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Cost-effectiveness of treating peripheral arterial disease and critical limb ischemia

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ABSTRACT

Introduction: Peripheral arterial disease of the lower limbs is characterized by high treatment costs and intensive resource use. Cost-effectiveness analyses are important for comparing treatments for patients with peripheral arterial disease characterized by critical limb ischemia. **Objective:** The objective of this study was to compare the cost-effectiveness of conservative, endovascular, and surgical treatments in patients with critical limb ischemia. **Methods:** Data were analyzed from patients with critical ischemia treated between January 2020 and December 2021. Patients were treated conservatively, endovascularly, or surgically. Data regarding hospital stay duration and treatment costs were analyzed. **Results**: 220 patients were treated—14 conservatively, 158 via endovascular means, 34 via revascularization surgery, and 14 initially via endovascular attempt followed by surgical treatment in the same hospitalization. The cost per limb preserved for endovascular treatment was USD 3813, for surgical treatment was USD 5939, and for endovascular+surgical treatment was USD 15779 ($p<0.01$). The incremental cost-effectiveness ratio of surgical treatment compared to endovascular was USD 2291, and for endovascular+surgical compared to endovascular, it was USD -1001. **Conclusion:** Performing surgeries after failed angioplasties leads to increased costs without corresponding improvements in outcomes.

Keywords: Cost-effectiveness evaluation; Critical limb ischemia; Peripheral arterial disease.

INTRODUCTION

Population studies show the prevalence of peripheral arterial disease (PAD) of the lower limbs affects between 10 and 21% of people over 60 years old[1]. In the past three decades, there has been a 17% increase in PAD among women and a 24% increase among men[2]. By contrast, the prevalence of coronary and cerebral atherosclerotic disease has decreased during this period. The growing prevalence of PAD is due to increased longevity, higher rates of diabetes, and lifestyle factors that contribute to arterial blockages[3]. Critical limb ischemia (CLI) represents the most advanced stage of PAD, with a reported prevalence of 1.3% in the adult population and an annual incidence of 0.3/1000 inhabitants[4].

Due to its critical nature, involving difficult-to-treat pain and a risk of amputation, the treatment of CLI is characterized by intensive care. It commonly requires multidisciplinary teams focused on restoring limb functionality, which involves intensive hospital resource use, including endovascular treatment equipment, open surgical revascularization procedures, intensive care, advanced antibiotics, wound care, and prolonged hospital

stays. In recent decades, endovascular treatment has advanced significantly due to its minimally invasive nature, however, long-term results in limb preservation are not superior to surgical procedures[5]. Concern over the costs involved in treating ischemic patients has been raised in publications from several countries, involving both public and private healthcare systems[6].

Outcomes studied in CLI treatments vary from procedural patency to patient-centered outcomes like limb preservation and quality of life. Cost analyses are more common when studying different types of endovascular equipment but less common when comparing treatments, especially in middle- or low-income countries[7]. The burden of CLI is substantial, and healthcare resources are limited, as reported in European countries and Brazil[8,9,10]. Thus, cost-effectiveness analysis of CLI treatments should be considered when making treatment decisions.

In this study, we sought to quantify the cost-effectiveness of CLI treatments aimed at limb preservation. The main goal was to compare costs among treatments through the incremental cost-effectiveness ratio (ICER). Additionally, we compared patients whose outcome was limb preservation to those whose outcome was a combination of major amputation or death.

METHODS

This was a cross-sectional study with data from patients treated in a tertiary hospital between January 2020 and December 2021. The research protocol was approved by the local ethics committee under number 5.476.722, in accordance with Resolution 466/12 of the National Health Council.

Data were collected from all patients over 18 years of age with CLI treated during the study period. Patients from both public and private healthcare systems were included. Those with incomplete medical records or who declined participation were excluded. Data on epidemiology, vascular procedures performed—type of treatment, hospital stay duration, and treatment costs—and vascular outcomes—limb preservation, major amputation, or death—were collected. Clinical data were gathered from electronic medical records and, when necessary, confirmed via phone calls or in-person consultations. Hospital treatment costs were obtained from the hospital's finance department. These costs were associated with patient hospitalization and outpatient follow-up at the wound care center and were individualized per patient, regardless of the funding source (public or private). Brazilian federal law 13709/2018 (General Data Protection Law) was followed to ensure confidentiality.

For group comparison, patients were categorized according to the treatment they received. The Conservative group was treated at the hospital's wound care center for ischemic ulcer care without revascularization procedures. The Endovascular group underwent endovascular treatments such as balloon angioplasty and stent implantation, followed by wound care. The Surgery group was treated with bypass surgery for limb revascularization, using either saphenous vein grafts or prosthetics. The Endo+Surgery group comprised patients who underwent endovascular treatment but required open surgical revascularization during the same hospitalization. The groups were compared based on epidemiological characteristics, outcomes, and treatment costs. Patients were allocated to treatment groups according to local protocol, based on national and international guidelines[10,11].. Those directed to conservative treatment had an ankle systolic pressure > 70 mmHg and were classified with Grade 1 ulcers based on the Wound, Ischemia, and Foot Infection (WIFI) classification system)[12].

Cost-effectiveness analysis compared the average hospital stay cost per treatment, the cost per negative outcome (defined as major amputation and death combined), the cost per limb preserved, and the ICER. Hospital stay duration was the main component of

total hospital costs. The combined outcome of major amputation and death was used as a negative outcome for advanced PAD cases[10]. ICER compares the costs and results of two interventions, calculated as the cost difference between two interventions divided by the difference in their outcomes [ICER = (cost of intervention A) – (cost of intervention B) / (outcomes of intervention A) – (outcomes of intervention B)]. [13]The Endovascular and Surgery groups were analyzed separately for patients with limb preservation versus those with amputation or death.

The data related to treatment costs were obtained in Brazilian Reais (BRL) and converted to US Dollars (USD). The average USD value for 2020 and 2021 in Brazil was used, with the average rate being 1 USD to 5.27 BRL. We used the Shapiro-Wilk test for normality analysis, continuous variables were analyzed using the Kruskal-Wallis or Mann-Whitney tests, as appropriate; categorical variables were analyzed using the chi-square trend test or Fisher's test. The data were organized in Microsoft Excel® spreadsheets, and we used the statistical software GraphPad Prism® 9 and R version 4.2.2. The data were double-checked by the authors and the hospital's cost department.

RESULTS

Data from 220 patients treated between January 2020 and December 2021 were analyzed, most of them treated endovascularly (158 cases, 71.8%). The Surgery group had longer hospital stays compared to the Endovascular group (20.4 days vs. 11.2 days, p<0.001). There was no difference in limb preservation rates between the groups. The patients who required surgery after endovascular attempts had the longest hospital stays, averaging 47 days, and also had the highest mortality rate.

Among the 158 patients treated via endovascular means, the composite outcome of amputation or death occurred in 20 (12.6%) (Table 2). Among the 34 patients treated with conventional surgery, the composite outcome of amputation or death occurred in 4 (28.6%) (Table 3). When analyzing age, gender, percentage of diabetics, length of hospitalization, and treatment costs, there were no significant differences between the groups with limb preservation and those who progressed to amputation or death, regardless of whether they were treated endovascularly or surgically.

The group of patients who required surgery after an endovascular attempt had the highest treatment costs, with an average of USD 19,843 or USD 537 per day of hospitalization (Table 4). Surgical treatment had higher overall costs compared to endovascular treatment (USD 5,986 vs. USD 3,924, $p < 0.01$), but the cost per day was lower (USD 487 vs. USD 745, $p < 0.01$). However, the endo+surgery group did not show a significant difference in daily treatment costs compared to the surgery group (USD 537 vs. USD 487, $p = 0.15$). Our data show that the average daily cost of endovascular treatment was the highest, even when compared to the endo+surgery group (USD 745 vs. USD 537, $p < 0.01$).

The ICER (Incremental Cost-Effectiveness Ratio) of USD 178 per limb preserved for endovascular treatment compared to conservative treatment shows that, although the treatment cost was higher, the outcomes were better (Table 4). Similarly, the ICER of USD 291 per limb preserved for surgical treatment compared to conservative treatment demonstrated improved cost-effectiveness. When comparing surgical treatment to endovascular treatment, there was a significant increase in costs with only a slight improvement in effectiveness, as shown by the ICER of USD 2,291 per limb preserved. Regarding the cost increase for the endo+surgery group, there was a significant rise in costs compared to both endovascular and surgical treatments, without an increase in efficacy, as evidenced by the negative ICER.

The average cost per limb preserved and per negative outcome increased across the treatment groups (Figure 1). Conservative treatment had the lowest cost per limb preserved, followed by endovascular and surgical treatment. Patients who required both endovascular and surgical approaches had the highest cost per limb preserved (Table 4).

Table 1. Demographic, hospitalization, and outcome data of 220 patients with critical limb ischemia treated between 2020 and 2021.

	Conservative Groupe n=14	Endovascular Group n= 158	Surgery Group n=34	Endo+Surgery Group n=14	p-value
Age (Years)	71,2 (62; 80,4)	69,6 (67,5; 71,7)	71,3 (67; 75,7)	68,9 (61; 76,8)	0,79
Female gender	8 (57%)	67 (42%)	12 (35%)	4 (29%)	0,12
Diabetic patients	12 (85,7%)	145 (91,8%)	29 (78,4%)	13 (92,8%)	0,18
Length of hospital stay (day)	-	11,2 (8,8; 13,6)	20,4 (15; 25,8)	47,0 (37,7; 56,3)	< 0,001
Limb preservation	10 (71,4%)	138 (87,3%)	30 (88,2%)	10 (71,4%)	0,09
Major amputation	4 (28,6%)	12 (7,6%)	2 (5,8%)	1 (7,1%)	0,17
Death	0	9 (5,7%)	2 (5,8%)	4 (28,6%)	0,005
Negative outcome (amputation/death)	4 (28,6%)	20 (12,6%)	4 (11,7%)	4 (28,6%)	0,76

Data for continuous variables presented as mean (95% confidence interval).

Table 2. Comparison between the group with amputation/death outcome and the limb preservation group among patients with critical limb ischemia treated endovascularly.

Endovascular Group	Limb Preservation Group n= 138	Amputation/ Death Group n = 20	p-value
Age (years)	69,2 (66,9; 71,4)	72,6 (65,8; 79,3)	0,28
Female gendeer	62 (44,9%)	5 (25%)	0,09
Diabetics	127 (92%)	18 (90%)	0,78
Hospitalization duration (days)	10,4 (8,2;12,8)	16,2 (9,4; 22,9)	0,39
Treatment cost (USD)	3.889 (3.339; 4.440)	4.148 (2,449; 5.847)	0,93

Continuous variables are presented as mean (95% confidence interval). Categorical data analyzed using Fisher's exact test. USD: US dollars.

Table 3. Comparison between the group with amputation/death outcome and the limb preservation group among patients with critical limb ischemia treated surgically.

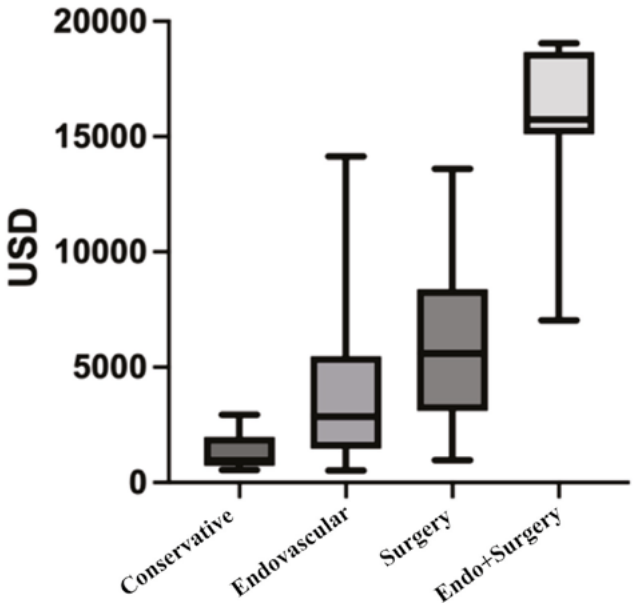
Surgery Group	Limb Preservation Group n = 30	Amputation/ Death Group n = 4	p-value
Age (years)	72,6 (68,1; 77,1)	63,5 (37,5; 89,5)	0,30
Female gendeer	10 (33,3%)	2 (50%)	0,60
Diabetics	25 (83,3%)	4 (100%)	0,99
Hospitalization duration (days)	21 (15; 26,9)	20,5 (1; 42,4)	0,86
Treatment cost (USD)	5.939 (4.603;7.276)	7.605 (2.057; 13.153)	0,32

Continuous variables are presented as mean (95% confidence interval). Categorical data analyzed using Fisher's exact test. USD: US dollars

Table 4. Cost-effectiveness analysis of 220 patients with critical limb ischemia divided by treatment groups.

	Conservative Group n = 14	Endovascular Group n = 158	Surgery Group n = 34	Endo+ Surgery Group n = 14	p-value
Treatment cost (USD)	1.089 (793; 1.383)	3.924 (3.403; 4.445)	5.986 (4.743; 7.229	19.843 (14.473; 25.212)	< 0,001
Ayerage cost per Day of hospitalization (USD)	-	745 (616; 875)	487 (279; 696)	537 (219; 856)	< 0,001
Average cost per negative outcome (amputation or death) (USD)	527 (153; 900)	4.613 (2.730; 6.495)	7.605 (2.056; 13.154)	27.155 (11.930; 42.380)	< 0,001
Cost per limb preserved (USD)	1.313 (736; 1.891)	3.813 (3.279; 4.346)	5.939 (4.603; 7.276)	15.779 (12.969; 18.590)	< 0,01
ICER (comparison with conservative treatment)	NA	178	291	NA	NA
ICER (comparasion with endovascular treatment)	NA	NA	2.291	- 1.001	NA
ICER (comparison with surgical treatment)	NA	NA	NA	- 825	NA

Values reported in USD, mean (95% confidence interval). Continuous variables presented as mean (95% confidence interval). ICER: incremental cost-effectiveness ratio. NA: not applicable.



DISCUSSION

Main Findings

This study shows that both endovascular and surgical treatments present good cost-effectiveness for treating patients with critical limb ischemia (CLI). Among the interventions for CLI treatment, the endovascular approach had the best cost per limb preserved. Surgical treatment resulted in higher costs with only a slight increase in efficacy. When properly selected, conservative treatment for patients with ischemic ulcers proved to be low-cost with an acceptable limb salvage rate. Patients who required both endovascular and surgical approaches had the highest hospitalization costs without a corresponding increase in effectiveness regarding limb salvage.

ICER is used to compare treatments. A positive ICER means there was an increase in costs with a corresponding improvement in the effectiveness or outcomes of the intervention being compared[15]. Our data show that both endovascular and surgical treatments led to increased costs with improved outcomes compared to conservative treatment. Surgical treatment had a larger cost increase compared to endovascular treatment, with an ICER of USD 2,291 per limb preserved. There is substantial variability in ICER values when comparing different types of treatments for limb ischemia[8,15,16]. One factor explaining the high ICER for surgical treatment compared to endovascular is the longer hospital stay for these patients.

Patients who required surgery after a failed endovascular attempt had the highest daily treatment costs, cost per limb preserved, and, most notably, cost per negative outcome (major amputation or death). When comparing this group to patients treated only endovascularly, the ICER was negative, indicating increased costs with worse outcomes. Similarly, comparing this group to patients treated only surgically also showed a negative ICER, reflecting a decline in cost-effectiveness. One factor influencing these results was the prolonged hospitalization. These findings are consistent with studies showing that multiple revascularization attempts and multiple hospitalizations within a short period significantly increase the cost of procedures and impact the cost-effectiveness of treatments for limb ischemia[8,16,17].A 5-year cost projection analysis by Vadia et al. showed that early endovascular intervention is effective in reducing costs and improving outcomes compared to multiple interventions[7]. Data from a prospective cohort of elderly patients also demonstrated the efficacy of endovascular treatment when performed before a patient's health condition deteriorates[8].Clique ou toque aqui para inserir o texto.

Cost-Effectiveness of Endovascular Treatment

Several studies indicate that endovascular treatment for CLI is cost-effective, reflecting lower costs compared to other treatments with similar or better efficacy[15,18,19]. There is a trend toward reduced costs with endovascular treatment, although it is unclear if this benefit is sustained over time[6]. The cost-effectiveness of endovascular treatment seems to be due to shorter hospital stays associated with good limb preservation outcomes[8,20]. This finding aligns with our results, showing that despite the higher daily cost of endovascular treatment compared to surgery, the cost per limb preserved was lower in the endovascular group. Chase et al. point out that the intensive use of new endovascular technologies significantly increases costs without improving efficacy[21].

Endovascular treatment outcomes did not lead to differences in treatment costs. Among patients treated endovascularly, there was no difference in cost between those who achieved limb preservation and those who underwent amputation or died. Likewise, there was no difference in hospitalization duration between these groups, which undoubtedly contributed to the similar costs. It is noteworthy that the hospi-

talization period in our study was longer than in other published studies, particularly among those who progressed to amputation or death[8,22]. Our practice has been to keep patients hospitalized for an extended period to treat ischemic lesions due to limited outpatient wound care availability.

Cost-Effectiveness of Surgical Treatment

Surgical bypass revascularization provides superior long-term results compared to endovascular treatment in terms of reconstruction patency and limb salvage[5,23]. However, surgery requires a longer hospital stay, a fact confirmed by our data[24]. Although there was no difference in hospital stay duration between patients who achieved limb preservation and those who progressed to amputation/death, the extended hospitalization influenced treatment costs. In some published series, the cost of lower limb revascularization was higher among those who underwent amputation, considering post-hospitalization expenses and rehabilitation costs[15,18,25]. Such expenses were not analyzed in our study, which may explain the lack of cost differences.

Surgical Revascularization After Endovascular Failure Increases Costs Without Improving Efficacy

Our data show that multiple revascularization attempts, especially surgery following a failed endovascular attempt, result in increased costs without improving outcomes. This emphasizes the importance of properly selecting patients for angioplasty or surgical revascularization. The strategy of attempting endovascular treatment for all patients, known as "endovascular-first," has been used in several centers. Mathlouti et al. found no difference between the "endovascular-first" and "bypass-first" approaches in a retrospective analysis of patients with CLI[26]. In another retrospective analysis of patients with infragenicular disease, those treated with a "bypass-first" approach had a lower amputation rate [27]. The BEST-CLI study highlighted the importance of proper patient selection, as those with suitable saphenous veins for revascularization had better limb-related outcomes[5].

Study Limitations

The main limitation is the lack of access to post-hospitalization treatment costs. Several important factors, such as rehabilitation time, return to daily activities or work, physiotherapy sessions, post-amputation rehabilitation, prosthetics, and home care, were not included in our analysis. Another limitation was the smaller number of patients treated surgically compared to those treated endovascularly; despite being able to compare the groups, the difference in sample sizes limited the analysis and the identification of confounding factors. Only patients from a single hospital center were studied, limiting the external validity of the data. Another significant limitation in interpreting our data is the lack of sensitivity analysis between groups, increasing the uncertainty of the analysis. However, we believe the cost and outcome differences described between the groups provide useful insights for teams managing patients with advanced PAD.

CONCLUSION

The average cost per limb preserved increased across conservative, endovascular, and surgical treatments for critical limb ischemia. Performing revascularization surgeries after failed endovascular treatment significantly increases costs without corresponding improvements in outcomes, underscoring the importance of proper intervention selection. Defining the treatment approach early is crucial for achieving effective limb preservation, whether through endovascular or surgical revascularization. Future studies considering post-hospitalization costs and conducting sensitivity analyses between treatment groups could better quantify the resources needed for limb salvage.

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THE AUTHORS DECLARE THAT THERE IS NO CONFLICT OF INTERESTS IN RELATION TO THIS ARTICLE.