of limb salvage. Although only 19% of patients without dead muscle required eventual amputation, all patients with dead muscle at the time of fasciotomy required amputation. Additionally, most fasciotomy wounds can be closed in a delayed primary fashion, decreasing the associated morbidity.

Our series suggests that the majority of patients with ALI are successfully revascularized, expeditious transfer to another center is safe, and fasciotomy should be performed, particularly in embolic arterial occlusion. Although other studies have examined outcomes in ALI, few have examined the impact of transfer from another hospital,[12,13] and only one has attempted to evaluate the safety of transfer, especially in patients with prolonged transfer times.[13] Unlike previous studies, our series is a larger, more contemporary study that not only analyzes outcomes in ALI related to the severity of ischemia on presentation, transfer status, ischemia time, and level of disease, but also includes information on fasciotomy characteristics.

Given the retrospective nature of this review, multiple limitations exist, including the possibility that data obtained from chart review are missing or inaccurate. Additionally, although we attempted to define ischemic time by including both time to operation and transfer times, we were unable to record the true ischemic time, which begins at the time of symptom onset. Further limitations include the absence of comorbidity analysis, which may influence outcomes, and the lack of long-term follow-up, which would provide further information regarding the safety and efficacy of revascularization and fasciotomy following ALI. Despite these limitations, this review is an important analysis of outcomes in ALI given the unique role that Harborview Medical Center serves in receiving transfers from a wide geographical area.

Future areas of investigation include following these patients longitudinally to determine the long-term outcomes after revascularization of ALI in patients transferred to a quaternary referral center, as well as the factors that are associated with prolonged time to operation. The former would allow for a better understanding of the long-term burden of disease and would provide further information regarding the safety of revascularization after transfer. The latter subject represents a possible quality improvement project that may identify factors that impede rapid revascularization.

CONCLUSIONS

Limb salvage for thrombotic and embolic acute lower extremity limb ischemia in the modern era is excellent, and factors predictive of limb salvage include Rutherford class 1 and 2 ischemia on presentation, as well as the presence of viable muscle at the time of fasciotomy. Furthermore, the rates of limb salvage remain high in patients treated for ALI after transfer from another facility, providing evidence for referring physicians that transfer is a safe option if necessary. Last, our series suggests that prophylactic fasciotomies, with a high rate of successful delayed closure, provide valuable predictive information regarding amputation based on the viability of muscle encountered.

AUTHOR CONTRIBUTIONS

Conception and design: SA, NT, BS, NS
Analysis and interpretation: JH, DE, SA, EQ, NT, BS, NS
Data collection: DE, SA, NS
Writing the article: JH, DE, NS
Critical revision of the article: SA, EQ, NT, BS, NS
Final approval of the article: JH, DE, SA, EQ, NT, BS, NS
Statistical analysis: SA, EQ, NS
Obtained funding: Not applicable
Overall responsibility: JH

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