Acute Occlusion of Abdominal Aorta: Duration of Bilateral Limb Ischemia and its Influence on Early-Term and Mid-Term Outcomes

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Abstract

Background To investigate the influence of duration of bilateral acute limb ischemia (BALI) due to acute aortic occlusion (AAO) on the amputation-free survival in the early- and mid-term follow-ups (FUs).

Methods A retrospective analysis of patients treated due to primary occlusion of the infrarenal aorta and BALI was performed. Univariate analysis was used to determine the risk factors of adverse outcomes and to compare the duration of BALI between amputation-free survival and the non-amputation-free survival group. The log-rank test was used to compare amputation-free survival in the FU.

Results The data of 16 patients, with a mean age of 70 ± 11 years, were analyzed. Predominantly females (56.3%, 9/16) were included in the study. The median FU was 32 months (range, 26–108 months). The mean ischemia time was significantly shorter in the amputation-free survival group compared to that in the non-amputation-free survival group (7.4 ± 3.5 hours vs. 22.4 ± 16.3 hours, $p = .01$). The time frame for successful bilateral lower limb revascularization was at <11 h ($p = .001$, Cramer's $V = .71$). Amputation-free survival in the early- and mid-term FUs was improved, if the duration of BALI was < 11 hours (log rank test, $p = .006$).

Conclusions The duration of BALI due to AAO < 11 hours was shown to be associated with improved amputation-free survival in the early- and mid-term FUs.

Trial registration: The study was retrospectively registered in TCTR international registry (identification no. TCTR20210609002).

Background

Bilateral acute limb ischemia (BALI) due to the acute aortic occlusion (AAO) is a rare but life-threatening condition associated with a high mortality and amputation rate (1–4). The outcomes of treatment have slightly improved over the last decade, but they have remained low (4). Current guidelines recommend emergent revascularization of acute limb ischemia (ALI) secondary to AAO to improve outcomes (5).

Previously published series have analyzed heterogenic cohorts of patients with AAO and have failed to determine the time frame for successful revascularization, which may be crucial for alignment of prehospital care protocols and routing the patients to high-volume centers, thus improving outcomes (1, 6, 7).

For unilateral ALI, improved amputation and survival rates with a duration of ischemia up to 12–24 hours have been reported, despite the recognized optimal revascularization time being 4–6 hours (8–10). Considering large muscle mass ischemia due to AAO, reduced collateralization and pronounced multiorgan failure after reperfusion, the time frame for successful revascularization of BALI may vary.

The objective of this study was to investigate the influence of duration of BALI due to AAO on the amputation-free survival and to determine the time frame for successful bilateral lower limb

revascularization.

Methods

Study design

A retrospective, single-center analysis of prospectively collected clinical data of patients with BALI admitted between January 1, 2010, and January 1, 2019, was performed. The clinical and anamnestic data were retrieved from the medical documentation. Informed consent was obtained for the collection and processing of the clinical data, according to the principles of the Declaration of Helsinki. An approval for the retrospective analysis of the prospectively cumulated clinical data was received from the local ethics committee of Krasnodar Regional Clinical Hospital #1 (protocol no.115 – 23/05/2019). The study was retrospectively registered in TCTR international registry (identification no. TCTR20210609002, date of registration 09/06/2021).

Study Population

Patients with BALI due to primary acute occlusion of the infrarenal aorta were included in this study. Patients with unilateral ALI, BALI secondary to suprarenal aortic occlusion or bilateral occlusion of aortobifemoral grafts, or multiple acute simultaneous arterial occlusions of the upper and lower extremities were excluded (Fig. 1). All patients with unknown timepoints of symptom onset and/or thrombophilia were excluded.

Treatment Protocol

All patients who presented with viable lower limb musculature and reversible BALI were scheduled for revascularization. A decision of palliation was made for critically ill patients with uncontrolled hypotension and with extended bilateral buttock, thigh, and calf rigor. Primary thigh amputation with blood flow restoration in the deep femoral artery was performed in cases of irreversible calf ischemia.

After admission, all patients received full heparinization with a 100 IU/kg intravenous bolus, followed by a supporting dose of 1000 IU/hour under the control of the partial thromboplastin time (PTT). The therapeutic level of PTT was estimated to be 60–70 seconds.

Preoperatively, duplex ultrasound and/or contrast-enhanced spiral computed tomography angiography of the entire aorta, with a slice thickness of 1 mm, were performed to estimate the level and extension of occlusion (Fig. 2).

All operations were performed by certified vascular surgeons. The revascularization procedure was performed as an aortic thrombectomy through the standard transfemoral approach using the Fogarty balloon catheter. Intraoperative balloon catheter-mediated revision of the distal run-off was obligatory. All

patients received bilateral four-compartment calf fasciotomy after revascularization, with subsequent secondary wound closure.

Postoperatively, in-hospital full anticoagulation with intravenous heparin under PTT control was administered. After discharge, lifelong anticoagulation with oral anticoagulants was recommended.

Follow-up

The standard FU protocol included clinical and sonographic examinations before discharge and annually thereafter. All sonographic series were assessed by an independent collaborator for radiology. The control examination was performed by vascular surgeons.

All patients (100%, 5/5) who exhibited amputation-free survival within 30 days after revascularization were followed up until November 2020.

Definitions

“Acute” ischemia was defined as the sudden onset of lower extremity ischemic symptoms lasting less than 2 weeks.⁽⁵⁾ The grade of acute lower extremity ischemia was classified using international clinical and sonographic criteria.⁽¹¹⁾

Technical success was defined as the prompt restoration of antegrade arterial flow in a target vessel based on the absence of residual arterial stenosis > 40% on postoperative duplex examination.

Procedural success was defined as technical success without complications.⁽¹¹⁾

Duration of ischemia was defined as the period between symptom onset and flow restoration (in case of revascularization) or until decision-making (in case of palliation).

The definition of early-term FU (up to 30 days) and mid-term FU (1–5 years) was made respective to current reporting standards.⁽¹²⁾

Myocardial infarction (MI) was defined as myocardial necrosis accompanied by a rise and/or fall in cardiac biomarker values (preferably, cardiac troponin), clinical symptoms of ischemia, new significant ST segment-T wave (ST-T) changes, and a new left bundle branch block or development of pathological Q waves on electrocardiogram.⁽¹³⁾

Statistical analysis

Statistical analyses were performed using SPSS version 25.0 (SPSS, Inc., Chicago IL, USA). Continuous data were presented as mean and standard deviation (mean $\pm$ SD). Categorical variables were presented as absolute numbers and percentages. A crosstab analysis was performed to characterize the sample.

Univariate analysis was performed to find differences between the compared groups using the χ^2 -test in the case of the categorical data and the Mann-Whitney U test in the case of the continuous data. Cramer's V coefficient was used to measure the effect size of the differences. Values below .1, .1-.2.9, .3-.4.9, and above .5 were considered little if any, low, moderate and large effect sizes respectively (14). The Kaplan-Meier curve was used to present survival. The log-rank test was used to compare amputation-free survival between groups. The level of significance for all the statistical tests was determined as $p < .05$.

Results

A total of 16 patients, with a mean age of 70 ± 11 years and predominantly females (56.3%, 9/16), were included in the study. The majority of patients had arterial hypertension and coronary artery disease (68.8%, 11/16 and 62.5%, 10/16, respectively). In all, 56.3% (9/16) of patients had grade 2 BALI (Table 1). BALI due to embolization was diagnosed in 62.5% (10/16) of cases. Atrial fibrillation (AF) was observed in 43.8% (7/16) of patients, and thrombogenic thoracic aorta was observed in 18.8% (3/16) of patients. A history of peripheral arterial disease (PAD) was estimated in almost one-third of patients (31.2%, 5/16). All demographic data are cumulated in Table 1. Neither malignancy nor preoperative ambulatory anticoagulation were reported. The mean duration of BALI was 17.7 ± 15.2 hours.

Table 1
Demographic data^a

Characteristics		Total n = 16 % (n/N)
Gender	male	43.7 (7/16)
	female	56.3 (9/16)
Age, years		70 ± 11
Etiology	Emboli	62.5 (10/16)
	Thrombosis	37.5 (6/16)
Rutherford grade of ischemia	2b	56.3 (9/16)
	3	43.7 (7/16)
PAD		31.2 (5/16)
AF		43.8 (7/16)
Thrombogenic thoracic aorta		18.8 (3/16)
Congestive heart disease		43.7 (7/16)
Coronary heart disease		62.5 (10/16)
Arterial hypertension		68.8 (11/16)
Stroke		25.0 (4/16)
Hypercholesterinemia		43.7 (7/16)
CRI		18.7 (3/16)
Diabetes mellitus		37.5 (6/16)
^a Categorical data are presented as absolute numbers and percentage; continuous data are presented in mean ± SD		
<i>PAD</i> , peripheral arterial disease; <i>AF</i> , atrial fibrillation; <i>CRI</i> , chronic renal insufficiency		

30-day Outcomes

Of the patients, 56.3% (9/16) of them underwent operations, with 43.8% (7/16) experiencing transfemoral thrombectomy. Technical success with regard to revascularization was achieved in 100% (7/7) of cases, and procedural success was achieved in 71.4% (5/7) of cases. Two patients experienced mortality after thrombectomy on the first postoperative day due to MI; thus, mortality in the revascularization group was 28.6% (2/7).

Unilateral and bilateral thigh amputations of the lower extremities were performed in 12.5% (2/16) of patients due to irreversible calf ischemia. One amputation of the single lower limb was performed on a patient with BALI of 63.5 hours duration. This patient was discharged and experienced ambulatory mortality due to pulmonary embolism on postoperative day 24. A second patient received bilateral amputations after BALI of 37.5 hours and endured mortality on the second postoperative day due to multiorgan failure.

Patients scheduled for palliative therapy accounted for 43.8% (7/16) of the sample size. In this group, in-hospital mortality reached 100% (7/7) and was due to multiorgan failure (85.7%, 6/7) and MI (14.3%, 1/7). The overall 30-day mortality rate was 62.5% (10/16). The amputation-free survival rate was 31.3% (5/16).

After dividing the patients into group A (amputation-free survivals) and group B (non-amputation-free survivals), a univariate analysis of risk factors for amputation and mortality was performed. The duration of ischemia was significantly shorter in group A as compared to group B (7.4 ± 3.5 hours vs. 22.4 ± 16.3 hours, $p = .01$) (Table 2). Revascularization and lower grade of BALI improved amputation-free survival ($p = .002$ and $p = .03$, respectively) (Table 2).

Table 2
Univariate analysis of risk factors for amputation-free survival^a

Characteristics		Main group % (Total n = 5)	Control group % (Total n = 11)	P value
Gender	male	40	45.5	0.8
	female	60	54.5	
Age, years		64±16	73±7	0.2
Ethiology	Emboli	80	54.5	0.3
	Thrombosis	20	45.5	
Rutherford grade of ischemia	2b	55.6	44.4	0.03
	3	0	100	
PAD		60.0	18.2	0.09
AF		20.0	54.5	0.2
Coronary heart disease		60	63.6	0.9
Arterial hypertension		80.0	63.6	0.5
Stroke		20.0	27.3	0.7
Hypercholesterolemia		40	45.5	0.8
CRI		40	9.1	0.1
Diabetes mellitus		20.0	45.5	0.3
Acetylsalicylic acid		0	27.3	0.2
Revascularisation	performed	100	18.2	0.002
	not performed	0	81.8	
Duration of ischemia, h		7.4 ± 3.5	22.4 ± 16.3	0.01
^a Categorical data are presented as percentage; continuous data are presented in mean ± SD				
PAD, peripheral arterial disease; AF, atrial fibrillation; CRI, chronic renal insufficiency; h, hour				

The successful bilateral lower limb revascularization was at the time frame < 11h (p = .001, Cramer's V = .71) (Table 3).

Table 3
Assotiation between duration of BALI and outcome^a

Duration of BALI, h	Group A	Group B	Fisher's two-sided Chi-Square Test	Cramér's V Test
< 12	100	27	> .001	.67
> 12	0	73		
< 11	80	10	< .001	.71
> 11	20	90		
< 10	80	10	< .001	.71
> 10	20	90		
^a Categorical data are presented as percentage				
<i>BALI</i> , bilateral acute limb ischemia; <i>Group A</i> , amputation-free survivals; <i>Group B</i> , non amputation-free survivals				

Mid-term Outcomes

The median FU was 32 months (range, 26–108 months). All patients (100%, 5/5) who showed 30-day amputation-free survival were followed 24 months after revascularization, and 80% (4/5) of patients were followed after 30 months (Fig. 4). During the FU period, no mortality or vascular reinterventions were reported. One patient (20%, 1/5) received a unilateral thigh amputation on FU month 53 due to deterioration of known infrainguinal PAD and concomitant gangrene, despite aortoiliac arterial segment patency. At FU months 24 and 32, amputation-free survival remained persistent (31.3%, 5/16) as compared to 30-day outcome.

At the mid-term FU, the patients with a duration of BALI < 11 hours showed improved amputation-free survival (log rank test, $p = .006$) (Fig. 3).

Discussion

Experimental studies using canine models reported the irreversible metabolic failure of skeletal muscle with a duration of ischemia > 7 hours, which was in the line with recognized optimal time for revascularization of unilateral ALI (15).

However, previously published real-world studies have reported both improved amputation-free and survival rates due to collateralization, if the duration of unilateral ALI was up to 12 hours (8, 9).

Surowiec et al. reported a higher amputation rate in a group with acute aortic thrombosis, if the duration of BALI was > 24 hours, as compared to that in an emboli group (17.6%, 3/17 vs. 6.2%, 1/16, respectively) (16).

Dossa et al. failed to determine the critical issue of time of BALI ($p = .1$).⁽³⁾ In this study, a 6-hour threshold was used, which is similar to the experimental data and to the optimal revascularization time of unilateral ALI. However, this was a two-fold shorter time than the previously reported threshold for unilateral ALI (< 12 hours) (8, 9).

Crawford et al. failed to show the need for amputation based on the duration of BALI ($p = .74$) (1). In this work, the reported median transport time was 3.9 hours (range, 0.5–7.5 hours), which is shorter than that reported by Dossa et al. and shorter compared to the data of the current study (17.7 ± 15.2 hours). Moreover, in the study by Crawford et al., patients with cancer, thrombophilia, supra- and infrarenal aortic occlusion, and visceral ischemia were included, which might affect the outcome.

In the current study, the mean duration of BALI associated with improved amputation-free survival has been found to be similar to unilateral ALI (7.4 ± 3.5 hours). However, the time frame for improvement of amputation-free survival after AAO was shown to be shorter (< 11 hours) than previously reported for unilateral ALI (< 12 hours) (8).

In the current study, 30-day mortality in the revascularization group was almost two-fold higher than the recently reported largest series ($n = 693$) evaluated by Grip and colleagues (28.6% and 15.5%, respectively) (4). However, the study by Grip et al. included patients with in-hospital occlusions of grafts and/or stents, potentially presenting the shortest duration of BALI. In addition, 14% of patients experienced unilateral ALI due to AAO.

Grip et al. reported a mean postoperative FU of 5.2 ± 5.5 years, with an overall survival over 60% and 40% after 2 years and 4 years of FU, respectively. Of the patients, 59% (410/693) of them were followed for 2 years and 68.6% (337/693) for 4 years postoperatively (4).

The current study showed similar FU length and FU compliance (32 months [range, 26–108 months] and 80% (4/5), respectively), reporting improved amputation-free survival over the mid-term FU for patients, whom revascularization could have been performed < 11 hours after the onset of BALI (log rank test, $p = .006$).

The current study presents some limitations. The retrospective, non-randomized design may introduce selection bias. The small power of the study and different sizes of the compared groups may introduce analysis bias. Moreover, the small size of the cohort failed a multivariate analysis of risk factors. Very few patients reaching 5 years of FU made any long-term conclusions non-meaningful.

Conclusions

Larger studies are necessary; however, a duration of BALI due to AAO < 11 hours were shown be associated with improved amputation-free survival in the early- and mid-term FUs. Thereby, routing of patients with BALI due to AAO and prehospital care protocols should be adapted to this time frame to improve the outcomes.

Abbreviations

BALI: bilateral acute limb ischemia; AAO: acute aortic occlusion; FU: follow-up; ALI: acute limb ischemia; PTT: partial thromboplastin time; MI: myocardial infarction; PAD: peripheral arterial disease.

Declarations

Ethics approval and consent to participate: Informed consent was obtained for the collection and processing of the clinical data, according to the principles of the Declaration of Helsinki. An approval for the retrospective analysis of the prospectively cumulated clinical data was received from the local ethics committee of Krasnodar Regional Clinical Hospital #1 (protocol no.115 from 23/05/2019).

Consent for publication: not applicable.

Availability of data and materials: all data generated or analysed during this study are included in this published article.

Competing interests: the authors declare that they have no competing interests.

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Authors' contributions: DS was involved in conceiving the idea, study design, and managing the overall progress of the study. All authors have participated in data analysis and interpretation. DS, AA and CF drafted the first manuscript and then edited it by SB, RV, AB and VP. CF performed statistical analysis. All authors read and approved the final version of the manuscript.

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Figures

Figure 1

Flow Chart

Figure 2

CTA.Level of Occlusion of Terminal Aorta

Survival functions

Figure 3

Amputation free survival

Image not available with this version

Figure 4

The median FU was 32 months (range, 26–108 months). All patients (100%, 5/5) who showed 30-day amputation-free survival were followed 24 months after revascularization, and 80% (4/5) of patients were followed after 30 months (Fig 4). During the FU period, no mortality or vascular reinterventions were reported. One patient (20%, 1/5) received a unilateral thigh amputation on FU month 53 due to deterioration of known infrainguinal PAD and concomitant gangrene, despite aortoiliac arterial segment patency. At FU months 24 and 32, amputation-free survival remained persistent (31.3%, 5/16) as compared to 30-day outcome.