

Limb salvage with open surgical revascularization in acute ischemia due to thrombosed popliteal artery aneurysm

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1 **Abstract**

2 **Introduction:** Acute ischemia due to thrombosed popliteal artery aneurysm (PAA) is
3 associated with a high risk of limb loss. The aim of this study was to analyze the
4 outcome, in particular the limb salvage rate in patients undergoing urgent open surgery
5 for acute ischemia due to thrombosed PAA.

6 **Methods:** Retrospective analysis of consecutive patients undergoing urgent open
7 surgery for acute limb ischemia (Rutherford category \geq II) due to thrombosed popliteal
8 artery aneurysm between January 2007 and December 2016 at a tertiary referral center.

9 **Results:** Fifty-one patients (92% male) with a median age of 75 years (range 46-97)
10 were identified. Twenty patients (39%) presented with category IIa acute limb ischemia,
11 20(39%) with category IIb, and 11(22%) with category III. Four patients (8%)
12 underwent primary major amputation. Forty-seven (92%) underwent bypass surgery,
13 43/47(91%) using great saphenous vein. One-vessel runoff was present in 27/47 patients
14 (57%). Thirty-day mortality was 4% (n=2). Four patients needed major amputation
15 within 30 days, resulting in an overall 30-day major amputation rate of 16% (8/51, 95%
16 CI 7.0-28.6). No further major amputations were necessary during a median follow-up
17 of 41 months (range 4-114) resulting in an estimated four-year limb salvage of 84%.
18 One-year primary assisted and secondary bypass patency rate was 90% and 95%,
19 respectively. Estimated four-year primary assisted and secondary patency rate was 82%
20 and 87%, respectively.

21 **Conclusion:** Rapid open surgical revascularization in patients with acute limb ischemia
22 due to a thrombosed popliteal artery aneurysm results in good long-term limb salvage
23 rates, especially in Rutherford category IIa and IIb of acute ischemia. Revascularization
24 may be attempted in clinically severe cases not fulfilling all criteria to be classified as

25 category III. Such patients may in fact be borderline between IIb and III. Despite poor
26 runoff, good bypass patency rates and low rates of claudication can be achieved.

27 **Introduction**

28 Popliteal artery aneurysms (PAA) are relatively rare with a prevalence of approximately
29 1% in men aged 65–80 years,¹ accounting for more than 80% of all peripheral
30 aneurysms.² Acute limb ischemia (ALI) due to aneurysm thrombosis or distal
31 embolization is the most severe complication of a PAA.³ Revascularization is
32 challenging and usually performed by open surgery, although a complete endovascular
33 approach has been reported.⁴ As crural arteries are often occluded, options for complete
34 revascularization of the foot are limited possibly resulting in major amputation.
35 Amputation is associated with worse functional outcome, especially in elderly patients
36 with cardiovascular comorbidities.^{5,6} Furthermore, primary amputation offers no cost-
37 benefit compared to bypass surgery when considering the cost of the prosthesis and
38 rehabilitation.⁷ Thus, every effort should be taken to achieve limb salvage. The 2017
39 ESC Guidelines on the management of peripheral artery disease cover ALI, but specific
40 recommendations regarding PAA are lacking.⁸ In Rutherford category II urgent
41 revascularization is indicated. For patients with acute Rutherford category III limb
42 ischemia, the current recommendation is amputation. There are contemporary series
43 addressing outcome in ALI due to thrombosed PAA.^{9,10} These registry papers may
44 underestimate the amputation rate of thrombosed popliteal artery aneurysms because
45 they either excluded primary amputations or lack adequate follow-up.^{9,10} In other
46 articles reporting the open surgical management of PAA, follow-up of patients
47 presenting with acute ischemia is poor as well.¹¹ The use of preoperative thrombolysis
48 in ALI due PAA is controversial and a significant benefit has not been shown in a
49 recent systematic review.¹¹ We therefore aim to analyze perioperative as well as long-
50 term outcome of patients undergoing urgent open surgery for ALI due to thrombosed
51 popliteal artery aneurysm, assessing limb salvage and mortality.

52 **Materials and Methods**

53 This study was approved by the local ethics committee (ID 2017-01529). Consecutive
54 patients with Rutherford category IIa, IIb, and III ALI due to thrombosed PAA
55 undergoing urgent surgery between January 2007 and December 2016 were identified
56 and reviewed retrospectively. Patients with category I ischemia were excluded.

57 Popliteal artery aneurysm was defined as a popliteal artery diameter of ≥ 13 mm and \geq
58 1.5 times the diameter of the upstream and downstream segments measured on
59 ultrasound or computed tomography (CT) images. The diagnostic algorithm for ALI
60 and suspected PAA thrombosis included clinical examination and duplex ultrasound.
61 Preoperative CT angiography was performed at the discretion of the treating vascular
62 surgeon to assess the extent of thrombosis and potential target vessels. The revised
63 Rutherford category of acute ischemia¹² was preoperatively assessed by the treating
64 vascular surgeon based on sensorimotor function and Doppler assessment. Of note,
65 category III is named “irreversible” consisting of major tissue loss or permanent nerve
66 damage (inevitables), profound sensory loss (anesthetic), profound muscle weakness
67 (paralysis, rigor), and inaudible arterial and venous Doppler signals. Patients with
68 Rutherford categories IIa, IIb and III were scheduled for urgent (IIa) or emergent (IIb
69 and III) surgery.

70 **Operative technique**

71 Intraoperative angiography was performed to assess target vessels. In case of severe
72 thrombosis without a suitable distal target vessel, all crural vessels were dissected and
73 selective thrombectomy with or without intra-arterial thrombolysis was performed.
74 Depending on the surgeon’s preference, between 100’000 and 500’000 IU Urokinase
75 (Medac GmbH, Wedel, Germany) were delivered into the popliteal or crural arteries. If

76 available, the ipsi- or contralateral great saphenous vein was used as a bypass graft.
77 Arm veins were used as a second choice. If autologous vein material was unavailable,
78 Omniflow[®] II (LeMaitre Vascular, Burlington, MA, USA) or ePTFE (BARD Peripheral
79 Vascular, Temple, AZ, USA) was used. The standard anticoagulation and anti-platelet
80 regimen consisted of oral anticoagulation with coumadin and acetylsalicylic acid for at
81 least three months and acetylsalicylic acid alone thereafter. In case of severely
82 compromised (1-vessel) runoff, lifelong oral anticoagulation was recommended.

83 **Data collection**

84 Preoperative, intraoperative and postoperative data were retrospectively collected from
85 hospital records. Standard follow-up after bypass surgery included outpatient duplex
86 ultrasound performed at one and three months. After that, patients were followed every
87 6-12 months in the outpatient clinic with duplex ultrasound performed at the discretion
88 of the treating physician, usually in case of claudication or drop in ankle brachial index
89 (ABI). Follow-up duplex ultrasound reports, ABI measurements, and information on
90 reinterventions for patients who were followed elsewhere were requested from those
91 institutions. Vital status or date of death was confirmed by contacting the patients'
92 primary care physician or extracted from communal databases. For all patients known to
93 be alive, a standardized telephone interview was performed at the beginning of March
94 2017 assessing for claudication or reinterventions at other institutions. Study end date
95 was defined to be March 6th, 2017. Major amputation was defined as any amputation
96 above the ankle. Patency was defined and assessed according to Rutherford.¹²

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100 **Statistical analysis**

101 SPSS Statistics 25.0 (IBM Corp., Armonk, NY, USA) was used for descriptive statistics
102 and GraphPad Prism 7.00 (GraphPad Software Inc., La Jolla California USA) for
103 Kaplan-Meier analysis and 95% confidence intervals using the asymmetrical method.
104 For univariate analysis, we stated proportions, for numerical data mean with standard
105 deviation (SD) or median with range. Patency rates and amputation-free survival were
106 estimated using the Kaplan-Meier method. For follow-up patency rates, only patients
107 with a graft (without in-hospital amputation) were included. Patients known to have
108 died during follow-up were reported separately with the median time to death. For all
109 other patients, follow-up completeness was assessed using the Follow-Up Index.¹³

110 **Results**

111 **Patient characteristics and presentation**

112 Fifty-one patients (92% male) with a median age of 75 years (range 46-97) were
113 identified. Comorbidities are listed in Table 1. The median size of the PAA was 33 mm
114 (range 13-80 mm). Six patients (12%) had already undergone open surgery for
115 contralateral PAA and in an additional 25 patients (49%), contralateral PAA was
116 detected at presentation or during follow-up. Twenty patients (39%) presented with
117 Rutherford category IIa acute limb ischemia, 20 patients (39%) with category IIb, and
118 11 patients (22%) with category III.

119 **Treatment / surgical procedures**

120 Four patients (8%) underwent primary major amputation due to lack of patent outflow
121 vessels on intraoperative angiography images and severe ischemia (Rutherford category
122 IIb in one and category III in three patients). In the remaining 47 patients,
123 revascularization surgery was performed with 44 bypass and 3 interposition grafts.
124 Great saphenous vein (GSV) was used in 43/47 patients (91%). Other grafts used are
125 listed in Table 2. The distal target vessel was the below-knee popliteal artery in 26
126 patients (55%) and the crural arteries in the remaining patients (Table 2). The surgical
127 approach was medial in 44/47 (94%) and posterior in 3/47 (6%). All bypasses were
128 routed orthotopically. Intraoperative intra-arterial thrombolysis was used as an adjunct
129 in 17 patients (36%) with more severe limb ischemia (3 with category IIa, 7 with
130 category IIb, and 7 with category III; No intraoperative thrombolysis in 17 patients with
131 category IIa, 13 with category IIb, and 4 with category III, $p=0.007$). Fasciotomy due to
132 compartment syndrome was performed in 15/51 patients (29%). Two patients
133 underwent preoperative local thrombolysis, which is not consistent with our standard

134 approach. In these two patients, the diagnosis of PAA had not been established at
135 admission. Mean length of hospital stay was 14 days (SD 11).

136 After revascularization, 12 patients (26%) had three-vessel runoff, five patients (11%)
137 had two-vessel runoff, and 27 patients (57%) had one-vessel runoff, as assessed on
138 intraoperative angiography. Three patients (6%) had no patent runoff vessel with bypass
139 outflow to the foot through collaterals only, representing an unsuccessful
140 revascularization (Figure 1). In these three patients, the bypass target was the below-
141 knee popliteal artery in one and the peroneal artery in two patients.

142 **30-day outcomes**

143 **Limb salvage.** Four patients needed secondary major amputation within 30 days,
144 resulting in an overall 30-day major amputation rate of 16% (8/51; 95% CI 7.0-28.6).
145 Excluding the primary amputations, the 30-day major amputation rate was 9% (4/47).
146 Two of those undergoing secondary major amputation were patients with collateral
147 perfusion only and progressive tissue loss despite a patent bypass. The remaining two
148 patients had one-vessel runoff after initial revascularization; in one the bypass failed
149 after one day and in the other amputation became necessary due to progressive necrosis
150 of the foot while the bypass was patent.

151 The third patient with collateral only flow to the foot, the bypass remained patent but
152 amputation was recommended due to progression of necrosis. However, the patient
153 denied amputation and died three months later due to septic complications.

154 Category IIb and III limb ischemia at presentation was significantly associated with 30-
155 day major amputation (8/31 with category \geq IIb versus 0/20 with category IIa, $p=0.02$).
156 Overall, of eleven patients presenting with category III ischemia, six patients (55%)
157 underwent primary or secondary amputation and one denied the recommended

158 amputation (mentioned above). In the remaining four patients (36%) with category III
159 ischemia and in 18/20 (90%) with category IIb limb salvage was successful.

160 **Mortality and morbidity.** Two patients died within 30 days of surgery, resulting in a
161 30-day mortality of 4%. One patient died from congestive heart failure due to severe
162 aortic stenosis after successful limb revascularization and one patient died due to multi-
163 organ failure after denying surgery for complicated diverticulitis after primary
164 amputation. Non-fatal in-hospital complications included surgical site hematomas (5),
165 delirium (3), and surgical site bleeding needing reintervention (1), false aneurysm (1),
166 muscle necrosis of the anterior tibial muscle (1), wound infection (1) and pneumonia
167 (1), respectively. No patient experienced acute renal failure requiring hemodialysis.

168 **Follow-up**

169 Seventeen patients died during follow-up after a median of 14 months (range 0-93
170 months, IQR 42 months). Thirty-two patients were alive at the study end date (March
171 6th, 2017) with a median follow-up of 41 months (range 4-114 months) and a Follow-up
172 Index of 0.99.

173 During follow-up, no further major amputations were necessary, resulting in an
174 estimated four-year limb salvage of 84%. Excluding primary amputations, the estimated
175 four-year limb salvage was 91%. Of 32 patients alive at the end of follow-up, 28 were
176 free of major amputation and estimated four-year amputation-free survival was 52%
177 (Figure 2). Two minor amputations were performed two and four years after initial
178 revascularization.

179 Of 28 amputation-free survivors, one patient reported claudication after 500 meters
180 (Fontaine classification IIa) at the end of follow-up while all other patients were free of
181 claudication. The four patients with limb salvage in category III ischemia were

182 ambulating without complains after revascularization but three died during follow-up
183 after a median of 1.9 years (median age at presentation 89 years); one was alive and free
184 of claudication at the study end date (3.5 years after revascularization).

185 **Graft patency.** Estimated 1-year primary assisted and secondary patency rate was 90%
186 and 95%, respectively. Estimated 4-year primary assisted and secondary patency rate
187 was 82% and 87%, respectively (Figure 3).

188 **Re-interventions.** Three re-interventions were performed for primary assisted patency:
189 an anastomotic stenosis was treated with a stent in two patients and with an open patch
190 plasty in one patient. Seven patients had bypass occlusion after a median of 36 months
191 (range 0-97) after initial revascularization. In four patients, a bypass thrombectomy was
192 performed. In three of those, a focal stenosis was identified as the cause of bypass
193 occlusion and was treated with patch plasty. Three patients underwent a redo bypass
194 procedure after failed bypass salvage and of these, two underwent a second redo bypass
195 procedure and additional endovascular interventions due to repeated bypass failure.

196 **Discussion**

197 In this single-center retrospective series, we report the outcome of 51 patients with
198 acute limb ischemia due to a thrombosed popliteal aneurysm. Revascularization in this
199 setting remains a surgical challenge since runoff is usually poor and patients may be
200 admitted with considerable time delay. Patients with popliteal artery aneurysms may
201 have multiple silent and time-shifted thromboembolic events before presenting with
202 acute ischemia due to complete aneurysm thrombosis.^{14,15} This results in very poor
203 outflow complicating revascularization. In our series, 57% of the patients had one-
204 vessel runoff, and 6% had no patent vessel in the lower leg. Similarly, Lilly and
205 colleagues described decades ago that arterial anatomy below popliteal aneurysms is
206 distinctly abnormal in 90% of the cases with 86% of patients with severe ischemia
207 having only single-vessel runoff.¹⁵

208 Thirty-day major amputation rate in our series was 16% (95% CI 7.0-28.6) with four
209 patients undergoing primary amputation and four patients undergoing secondary
210 amputation after attempted revascularization. As no further major amputations were
211 necessary during follow-up, four-year estimated limb salvage rate was 84%. A
212 multicentric Italian study from 2013 reported a two-year limb salvage rate of ALI due to
213 PAA treated surgically of 81.5% (41 patients).¹⁶ Similarly, a systematic review by
214 Kropman et al. reported a five-year limb salvage rate of 74%.¹⁷ A Swedvasc report
215 showed a similar one year amputation rate of 13.4% (including primary amputation),
216 but the follow up at one year was only 87% and the patient cohort was markedly
217 different (13.2% category I patients).⁹

218 A Vascunet report with data from eight countries, excluding primary amputations,
219 showed a discharge / 30-day amputation rate of 6.5%.¹⁰ However, category of ischemia

220 is not reported. Excluding primary amputations in our series, the one-year amputation
221 rate was 9%.

222 Estimated four-year primary assisted and secondary patency rates in our series were
223 82% and 87% respectively. This is in line with Kropman's findings of a five-year
224 secondary patency of 80%.¹⁷ In our series 96% of patients without major amputation
225 denied any claudication symptoms at follow-up, which is also satisfactory, considering
226 the high prevalence of outflow vessel obstruction in these patients.

227 Clinical assessment and categorization according to Rutherford et al. is crucial when
228 reporting acute limb ischemia. Eleven patients were preoperatively classified as
229 category III. This would actually deem their ischemia irreversible leading to
230 amputation.^{8,12} As four patients were salvageable in our series we must, retrospectively,
231 assume that these cases were initially misclassified and did not show all the
232 characteristics described by Rutherford et al. and therefore were severe category IIb
233 patients. Only the postoperative course may have definitely showed that these cases
234 were only mimicking category III, and were therefore salvageable. However, if no
235 runoff can be achieved intraoperatively by means of thrombectomy and thrombolysis,
236 placement of a bypass seems not advisable.

237 Preoperative thrombolysis has extensively been discussed for ALI due to thrombosed
238 PAA.¹⁸ A recent systematic review could not show significant reduction of amputations
239 after preoperative thrombolysis. Five-year primary patency rates, secondary patency and
240 limb salvage rates were not different after thrombolysis when compared to patients who
241 did not undergo thrombolysis.¹⁷ Many open surgical series included in this review had
242 low patient numbers and acute ischemia was classified only in 122 of 895 patients.¹⁷ In
243 other series investigating this issue, data on the severity of ischemia is lacking.³
244 Neurologic deficits (Rutherford category IIb and III) are well-known indications for

245 emergent revascularization.¹² Preoperative thrombolysis may only lead to a better
246 outcome in patients with less severe ischemia who per se have better outcomes
247 regarding limb salvage. We only included patients with limb-threatening ischemia
248 (Rutherford category \geq II) in our series. These patients should be treated immediately
249 because of the considerable threat of permanent neuromuscular and tissue damage.⁸
250 Preoperative thrombolysis may lead to a delay in open surgical revascularization.¹² Our
251 data does not add knowledge to the topic of preoperative thrombolysis, since it was only
252 performed in two cases.

253 Open bypass surgery is the standard treatment for ALI due to thrombosed PAA at our
254 institution. A complete endovascular approach has been reported in the literature. The
255 largest series by Fargion and colleagues included six patients.⁴ One patient died shortly
256 after early stent thrombosis and major amputation. The remaining five patients showed
257 a primary patency rate of 60% and a secondary patency rate of 80% after a mean
258 follow-up of 28.6 months. The authors state that this approach is an alternative in
259 selected high-risk patients with specific anatomic requirements, but should not replace
260 GSV bypass as the gold standard.⁴

261 Another important issue is the association of PAA with other aneurysms, especially
262 contralateral PAA or AAA.¹¹ Sixty-one percent of patients in our series had
263 contralateral PAA. Six patients had already undergone open surgery for contralateral
264 PAA when presenting with acute limb ischemia due to PAA thrombosis on the other
265 side. Median time from previous PAA surgery to contralateral PAA thrombosis was
266 nine years. This emphasizes the importance of life-long follow-up in these patients, not
267 only to assess bypass patency after PAA repair but for surveillance of aneurysmal
268 disease of the contralateral leg and other associated aneurysms. In an elective setting,
269 PAA can be treated with a low morbidity and mortality and excellent long-term

270 outcomes which are far superior to the results in acute ischemia.^{11,19} Therefore, we aim
271 to search for PAA in patients with known aneurysms at other sites and operate them
272 electively at a diameter of 20mm.

273 **Limitations.** As this is a retrospective single-center study, certain factors may limit the
274 generalizability of the study results. The limited number of patients is reflected by the
275 broad 95% CI in our results. A future large multicentric collaboration could allow for
276 analyses of subgroups to provide more insight concerning the best treatment option for
277 each patient. The category of acute ischemia was documented by the treating vascular
278 surgeon. We assume misclassification for some category III patients, since they were
279 not all amputated. Because this is a retrospective analysis we cannot perform a detailed
280 clinical re-assessment of these cases and had to rely on the clinician's evaluation
281 provided back then. However, publications in this field suffer from this particular bias
282 as well, e.g. some do not report the category of ischemia of the patients included.

283 There is no comparator group, since all patients were treated by open surgery. The
284 selection of graft material, surgical technique, the use of thrombolysis and the
285 anticoagulation and anti-platelet regimen were at the discretion of the vascular surgeon
286 who operated and therefore not standardized. Although regular follow-up visits in our
287 outpatient clinic were documented in most patients, some were followed at other
288 institutions and therefore clinical and ultrasound follow-up was not standardized. Thus,
289 asymptomatic bypass occlusion might not have been detected in some patients. Causes
290 of death are not known in most of the diseased patients. Furthermore, over the span of
291 ten years substantial improvements in interdisciplinary treatment have been achieved.
292 This might have led to less time to intervention and hence higher limb salvage rates.
293 Due to the small study population, we did not analyze trends over time. The time from
294 symptom onset until revascularization is an important issue in ALI. Most of the patients

295 had gradually worsening symptoms and were not able to report a precise time of
296 symptom onset. A strength of the present study is the defined study end date with
297 almost complete follow-up (Follow-Up Index 0.99) and standardized telephone
298 interviews with all surviving patients at the end of follow-up.

299

300 **Conclusion.** Rapid open surgical revascularization in patients with acute limb ischemia
301 due to thrombosed popliteal artery aneurysm results in good long-term limb salvage
302 rates in our series, especially in Rutherford category IIa and IIb of acute ischemia.
303 Revascularization may be attempted in clinically severe cases not fulfilling all criteria to
304 be classified as category III. Such patients may in fact be borderline between IIb and III.
305 Despite poor runoff, good bypass patency rates and low rates of claudication can be
306 achieved.

307 **What this study adds to the current evidence**

308 This study represents a single-center series of open surgical management of acute
309 presentations of thrombosed popliteal artery aneurysm. It stands out from other
310 contemporary reports due to inclusion of patients with severe ischemia and a complete
311 follow-up (median 41 months, Follow-up Index 0.99). Rapid open surgical
312 revascularization without preoperative thrombolysis can lead to good rates of limb
313 salvage and bypass patency despite poor runoff.

314

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318

319 **Conflict of Interest**

320 The authors declare no conflict of interest.

321

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325

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388

389

390 **Tables**

391 **Table 1**

Demographic data	
Number of patients, n (%)	51 (100%)
Age (years), median (range)	75 (46-97)
Male, n (%)	47 (92%)
Comorbidities, n (%)	
Coronary artery disease	22/51 (43%)
Previous vascular surgery	11/51 (22%)
Hypertension	40/51 (78%)
Diabetes	8/51 (16%)
Dyslipidemia	27/51 (53%)
Smoking	31/51 (61%)
GFR \leq 60ml/min	5/51 (10%)
COPD	3/51 (6%)

392

393 **Table 2**

Parameter	Proportion	%
Rutherford classification of acute ischemia at presentation		
IIa	20/51	39
IIb	20/51	39
III	11/51	22
Existing contralateral PAA		
Previous surgery	6/31	19
Intra-arterial thrombolysis		
Preoperative	2/51	4
Intraoperative	17/51	33
Type of surgery		
Primary amputation	4/51	8
Bypass / interposition graft	47/51	92
GSV	43/47	91
Omniflow	2/47	4
Omniflow with cephalic vein	1/47	2
PTFE with GSV	1/47	2
Approach		
Medial	44/47	94
Dorsal	3/47	6
Target vessel		
Below-knee popliteal artery	26/47	55
Anterior tibial artery	2/47	4
Tibioperoneal trunk	5/47	11
Posterior tibial artery	4/47	9
Peroneal artery	6/47	13
Combined	4/47	9

394

395 **Figure and Table Legends**

396 **Table 1.** Demographic data and comorbidities (Abbreviations: GFR = glomerular
397 filtration rate, COPD = chronic obstructive pulmonary disease)

398 **Table 2.** Clinical presentation and surgical data (Abbreviations: GSV = great saphenous
399 vein, PTFE = Polytetrafluoroethylene)

400 **Figure 1:** Distribution of patent crural vessel after revascularization.

401 **Figure 2:** Kaplan-Meier estimate of amputation-free survival including 95% confidence
402 intervals (dotted lines).

403 **Figure 3:** Kaplan-Meier estimates of primary assisted and secondary patency rates.