Endovascular therapy for acute limb ischemia

Vikram S. Kashyap, MD,[a] Ramyar Gilani, MD,[a] James F. Bena, MS,[b] Mohsen Bannazadeh, MD,[a] and **Timur P. Sarac, MD,[a]** *Cleveland, Ohio*

Background: **Acute limb ischemia (ALI) of the lower extremities remains a challenging clinical dilemma. Treatment of ALI has shifted toward endovascular therapies. The purpose of this study was to assess outcomes in patients treated for ALI with intra-arterial thrombolysis and/or adjuvant endovascular techniques.**

Methods: **Consecutive patients with ALI of the lower extremities treated via endovascular intra-arterial methods between January 1, 2005 and September 30, 2007 were identified and reviewed. Comparisons of success, thrombolysis days, and all 30-day outcomes except mortality were performed using generalized estimating equations with logistic and proportional odds regression. Thirty-day mortality was assessed using logistic regression. Long-term patency, limb salvage, and survival were assessed using time-to-event methods, including Kaplan-Meier estimation and Cox proportional hazards models.**

Results: **The analyzed dataset included 129 limbs treated in 119 patients presenting with ALI (class I 68%, class IIa 23%, class IIb 9%). The mean follow-up was 16.8 months (range: 0-43 months). Technical success was achieved in 82% cases. The 30-day mortality rate was 6.0% with all 30-day deaths occurring in females ($P = .002$). One (0.76%) central nervous system hemorrhage (CNS) was noted in this cohort. Primary patency for the entire cohort at 12 and 24 months was 50.1% (95% confidence interval [CI], 39.5-60.7) and 37.7% (95% CI, 26.2-49.1), respectively, while secondary patency was 74.0% (95% CI, 64.9-83.1) and 65.3% (95% CI, 54.5-76.2). Multivariable analyses identified patients presenting with femoropopliteal (hazard ratio [HR] 2.63) or tibial thrombosis (HR 2.80); graft thrombosis (vs native artery thrombosis, HR 2.57) and long-term dialysis (HR 3.66, 95% CI, 2.35-5.71, $P < .001$) were associated with poorer primary patency rates. Cumulative limb salvage at 24 months was 68.8% (95% CI: 59.5-78.1) with female gender (HR 3.34, $P = .002$) and thrombolysis ≥3 days (HR 2.35, $P = .019$) associated with an increased risk of limb loss. Overall 36-month survival was 84.5% (95% CI: 77.5-91.6). Women had decreased survival rates both in the short- and midterm (HR 6.29; 95% CI, 1.78-22.28; $P = .004$).**

Conclusions: **Endovascular therapy with thrombolysis remains an effective treatment option for patients presenting with lower extremity ALI. Thrombolysis should be limited to <3 days. Female gender negatively affects the rates of limb salvage and survival. (J Vasc Surg 2011;53:340-6.)**

Patients with peripheral arterial disease (PAD) of the lower extremities often suffer from chronic conditions including claudication, rest pain, or ulceration. A small subset of patients may suffer from acute limb ischemia (ALI), which can lead to loss of limb and life without prompt treatment.[1] This devastating condition requires prompt identification of the acute arterial occlusion in the leg and effective treatment. It remains a challenging scenario for clinicians. In addition to the limb ischemia, the systemic sequalae from ischemia can lead to high morbidity and mortality rates.[1]

After therapeutic anticoagulation is achieved, traditionally, urgent surgical intervention follows employing thromboembolectomy, placement of a bypass graft, or other techniques to restore arterial flow to the extremity. Early operative intervention, however, is associated with a significant risk of perioperative mortality. Mortality rates in excess of 25% following open surgical repair for ALI were reported in the late 1970s.[2] Jivegard and colleagues corroborated these findings a decade later, documenting a 20% mortality rate in patients undergoing operative revascularization for acute limb ischemia.[3] In spite of advances in surgical technique and perioperative care, the current risk of morbidity and mortality following open surgical intervention continues to be significant. The mortality rate of surgical revascularization performed in the setting of ALI remains high, mostly because many patients poorly tolerate an extensive procedure performed without adequate preoperative preparation.[4,5] Cardiopulmonary complications occur with frequency, accounting for an unacceptably high mortality rate over midterm follow-up. Individuals who present with ALI comprise one of the sickest subgroups of patients that the vascular specialist is asked to treat.[6] Furthermore, operative strategies are often suboptimal. Residual thrombus has been demonstrated in a large fraction of vessels after open surgical thrombectomies.[7,8]

The development of effective medications to dissolve occluding thrombus led to the increasing use of thrombolytic therapy in patients with ALI. Randomized control trials have provided a rationale for thrombolysis as a first

From the Department of Vascular Surgery,[a] and Department of Quantitative Health Sciences,[b] Cleveland Clinic.

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Reprint requests: Vikram S. Kashyap, MD, Cleveland Clinic, Department of Vascular Surgery, H32, 9500 Euclid Avenue, Cleveland, OH 44195 (e-mail: kashyav@ccf.org).

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step in patients with ALI vs immediate operative revascularization.[4,9,10] Catheter directed thrombolysis offers several potential advantages to lessen the pitfalls of open techniques. By utilizing an endovascular approach and local anesthesia, the risks of general anesthesia are minimized within a subgroup of patients that are at their physiologic limits. In addition, enzymatic dissolution of thrombus allows for more effective clot resolution particularly within distal arterial beds that are often resistant to open thrombectomy. Successful clot dissolution will unveil a "culprit" lesion responsible for initiating thrombosis. Experience has shown that patency rates are markedly dependent on the discovery and treatment of such underlying lesions.[11]

We have pursued an aggressive approach to limb salvage in patients with ALI and preferentially use endovascular therapy in these patients with thrombolysis and/or percutaneous mechanical thrombectomy (PMT) devices. The advent of PMT has allowed removing clot burden quickly and restoring flow to the foot during the initial angiogram. The purpose of this study was to review our contemporary experience treating ALI via endovascular therapy. The specific goals of the study were to assess periprocedural safety, technical outcome, procedural durability, and survival of this group of patients.

PATIENTS AND METHODS

Patient population. After Institutional Review Board (IRB) approval, a retrospective review was performed of patients at the Cleveland Clinic Foundation (CCF) from January 1, 2005 to September 30, 2007 who presented with ALI. A prospectively collected registry was queried using current procedural terminology (CPT) codes to identify all patients treated with endovascular techniques for ALI of the lower extremities. In this two and a half year interval, we identified 129 limbs in 119 patients that were consecutively treated for lower extremity ALI at our institution. During this time frame, approximately 20 patients underwent surgical therapy for ALI due to surgeon preference. All clinical, perioperative, and demographic data were obtained through review of the hospital and physician electronic records. The original angiographic imaging was reviewed via captured and stored electronic images (MagicView; Siemens Medical Systems, Malvern, Pa). Preoperative data were obtained including demographics, atherosclerotic risk factors, symptoms, and other clinical variables. ALI was defined as the sudden onset or worsening of ischemic manifestations within the lower extremities due to arterial thrombosis or embolism. The involved segment was further classified as native vessel or graft, the latter including both autogenous and prosthetic conduits. Previous endovascular therapy or open surgery on the affected ischemic side was recorded. Rutherford's classification of ALI was determined based on the physician initial evaluation that adhered to the published criteria.[12]

Operative technique. Endovascular procedures were performed by the faculty of the Cleveland Clinic Department of Vascular Surgery. Procedural technical details for all included limbs (N = 129) were recorded. During this time period, recombinant tissue plasminogen activator (rt-PA, Activase; Genentech, Inc, San Francisco, Calif) was used universally for thrombolysis at a dose of 0.5-1.0 mg/h. Adjuvant procedures were often needed (91%) and included both endovascular and open techniques to treat the "culprit lesion" after thrombolytic dissolution of the thrombus. These included endarterectomy, open bypass revision, angioplasty, and stenting. PMT was evaluated as an individual entity and included power-pulse techniques.[13] The AngioJet devices (Possis, Medical Inc, Minneapolis, Minn) were preferentially used for PMT. Thrombolysis days were based on the total number of days a patient underwent thrombolysis. Technical success was dependent on the re-establishment of in-line blood flow to the foot. The requirement of a new surgical bypass constituted a technical failure.

Data analysis and follow-up. Periprocedure data, associated morbidity, and mortality within 30 days of the procedure were determined. Long-term follow-up documentation of patency included the presence of palpable femoral/distal artery pulses, resolution of symptoms, and/or noninvasive vascular laboratory testing. The last included ankle-brachial indices (ABI), pulse-volume recordings (PVR), and color-flow Doppler ultrasound. We are able to obtain reliable follow-up data for the vast majority of patients with noninvasive vascular laboratory testing in 101/129 limbs (78%). The average length of follow-up was 16.8 months (range 0-43 months).

Primary and secondary patency and limb salvage were determined in concordance with the Society for Vascular Surgery guidelines.[12] Primary end points evaluated at a limb level (N = 129) were primary patency, secondary patency, and limb salvage while survival was evaluated at a patient level (n = 119). Primary patency was defined as the ability to maintain uninterrupted patency of the reference limb vasculature. Secondary patency was defined as the re-establishment of flow in the setting of re-thrombosis. Limb salvage was defined as freedom from major amputation above the foot level. The majority of patients had objective noninvasive vascular laboratory testing at follow-up visits planned for every 6 months. Loss of patency was determined by a drop in ABI greater than 0.15, and/or Doppler ultrasound findings of occlusion in the treated segment. Failures underwent repeat angiography. In a small fraction of patients, the loss of previously palpable pulses and/or recurrent symptoms, prompted angiography. Mortality was verified using the Social Security Death Index database.

Statistical methods. Summaries of the categorical factors were described using frequencies and percentages. The mean and standard deviation were used to summarize continuous measure distributions. Comparisons of success, thrombolysis days, and all 30-day outcomes except mortality were performed using generalized estimating equations with logistic and proportional odds regression. Thirty-day mortality was assessed using logistic regression. Long-term patency, limb salvage, and survival were assessed using time-to-event methods, including Kaplan-Meier estima-

Table I. Patient baseline characteristics (n=119)

Patient variables	*n (%)*
Male	70 (59)
Hypertension	84 (71)
Diabetes	28 (24)
Hyperlipidemia	60 (50)
Smoking[a]	82 (69)
CAD	66 (55)
Arrhythmia	11 (9)
COPD	14 (12)
Dialysis dependent	5 (4)
	Mean (SD)
Age (year)	63.7 (14.4)
Creatinine (mg/dL)	1.0 (0.4)

CAD, Coronary artery disease; *COPD,* chronic obstructive pulmonary disease.
[a]Within 10 years.

Table II. Limb baseline characteristics (N = 129)

Limb variables	*Percentage, N (%)*
Rutherford class	
I	88 (68)
IIa	30 (23)
IIb[a]	11 (9)
Thrombosis vessel	
Native artery	36 (28)
Graft	93 (72)
Thrombosis location	
Aortoiliac (AI)	29 (22)
Femoropopliteal (FP)	51 (40)
Tibial (T)	29 (22)
Multilevel	20 (16)
Previous ipsilateral revascularization	
Endovascular therapy	54 (42)
Either open revascularization or endovascular therapy	106 (82)

[a]One limb was Rutherford class III.

Table III. Procedural details (N = 129)

Technical variable	*N (%)*
Contralateral access	77 (60)
PMT	60 (47)
Thrombolysis days	
0-1	63 (49)
1-2	50 (39)
≥3	16 (12)
Adjuvant procedure	118 (91)
Endovascular	69 (54)
Open	17 (13)
Combined	32 (25)
Technical success	106 (82)

PMT, Percutaneous mechanical thrombectomy.

tion and Cox proportional hazards models. Marginal models were used where appropriate to adjust for multiple limbs per patient, where appropriate. Tests assumed a significance level of 0.05. Analyses were performed using SAS (version 9.1; Cary, NC) and initial plots were created using R software (version 2.4; Vienna, Austria).

RESULTS

Patients presenting with ALI of the lower extremities had significant comorbidities along with a long history of peripheral arterial disease. During the study interval, 119 patients underwent thrombolysis for ALI. Ten patients had either both limbs or different arterial regions affected by ALI. These patients had a mean age of 64 years (Table I), were the majority male (59%), and carried the atherosclerotic risk factors of hypertension (71%), diabetes (24%), hyperlipidemia (50%), and smoking (69%). This cohort had severe pre-existing PAD. One hundred and six of the 129 limbs affected by ALI (82%) had either prior surgical revascularization or prior endovascular therapy in the ipsilateral extremity (Table II). Graft thrombosis predominated (93, 72%). Upon presentation, the majority of limbs were categorized as Rutherford class I (88, 68%) or class IIa (30, 23%) ischemia. However, 10 limbs fell under the category of Rutherford class IIb and 1 limb was class III. These 11 limbs were combined for statistical purposes. The involved segment was distributed among the segments of the lower limb arterial tree with the femoropopliteal location being most affected and a subgroup of limbs (20, 16%) having multilevel thrombosis.

Procedural details from the interventions performed are summarized in Table III. From a technical standpoint, cases were mostly done from a contralateral femoral approach (60%). PMT was utilized in nearly half the cases (47%) in addition to thrombolysis. This included PMT to reduce thrombus burden at the beginning of the thrombolysis and during thrombolytic check angiograms, as well as, PMT utilized to lace the thrombus with thrombolytic agent ("power-pulse technique").[14] There were no PMT-related complications including hemolysis. The total number of thrombolysis days was divided into three subgroups: most limbs underwent 0-1 days (63, 49%) or 1-2 days (50, 39%), while a few limbs required 3 or more days (16, 12%). In an overwhelming majority of cases (91%), an adjuvant procedure was performed to treat the "culprit lesion" leading to thrombosis. This was a purely percutaneous endovascular procedure in 56%, an open surgical procedure in 15% and a combined approach in 28%. Technical success was achieved in 106 (82%) of treated limbs. Univariable analyses found that the location of the thrombus was associated with technical success. Femoropopliteal thrombosis (odds ratio [OR] 0.27) and tibial thrombosis (OR 0.10) fared poorly compared with thrombosis in the aortoiliac location (P = .02). In the remaining patients not characterized as a technical success (n = 23), surgical revascularization was successful (n = 5) or medical therapy (ie, anticoagulation, n = 3) sufficed in preventing limb loss. Early amputation was needed in 11 limbs, and an additional four patients died after technically unsuccessful cases.

The early (30-day) outcomes indicate that overall, 82% of patients were alive and had their limb intact after endovascular treatment for ALI. However, this was associated with a risk for procedure-related complications. Access site

Table IV. Univariable summaries of the associations with 30-day amputation are shown

Factor	*Level*	*Amputation %*	*Odds ratio (95% CI)*	P *value vs reference*	P *value overall*
Female	No	9.7	1.00		.038
	Yes	24.1	2.91 (1.06, 7.97)	.038	
Hypertension	No	18.9	1.00		.76
	Yes	14.6	0.84 (0.27, 2.60)	.76	
Diabetes	No	17.4	1.00		.37
	Yes	10.7	0.51 (0.11, 2.23)	.37	
Dialysis	No	15.7	1.00		.77
	Yes	20	1.39 (0.15, 13.20)	.77	
Hyperlipidemia	No	21	1.00		.15
	Yes	10.9	0.49 (0.18, 1.30)	.15	
Arrhythmia	No	17.5	1.00		.21F
	Yes	0	NA	.21F	
COPD	No	17.9	1.00		.12F
	Yes	0	NA	.12F	
Smoking	No	18.9	1.00		.31
	Yes	14.6	0.57 (0.19, 1.68)	.31	
Graft thrombosis	No	14.3	1.00		.73
	Yes	16.5	1.21 (0.40, 3.64)	.73	
Previous endovascular therapy	No	20.8	1.00		.36
	Yes	9.3	0.28 (0.00, 1502.4)	.77	
Rutherford class	1	14	1.00		.55
	2a	13.3	0.89 (0.30, 2.65)	.84	
	2b	40	2.71 (0.38, 19.36)	.32	
Location	Al	6.9	1.00		.071
	FP	10.2	1.70 (0.28, 10.40)	.57	
	T	24.1	4.34 (0.70, 26.83)	.11	
	Multilevel	31.6	7.03 (1.13, 43.55)	.036	
Adjuvant procedure	No	45.5	1.00		.008
	Yes	13	0.17 (0.04, 0.62)	.008	
PMT	None	14.7	1.00		.31
	PMT	21.1	2.16 (0.65, 7.20)	.21	
	PMT/PowerPulse	10	0.74 (0.04, 12.92)	.84	
Thrombolysis days	0-1	9.7	1.00		.012
	1-2	16.3	2.25 (0.58, 8.74)	.24	
	≥3	40	9.38 (2.06, 42.83)	.004	
Age	10 year increase		0.81 (0.55, 1.19)		.29
Creatinine (nondialysis)	Per unit increase		0.19 (0.03, 1.38)		.10

AI, Aortoiliac; *CI,* confidence interval; *COPD,* chronic obstructive pulmonary disease; *F,* Fisher exact test; *FP,* Femoropopliteal; *PMT,* percutaneous mechanical thrombectomy; *T,* Tibial, which does not adjust for correlation within patient was used, due to non-convergence of the GEE logistic regression model. *P* values are from Wald tests of the odds ratio.

hematoma (11%), bleeding requiring transfusion (8%), and compartment syndrome (4%) occurred after ischemia-thrombolysis-reperfusion. A single patient (0.76%) developed intracranial bleeding. Mortality was observed in seven patients (6%), four occurring after amputation. All of the early mortalities occurred in female patients ($P = .002$). In addition to gender, technical failure was predictive of mortality (OR, 5.88; 95% confidence interval [CI], 1.23-33.3; $P = .03$).

Twenty limbs required early amputation (15.5%); 11 after unsuccessful thrombolytic cases, as outlined above. On univariable analysis, factors associated with early amputation are displayed in Table IV. These included female gender (OR, 2.91; 95% CI, 1.06-7.97; $P = .038$) and three or more thrombolysis days (OR, 9.38; 95% CI, 2.06-42.83; $P = .004$). Technical failure was also associated with 30-day amputation (OR, 8.33; 95% CI, 2.86-25.0; $P < .001$). Furthermore, an adjuvant procedure treating the "culprit lesion" was predictive of improved outcomes and decreased risk of amputation at 30 days (OR, 0.17; 95% CI, 0.04-0.62; $P = .008$). There was a trend for tibial thrombosis (OR 4.34) or multilevel thrombosis (OR 7.03) to increase the risk of amputation.

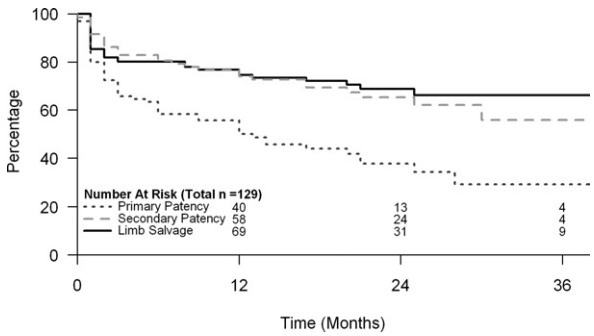

Fig 1. Kaplan-Meier estimates of primary patency, secondary patency, and limb salvage for the entire cohort are shown. Standard error <10% for all of the curves displayed.

Table V, A. The multivariable model for primary patency loss is summarized

Measure	*Level*	*Hazard ratio (95% CI)*	P *value vs reference*	P *value overall*
Dialysis	Yes	3.66 (2.35, 5.71)	<.001	<.001
Graft thrombus	Yes	2.57 (1.24, 5.33)	.012	.012
Location[a]	Fempop	2.63 (1.13, 6.12)	.025	.024
	Tibial	2.80 (1.09, 7.21)	.033	
	Multilevel	1.03 (0.38, 2.80)	.95	
Technical success	Yes	0.25 (0.11, 0.56)	<.001	<.001

P values are from the Cox proportional hazards model.
CI, Confidence interval.
[a]Compared to aortoiliac location.

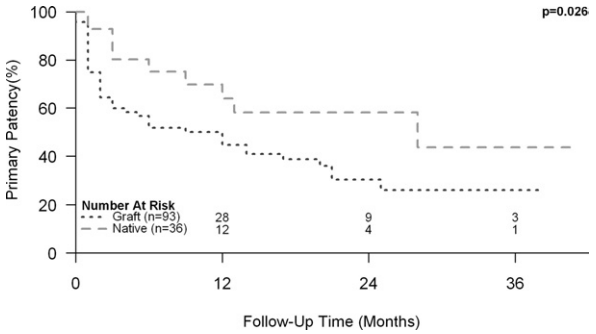

Fig 2. Kaplan-Meier estimates of primary patency comparing graft vs native artery thrombolysis. Standard error <10% for all of the curves displayed.

Primary patency, secondary patency, and limb salvage were assessed using time-to-event methods (Fig 1). Primary patency for the entire cohort at 12 and 24 months was 50.1% (95% CI, 39.5-60.7) and 37.7% (95% CI, 26.2-49.1), respectively. Secondary patency at 12 and 24 months was 74.0% (95% CI, 64.9-83.1) and 65.3% (95% CI, 54.5-76.2), respectively. A multivariable model for primary patency loss was constructed (Table V, A). Patients presenting with femoropopliteal (hazard ratio [HR] 2.63) or tibial thrombosis (HR 2.80), and graft thrombosis (vs native artery thrombosis, HR 2.57, Fig 2) were associated with poorer primary patency rates. Primary patency at 12 months was not achieved in each of the five patients requiring long-term dialysis (HR 3.66, 95% CI, 2.35- 5.71, $P <$ .001).

Limb salvage at 12 months was 74.6% (95% CI, 66.5-82.7) and at 24 months was 68.8% (95% CI: 59.5-78.1). Multivariable modeling (Table V, B) revealed that female gender (HR 3.34, $P = .002$) and thrombolysis ≥3 days (HR 2.35, $P = .019$) were associated with an increased risk of limb loss. As expected, initial technical success (HR 0.32) and performance of an adjuvant procedure (HR 0.30) were associated with lower rates of amputation long-term.

Survival of the entire cohort at 12 months was 85.7% (95% CI, 79.0- 92.5) and at 24 months and 36 months was 84.5% (95% CI: 77.5-91.6, Fig 3). Female patients were found to have decreased survival rates both related to early postprocedure deaths and during the first year in follow-up (HR 6.29; 95% CI, 1.78-22.28; $P = .004$). Chronic obstructive pulmonary disease (COPD) (HR 3.18) and each 10-year increase in age (HR 1.71) were the other variables found to be associated with decreased survival on multivariable modeling (Table V, C).

DISCUSSION

ALI of the lower extremities remains a challenging entity for clinicians with significant limb loss and mortality. Prospective randomized trials have shown that a thrombolysis-first strategy allows for rates of limb salvage and survival that rival open surgical revascularization.[4,9,10] Furthermore, advances in endovascular techniques have made the percutaneous treatment of underlying "culprit" lesions; thus, allowing the treatment of ALI with just an arterial puncture.

Our study re-confirms that thrombolysis can be performed relatively safely from the perspective of complications and with robust technical success. Our results indicate that a vast majority of patients (82%) treated with endovascular therapy can survive an episode of ALI with their limbs intact. In over 90% of cases, dissolution of the thrombotic occlusion with thrombolytic therapy uncovered a lesion that could be treated via either endovascular methods or with a limited surgical operation. Thrombolysis did not lead to a high rate of bleeding complications as often feared. Transfusion requirement (8.5%) and intracranial bleeding (0.76%) rates were low and compared favorably with results from open surgical revascularization for ALI.[3, 9, 15]

However, these results paint a sobering picture for some patients presenting with ALI. Survival in the near- and midterm was worse for females. This was skewed by the fact that all 30-day mortalities occurred in women. Additionally, review of the survival curves showed continued mortality in the first year after ALI for women, but not so for men. Whether the inflammatory milieu is more severe in females or that females with ALI represent a more virulent form of atherothrombosis remains unknown. Regardless, these results point to increased caution for thrombolysis in female patients. The 30-day amputation rate was 15.9%, which is not negligible but similar to other reports on ALI.[14, 16-18] Correlated with increased early amputation was female gender. Given anatomic differences in vessel size,

Table V, B. The multivariable model for limb loss is summarized

Measure	*Level*	*Hazard ratio (95% CI)*	P *value vs reference*	P *value overall*
Gender	Female	3.34 (1.58, 7.07)	.002	.002
Adjuvant procedure	Yes	0.30 (0.13, 0.72)	.007	.007
Thrombolysis days[a]	1-2	0.83 (0.35, 1.96)	.67	.013
	≥3	2.35 (1.15, 4.80)	.019	
Technical success	Yes	0.32 (0.16, 0.63)	.001	.001

P values are from the Cox proportional hazards model.
CI, Confidence interval.
[a]Compared to 1 day.

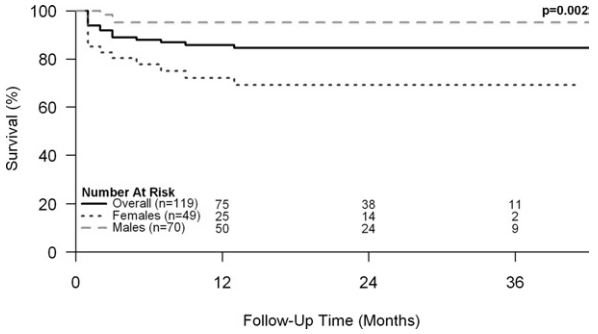

Fig 3. Kaplan-Meier estimates of survival for the entire cohort and by gender. Standard error <10% for all of the curves displayed.

Table V, C. The multivariable model for long-term survival is summarized

Measure	*Level*	*Hazard ratio (95% CI)*	P *value vs reference*	P *value overall*
Gender	Female	6.29 (1.78, 22.28)	.004	.004
COPD	Yes	3.18 (1.08, 9.31)	.035	.035
Age	10-year increase	1.71 (1.09, 2.69)	.021	.021

CI, Confidence interval; *COPD,* chronic obstructive pulmonary disease.
P values are from the Cox proportional hazards model.

female patients may tolerate less thrombus burden and therefore have poorer results with thrombolysis. In addition, 3 or more days of thrombolysis were associated with amputation. We suspect that this is due to greater thrombus burden and/or thrombus resistance to thrombolysis. Patients requiring three or more days of thrombolysis may have components of chronic thrombosis (despite their acute presentation) that is resistant to fibrinolytic therapy. Thus, these patients will not have complete dissolution of the thrombotic material but accrue increasing risk with persistent thrombolytic infusion.[11,19] This finding has led to a change in our practice of limiting arterial thrombolysis to <3 days. An aggressive posture for the treatment of ALI remains warranted, but thrombolysis should be stopped if patency is not restored in <3 days. Lastly, graft thrombosis treated with thrombolysis fared worse in regard to patency than native artery thrombosis. Although not directly evaluated given the small numbers, this may be explained by polytetrafluoroethylene (PTFE) bypasses in the femoropopliteal location and the increased loss of collaterals with thrombosis.

The outcome of patients with embolic vs thrombotic causes of arterial occlusion is of great interest. This could not be directly assessed in this study for multiple reasons. The decreasing prevalence of rheumatic heart disease underlies the diminishing impact of embolic causes for acute limb ischemia. Only 9% of our cohort had a documented arrhythmia and in reviewing the original images, only a handful of cases had clear intraluminal emboli with characteristic angiographic findings. However, in many cases, embolus with subsequent proximal and distal thrombosis may mimic in situ thrombosis. Thus, for our analyses, we stratified the patients between native arterial ALI vs graft thrombosis. We believe a portion of patients with native artery thrombosis were from embolic causes.

Kuoppala and colleagues reviewed their experience with thrombolysis for lower limb ischemia.[16] They compiled their outcomes in 220 cases in 195 patients. However, this included 31 patients with nonacute ischemia. The overall results were positive with high rates of successful restoration of blood flow, complete thrombus dissolution, and few major complications. During a medial follow-up of 32 months, 57 (26%) amputations were performed. Risk factors associated with amputations included diabetes, motor deficit on presentation and again, female gender.

In the United Kingdom, a national audit of thrombolytic cases over a 10-year period has been published.[18] The National Audit of Thrombolysis for Acute Leg Ischemia (NATALI) study compiled results in 1133 thrombolytic cases, mostly using rt-PA. The overall amputation-free survival (AFS) was 75%, with a 12% rate of amputation and a 12% rate of death in the first 30 days. Mirroring our findings, on multivariable analysis, female gender was associated with increased risk for mortality ($P = .006$). Also, increasing age, duration of ischemia, and Fontaine grade proved to be related to AFS.

The "power-pulse" technique has been used to limit ischemia time by restoring in-line blood flow as soon as feasible. Allie and colleagues have utilized a rheolytic PMT device to deliver either urokinase or tenecteplase at high pressure to lace the thrombus.[14] This theoretically allows better clot penetration and expedited fibrin degradation. Then, the PMT device is used to evacuate as much throm-

bus burden at the initial angiogram. In 49 patients with ileofemoral thrombosis, mean procedure times were only 73 minutes. Success rates were high and limb salvage at 30 days was 91%. Similarly, Ansel and colleagues described their experience with PMT in 99 consecutive patients.[17] In a majority of patients (71%), a substantial to complete amount of the thrombotic occlusion was removed on initial therapy with only 37% requiring additional thrombolysis. Multiple studies appear to signal a shift from thrombolysis only to PMT/thrombolysis to hasten reperfusion with acceptable early results.[20] In our experience, only 20 limbs underwent the "power pulse" technique while an additional 38 limbs had PMT used during their endovascular procedures. We did not show a benefit with PMT in our analysis. However, it is likely our study suffers from a selection bias in that the PMT devices were used in more recent patients with greater clot burden and progressively worsening ALI symptoms.

Admittedly this study is with several important limitations. First, it represents a retrospective review of database and medical records without comparable controls. Many of the patients were from outside institutions transferred to our tertiary care facility. Thus, our cohort may not represent the normal ALI population and our results may not be generalizable. Many of the patients had multiple procedures in the past with variables that may not have been accounted for. Patients living far away limited follow-up in some instances, and the planned post-procedure vascular laboratory testing was not obtained in all patients. Despite these limitations, we feel this study further validates the role for endovascular therapy in the treatment of ALI. Although significant advances have been made in endovascular therapeutic modalities, ALI of the lower extremities still carries significant morbidity and mortality. Limiting the duration of thrombolysis and employing increased vigilance in our female patients may further improve outcomes.

AUTHOR CONTRIBUTIONS

Conception and design: VK, RG, TS
Analysis and interpretation: VK, RG, JB, MB, TS
Data collection: VK, RG, MB
Writing the article: VK, RG
Critical revision of the article: VK, RG, JB, MB, TS
Final approval of the article: VK, RG, JB, MB, TS
Statistical analysis: VK, JB
Obtained funding: VK
Overall responsibility: VK

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