Analysis of the results of endovascular and open surgical treatment of acute limb ischemia

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ABSTRACT

Objective: The objective of this study was to evaluate the long-term estimates of limb salvage and survival in patients with acute limb ischemia (ALI) receiving open surgery or endovascular revascularization.

Methods: This was a retrospective consecutive cohort study of patients with ALI who underwent open surgery or endovascular treatment at the Vascular and Endovascular Surgery Unit, Hospital do Servidor Público Estadual (São Paulo, Brazil), between July 2010 and July 2016. The overall mortality, limb salvage, and survival rates at 720 days were analyzed in both the open surgery (group 1) and endovascular treatment (group 2) groups.

Results: A total of 69 patients were admitted for a limb salvage procedure. The mean follow-up period was 822 ± 480.5 days. All of the analyses were performed at 720 days. Of the 69 patients, 46 (66.6%) were in group 1 and 23 (33.4%) in group 2. The clinical characteristics were similar between the groups, except for higher rates of chronic kidney disease ($P = .04$) and arrhythmia ($P = .01$) in group 1. Group 1 had a higher postoperative ankle-brachial index ($P = .03$). Concerning the Rutherford classification, group 1 had a higher prevalence of Rutherford IIB ALI ($P = .003$). The preoperative creatine kinase level was higher in group 1 than in group 2 (780 [range, 198-6546] mg/dL and 245 [65-78] mg/dL, respectively). A creatine kinase level >200 mg/dL was seen in 65.2% and 47.8% of patients in group 1 and group 2, respectively ($P = .028$). The limb salvage and overall survival estimates at 720 days were similar between group 1 and group 2 (79.2% vs 90.6% [$P = .27$] and 53% vs 60.8% [$P = .45$], respectively). The overall mortality rate was 10.1% (seven patients) within the first 30 days, and it was higher in group 1 (six patients [13.0%]; $P = .03$).

Conclusions: Both open surgery and endovascular procedures are safe treatments of patients with ALI, with acceptable limb salvage and survival rates. No previous study has suggested the preferred treatment of ALI. However, based on this study and the overall literature, endovascular treatment may be the preferred treatment of patients with Rutherford I and IIA ALI; open surgery may be the best option for ALI due to arterial embolism and for Rutherford IIB acute arterial thrombosis because of a greater urgency to restore blood flow. (J Vasc Surg 2019;69:843-9.)

Keywords: Acute limb ischemia; Arterial embolism; Arterial thrombosis; Endovascular surgery; Arterial surgery

Acute limb ischemia (ALI) represents one of the most common emergencies in vascular surgery. Some studies have shown an incidence of 22 per 100,000 patients per year.[1] The treatment of ALI is still a challenge for vascular surgeons, considering the clinical gravity of patients admitted with this condition and the vast therapeutic modalities available. The reported major amputation rates range from 15% to 50%.[2]

During past years, endovascular treatment, especially catheter-directed thrombolysis (CDT), has shown similar efficacy to open surgical revascularization in terms of limb salvage and mortality rates in patients with ALI.[3] However, endovascular treatment has some limitations associated with the time required to remove the thrombus and the higher risk of hemorrhagic complications.[4]

The main objective of this study was to determine the long-term estimates of limb salvage and survival in patients with ALI receiving open surgery vs endovascular revascularization.

METHODS

This study was approved by the research ethics committee. Informed consent of the patients was obtained for the study. The design of the study was a retrospective consecutive cohort study of patients with ALI who underwent open surgery or endovascular treatment at the Division of Vascular and Endovascular Surgery, Hospital do Servidor Público Estadual (São Paulo, Brazil), between July 2010 and July 2016. All of the patients' data, comprising demographic and epidemiologic characteristics and outpatient follow-up results, were collected from the vascular surgery service database using Microsoft Access (Microsoft, Seattle, Wash). Whenever it was necessary, the hospital records database were also consulted. The details of the surgical procedures were obtained from the database and patients' records.

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The inclusion criteria were patients with ALI who had undergone open surgery or endovascular revascularization classified according to the Rutherford system as I, IIA, or IIB.[5] Arterial duplex ultrasound or arteriography was performed to determine the cause of ALI, according to the decision of the vascular surgeon who admitted the patient to the emergency department and who was also responsible for selecting the most appropriate intervention to treat the patient's condition. The arteriography procedures were re-evaluated to confirm the precise execution of the departmental protocols. Moreover, the arteriography procedures were classified according to the TransAtlantic Inter-Society Consensus II classification, as were the diameters and lengths of the catheter balloons and stents used to repair the arterial lesions and other factors associated with the endovascular treatments.[6,7]

Irreversible limb ischemia, classified as Rutherford III,[5] was the only exclusion criterion, for which the only possible treatment was major amputation.

Based on the treatment performed, the patients were classified into two groups: open surgical revascularization (group 1), mainly including bypass surgery and embolectomy; and endovascular treatment (group 2). The endovascular treatment was CDT, following our department surgery protocols, using intra-arterial recombinant tissue-type plasminogen activator at a loading dose of 10 mg to the maximum of 20 mg in the operating room by the pulse-spray technique, followed by a dose of 1 mg/h in the intensive care unit. All patients received intravenous unfractionated heparin (UFH) at a loading dose of 80 units/kg in the operating room, followed by infusion at 300 to 500 units/h intravenously in the intensive care unit. The infusion dose of UFH was adjusted to achieve the therapeutic activated partial thromboplastin time established by the hospital laboratory every 4 to 6 hours. Arteriography controls were performed every 12 hours for 48 hours, the maximum time of intra-arterial thrombolysis. The catheter of choice was the Fountain Infusion System (Merit Medical Systems, South Jordan, Utah). The fibrinogen levels were dosed every 4 to 6 hours, in a level of 200 to 400 mg/dL. If the level was <200 mg/dL, intra-arterial thrombolysis was immediately suspended.

Initial technical success using CDT was defined as no more than 30% residual stenosis and prompt restoration of blood flow in a formerly stenotic or occluded artery. Procedures such as angioplasty and stent replacement were performed whenever needed.

All of the patients were scheduled for follow-up at the hospital at 15 days and at 1 month, 3 months, 6 months, and 12 months after discharge. The patients were followed up every 6 months after the first year and every 12 months after the second year, at which clinical visit the following clinical criteria were evaluated: pulse palpation, ankle-brachial index, and presence of symptoms.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective, single-center cohort study
- **Key Findings:** Endovascular and open surgical revascularizations in 69 patients presenting with acute limb ischemia resulted in similar 6-year survival (53% vs 60.8%) and limb salvage rates (79.2% vs 90.6%). Patients with arrhythmia and more advanced disease (Rutherford IIB) were more frequently treated by open surgery.
- **Take Home Message:** This study suggests that acute limb ischemia can be treated by either endovascular or open surgical techniques, with similar long-term survival and limb salvage rates. Those with emboli or more severe ischemia may benefit more from open surgical treatment.

Statistical analyses were performed using SPSS 15.0 for Windows (SPSS Inc, Chicago, Ill). Frequencies and descriptive statistics were analyzed. The χ^2 test and Student *t*-test were used to compare the univariate analysis data. Survival curves to estimate limb salvage and survival rates were constructed using the Kaplan-Meier method. A P value $<.05$ was considered statistically significant. The Mann-Whitney and Wilcoxon tests were used as nonparametric tests. All of the analyses were conducted within 720 days of the procedure.

RESULTS

A total of 86 patients were admitted to the emergency department with ALI between July 2010 and July 2016. Seventeen patients diagnosed with Rutherford III irreversible ALI were excluded. All of these 17 patients were submitted to a primary major amputation, without an attempt at revascularization, because of irreversible limb ischemia. Thus, 69 patients were scheduled to undergo a limb salvage procedure. The mean clinical follow-up period was 822 ± 480.5 days. All of the analyses were conducted at 720 days. Of the 69 patients, 46 (66.6%) were classified in group 1 and 23 (33.4%) in group 2. The clinical characteristics of the patients are shown in Table I, and the perioperative and postoperative data are listed in Table II.

The clinical characteristics were similar between the two groups, except for a higher prevalence of chronic kidney disease in group 1 ($P = .04$) and a higher incidence of arrhythmia in group 1 ($P = .01$; Table I). Group 1 had a higher postoperative ankle-brachial index ($P = .03$) and a higher prevalence of Rutherford IIB ($P = .003$). The femoropopliteal segment was the segment most affected by acute arterial occlusion (63.5%). There was a higher incidence of aortoiliac occlusion in group 1 ($P = .04$). The main cause of ALI was arterial embolism in group 1 (64.5%) and native arterial thrombosis in group

Table I. Clinical characteristics

Variable	Total (N = 69)	Group 1 (n = 46; 66.6%)	Group 2 (n = 23; 33.4%)	*P* value
Age, years	75.53 ± 11.96	72.85 ± 8.3	73.48 ± 7.2	.73
Female	43 (62.3)	28 (60.8)	15 (65.2)	.45
Hypertension	62 (89.8)	43 (93.4)	19 (86.3)	.57
Diabetes	30 (43.4)	20 (43.4)	10 (43.4)	.41
Ischemic heart disease	15 (21.7)	10 (21.7)	5 (21.7)	.54
Chronic renal failure	12 (17.3)	11 (23.9)	7 (4.3)	.04
Arrhythmias	16 (23.1)	15 (32.6)	1 (4.3)	.01

Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation.

Table II. Perioperative and postoperative data

Variable	Total (N = 69)	Group 1 (n = 46; 66.6%)	Group 2 (n = 23; 33.4%)	*P* value
Preoperative ABI	0.35	0.30	0.42	.14
Postoperative ABI	0.8	0.9	0.7	.03
Rutherford class				
I	9 (13)	3 (6.5)	6 (26)	.03
IIA	30 (43.5)	19 (41.3)	11 (47.8)	.09
IIB	30 (43.5)	24 (52.2)	6 (26)	.003
Surgical complications	17 (24.6)	13 (28.3)	4 (17.4)	.04
Segment occluded				
Aortoiliac	23 (33.3)	17 (37)	5 (21.7)	.04
Femoropopliteal	44 (63.8)	28 (60.8)	17 (67.5)	.10
Infrapopliteal	2 (2.9)	1 (2.2)	1 (4.3)	.09

ABI, Ankle-brachial index.
Categorical variables are presented as number (%).

2 (86.9%). There was one case of acute bypass occlusion and two cases of acute stent occlusion in group 2.

Group 1 had the highest rate of surgical complications (35.5%; *P* = .04), the most common of which was wound infection, which occurred in eight patients (13%). In group 2, there was one case of wound infection due to an infected fasciotomy and one fatal case of hemorrhagic stroke. There were six cases of pneumonia (four in group 1 and two in group 2). The preoperative creatine kinase level was higher in group 1 than in group 2 (780 [range, 198-6546] mg/dL and 245 [65-78] mg/dL, respectively). A creatine kinase level >200 mg/dL was seen in 65.2% and 47.8% of patients in group 1 and group 2, respectively (*P* = .028). There were 11 patients who underwent fasciotomy, 8 patients in group 1 (17.3%) and 3 patients in group 2 (13%), with no statistical differences between these groups (*P* = .46). The findings at fasciotomy did not influence amputation (*P* = .61), as seen in Table III in a Cox regression.

Regarding open surgical procedures, embolectomy was most commonly performed (58.7%), followed by bypass surgery (41.3%) in group 1 (Table IV). In group 2, the prevalence of CDT was 65.2%; 34.8% were treated with primary angioplasty, followed by stent placement. Recombinant tissue-type plasminogen activator (Actylise) was the fibrinolytic agent of choice. The medium CDT duration was 12 (range, 1-36) hours. UFH was used in 74.6% and enoxaparin in 25.4% of patients postoperatively, with no differences between the groups (*P* = .15). Intravenous alprostadil (Prostavasin) was used in 5.6% of patients in both groups (*P* = .40). In group 2, stents were used in 16 patients (60.5%). The results of the endovascular procedures are listed in Table V.

The overall mortality rate (OMR) was 10.1% (seven patients) within the first 30 days. Group 1 had a higher OMR (six patients [13.0%]; *P* = .03). The causes of death in group 1 were heart attack (n = 2), pneumonia (n = 2), and sepsis (n = 2). The median creatine kinase level in those patients was 1980 (678-3532) mg/dL; thus, all had creatine kinase levels higher than 200 mg/dL. In group 2, there was one death due to hemorrhagic stroke. During the study period, there were 12 amputations, and the prevalence of above-the-knee amputations was 85%, with no differences between the groups (*P* = .15).

The limb salvage and overall survival estimates at 720 days were similar between group 1 and group 2 (79.2% vs 90.6% [*P* = .27] and 53% vs 60.8% [*P* = .45], respectively; Figs 1 and 2). The causes of death at 720 days in group 1 were hemorrhagic shock (2.2%) due to massive intestinal bleeding, septic shock (2.2%),

Table III. Cox regression analysis of factors associated with the limb salvage rate

	Univariate analysis				Multivariate analysis			
Variable	B	HR	95% CI	*P*	B	HR	95% CI	*P*
Rutherford classification	0.517	6.00	0.128-2.767	.068	0.597	7.00	0.226-10.060	.880
Female sex	0.299	0.830	0.262-2.297	.547	1.296	1.03	0.820-4.681	.642
Chronic kidney disease	13.759	10.42	0.680-2.051	.714	8.11	3.71	0.538-4.567	.831
Diabetes	0.984	0.869	0.221-1.501	.864	0.885	0.906	0.411-14.294	.831
Segment occluded	13.230	0.913	0.331-1.429	.649	1.032	0.571	0.331-4.234	.552
Fasciotomy	0.401	0.803	0.231-0.803	.615	0.249	0.252	0.619-1.429	.618
Type of surgery	0.686	0.913	0.542-1.543	.936	0.711	0.915	0.339-12.230	.437

CI, Confidence interval; *HR*, hazard ratio.

Table IV. Open surgical bypasses (N = 19)

	No. (%)
Proximal anastomosis	
Aorta	1 (5.3)
Axillary	1 (5.3)
Iliac	1 (5.3)
Common femoral	10 (52.5)
Superficial femoral	3 (15.8)
Profunda femoris	3 (15.8)
Distal anastomosis	
Common femoral	7 (36.9)
Popliteal	6 (31.5)
Tibioperoneal trunk	1 (5.3)
Anterior tibial	1 (5.3)
Posterior tibial	2 (10.5)
Peroneal	2 (10.5)
Arterial substitute	
PTFE	8 (42.1)
Dacron	2 (10.5)
Great saphenous vein	8 (42.1)
Cephalic vein	1 (5.3)

PTFE, Polytetrafluoroethylene.

Table V. Endovascular procedures

	No. (%)
Arterial segment treated	
Iliac	6 (26)
Femoropopliteal	13 (56.5)
Infrapopliteal	4 (17.5)
Procedures	
Angioplasty	8 (34.7)
CDT + angioplasty	11 (47.8)
CDT + bypass	1 (4.3)
CDT	3 (13)
Stents	
Balloon-expandable stent	6 (26.2)
Self-expandable stent	8 (34.7)
None	9 (39.1)

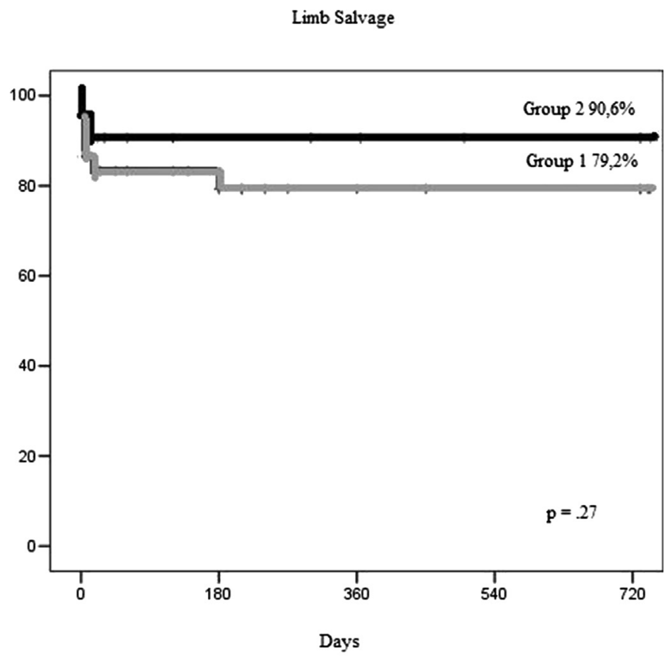
CDT, Catheter-directed thrombolysis.

acute coronary ischemia (2.2%), pneumonia (4.4%), and mesenteric thrombosis (2.2%) leading to acute bowel ischemia. In group 2, the causes of death at 720 days were hemorrhagic stroke (4.3%), septic shock (4.3%), and respiratory failure (4.3%).

A Cox regression analysis was performed to identify factors related to the limb salvage rate (Table III). None of them was associated with a worse limb salvage rate.

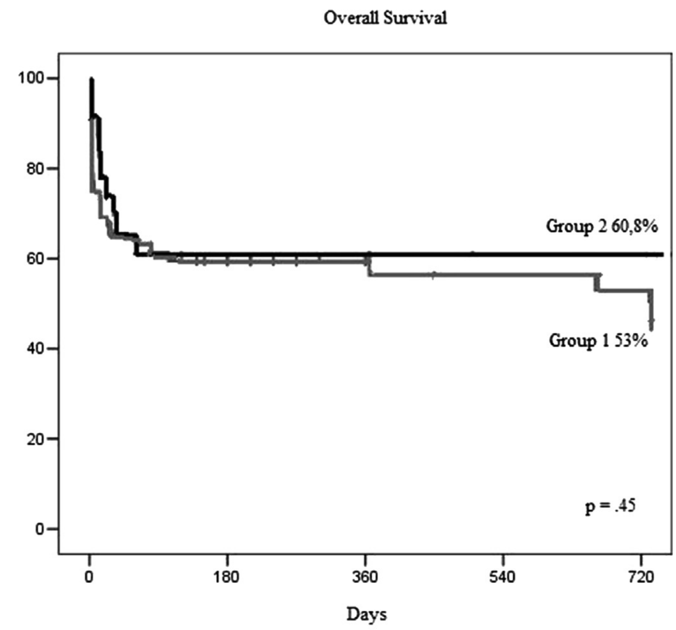
DISCUSSION

A vast amount of literature has been published on endovascular and open surgical procedures for ALI; however, there is no consensus regarding the best therapeutic strategy for this threatening condition. Ouriel et al[8] compared thrombolytic therapy with operative revascularization for treatment of ALI and found a better event-free survival rate at 12 months in the thrombolysis group than in the open surgery group (75% vs 52%; $P = .02$). The survival rate at 12 months was also better in the thrombolysis vs open surgery group (84% vs 58%; $P = .01$). On the other hand, in this study, the 12-month survival rates were statistically similar between the groups (53% and 60.8% in group 1 and group 2, respectively). However, group 1 had a higher 30-day OMR (13%; $P = .03$). This could be explained by the higher prevalence of patients assigned to Rutherford IIB, associated with a much worse clinical condition, in group 1 ($P = .003$). In support of the greater clinical severity in group 1, the creatine kinase level was higher in group 1 compared with group 2 ($P = .028$) because of more severe ischemia in group 1. All patients who died in group 1 presented with elevated creatine kinase levels (>200 mg/dL). Despite the worse condition of patients in group 1, the limb salvage rates were statistically similar between the groups. These results suggest that despite the greater clinical severity of patients who undergo open surgery, this treatment remains the proper indication for patients with Rutherford IIB ALI.



At risk Days	0	180	360	720
Group 1	46	20	14	12
Group 2	23	14	11	8

Fig 1. Kaplan-Meier curves for the limb salvage rate. The limb salvage rate at 720 days was 79.2% in group 1 and 90.6% in group 2 with a standard error <10%.



At risk Days	0	180	360	720
Group 1	46	18	18	11
Group 2	23	13	13	13

Fig 2. Kaplan-Meier curves for the survival rate. The survival rates at 720 days were 53% in group 1 and 60.8% in group 2 with a standard error <10%.

Taha et al[9] evaluated 154 limbs of 147 patients treated with endovascular repair (ER group) compared with 326 limbs of 296 patients treated with open repair (OR group). Among the Rutherford II patients, technical success was achieved in 90.7% of patients in the OR group vs 79.9% in the ER group ($P = .002$), with amputation rates of 10.0% vs 7.2% ($P = .35$) at 30 days and 16.3% vs 13.0% ($P = .37$) at 1 year, respectively. The 30-day OMRs were 13.2% (OR group) and 5.4% (ER group; $P = .012$). Similarly, in this study, the 30-day OMR was higher in group 1 (open surgery); however, the 12-month survival rates were similar between the groups, indicating that both treatments achieved similar results after hospital discharge. Obviously, it is important to note that in this cohort, the open surgery group had more patients with Rutherford IIB ALI and higher creatine kinase levels, which is a severe condition requiring prompt intervention to restore blood flow as soon as possible.

In a Cochrane review, Berridge et al[10] evaluated five trials involving 1283 patients, comparing thrombolysis and surgery for the initial treatment of ALI. There was no significant difference in the limb salvage or mortality rate at 30 days, 6 months, or 1 year between the surgery and thrombolysis groups. However, stroke was significantly more frequent at 30 days in the thrombolysis group (1.3%) compared with the surgery group (0%; odds ratio, 6.41; 95% confidence interval, 1.57-26.22). Participants treated by initial thrombolysis displayed an equivalent overall survival rate compared with initial surgery (odds ratio, 0.87; 95% confidence interval, 0.61-1.25). The authors concluded that initial treatment with either surgery or thrombolysis cannot be advocated universally on the basis of the available evidence. Their results are comparable to those of our study, in which the OMR in all patients was 10.1% (seven patients) within the first 30 days; group 1 had a higher OMR (six patients [13.0%]; $P = .03$). The most common surgical procedure in group 1 was embolectomy for arterial embolism as the main cause. The best way to treat arterial embolism remains traditional embolectomy surgery using Fogarty catheters. CDT cannot completely remove cardiac thrombi, preventing sufficiently prompt restoration of blood flow after the procedure. In our study, no cases of arterial embolism were treated with CDT.

In a recent review of patients treated with thrombolysis, Ebben et al[11] aimed to evaluate the treatment results and to identify possible predictors of outcome and bleeding complications. A total of 109 cases were evaluated. In 79% of cases, clinical improvement was observed. The limb salvage rates at 30 days and 6 months were 94% and 90%, respectively. Major bleeding complications were observed in 13% of cases. The median duration of thrombolysis was 27 (range, 4-68) hours. The overall mortality estimates at 30 days and 6 months were 7% and 16%, respectively, and there were no deaths related to bleeding complications. The main predictive factors related to a worse outcome were age, popliteal artery occlusions, and an advanced chronic vascular stage. Moreover, factors like age, female sex, and cardiac history were associated with increased risk of bleeding. In this cohort, in group 2 (endovascular treatment), the prevalence of CDT was 65.2%, and one case of bleeding occurred, which was caused by hemorrhagic stroke and led to death. A Cox regression analysis was performed to identify any other factors related to the limb salvage rate in our study (Table III), but no factors were associated with a worse limb salvage rate. However, in the univariate analysis, there was a statistical tendency toward an association between the Rutherford classification and a worse limb salvage rate ($P = .068$). Perhaps in a larger sample of patients, the Rutherford classification would have shown a significant impact on the limb salvage rate, although this variable was not significant in our multivariate analysis ($P = .880$). These results further suggest that patients with Rutherford IIB ALI have better outcomes with open surgical repair compared with CDT.

The clinical characteristics were similar between our two groups, except for higher rates of chronic kidney disease ($P = .04$) and arrhythmia ($P = .01$) in group 1. Group 1 had a higher postoperative ankle-brachial index ($P = .03$) and a higher rate of Rutherford IIB ALI ($P = .003$). Despite the higher 30-day OMR in group 1, the survival rates were similar at 720 days. These results indicate that open surgery is effective and safe in Rutherford IIB patients because of a necessity for prompt blood flow restoration, which cannot be achieved by pharmacologic intra-arterial fibrinolysis. Including not only the embolectomy surgery, indeed, we have shown about 19 cases of surgical bypass, including distal bypasses. Perhaps with the introduction of pharmacomechanical fibrinolysis and new endovascular systems and technologies, this scenario can be changed.

There are few studies on pharmacomechanical fibrinolysis. Leung et al[12] presented the results of rheolytic pharmacomechanical thrombectomy (PMT) for the management of ALI, as reported in the Peripheral Use of AngioJet Rheolytic Thrombectomy with a Variety of Catheter Lengths (PEARL) registry. Concerning this study, 147 procedures (52%) were performed without adjunct CDT. The limb salvage and overall survival rates were 81% and 91%, respectively, at 12 months. Moreover, the incidence of major bleeding was 9% at 12 months, and the prevalence of renal failure was 5%, also at 12 months. There were significantly better outcomes in patients without infrapopliteal disease and in those who underwent PMT without needing CDT. Besides, there were higher rates of technical success (88% vs 74%; $P = .021$), 12-month amputation-free survival (87% vs 72%; $P = .028$), and 12-month freedom from amputation (96% vs 81%; $P = .01$) in the PMT without CDT group. New studies are necessary to compare PMT with open surgery to establish the best treatment options for patients with this threatening condition.

Some important deficiencies can be observed in this study. It was a retrospective study, and the groups evaluated were not statistically similar in terms of certain clinical characteristics. There were no cases of PMT in this study, preventing a comparison of PMT with the other two treatments in patients with ALI. Notably, very few studies have analyzed clinical data and comparative surgical or endovascular procedure results in patients with ALI, thus necessitating further prospective and larger studies of this important and severe disease.

CONCLUSIONS

Both open surgery and endovascular procedures are safe treatments with acceptable limb salvage and survival rates. No study in the literature indicates the preferred treatment of ALI. However, based on this study and in the overall literature, endovascular treatment may be the preferred treatment of Rutherford I and IIA ALI, whereas open surgery may be the best option for ALI due to arterial embolism and for Rutherford IIB acute arterial thrombosis because of a greater urgency to restore blood flow.

AUTHOR CONTRIBUTIONS

Conception and design: RAS
Analysis and interpretation: RAS, MFM, FBN, MC, RS
Data collection: RDA, MJM, BPC
Writing the article: RAS
Critical revision of the article: RAS, MFM, FBN, MC, RDA, MJM, BPC, RS
Final approval of the article: RAS, MFM, FBN, MC, RDA, MJM, BPC, RS
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Overall responsibility: RAS

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