Eur J Vasc Endovasc Surg (2010) **39**, 452–457

REVIEW

Clinical Outcome of Acute Leg Ischaemia Due to Thrombosed Popliteal Artery Aneurysm: Systematic Review of 895 Cases

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Submitted 9 August 2009; accepted 10 November 2009
Available online 12 February 2010

KEYWORDS
Popliteal artery aneurysm;
Ischaemia;
Thrombosed

Abstract *Objectives:* A systematic review was performed to summarise outcomes of acute thrombosed popliteal artery aneurysms (PAAs) treated with thrombolysis or thrombectomy followed by bypass.
Methods: A systematic review was conducted of data on acute thrombosed PAAs dated 1 January 1990 through 30 June 2008 using the Cochrane Library, MEDLINE and EMBASE databases. Primary endpoint was limb salvage; secondary endpoints were mortality and patency of the bypasses.
Results: Eight prospective studies and 25 retrospective studies with 895 patients presenting with acute ischaemia were included. No randomised trials were included. The mortality rate after surgical repair was 3.2% (95% confidence interval (C.I.) 1.8–4.6). The amputation rate was 14.1% (95% C.I. 11.8–16.4). Thrombolysis before surgery did not result in a significant reduction of the number of amputations, compared with surgery (thrombectomy and bypass) alone. The mean primary patency rates of the bypasses at 1, 3 and 5 years were 79%, 77% and 74%, respectively, in the 'thrombolysis' group and 71% ($P = 0.026$), 54% ($P = 0.164$) and 45% ($P = 0.249$) in the 'thrombectomy' group. No distinction could be made regarding secondary patency and limb-salvage rates between the groups owing to insufficient data.

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doi:10.1016/j.ejvs.2009.11.010

Conclusions: Preoperative and intra-operative thrombolyses result in a significant improvement in 1-year primary graft patency rates, but do not result in a significant reduction for amputations compared with surgery alone.

Popliteal artery aneurysms (PAAs) are the most frequently encountered peripheral arterial aneurysms, with an incidence of 0.1—2.8%.[1—3] Many authors recommend elective surgical intervention in patients with asymptomatic aneurysms larger than 20 mm with mural thrombus because of the increased risk of thrombo-embolic complications.[4—9] Other authors suggest a diameter of 3 cm should be the cutoff point.[10,11] There is barely a need to exclude PAAs to prevent rupture; PAA rupture is rare compared with the rupture of abdominal aortic aneurysms.[4,8] The consequences of acute thrombosis of a PAA are both limb- and life-threatening. Because of thrombo-embolisation of the runoff arteries, an important risk of major amputation exists despite emergency interventions. Historically, surgical thrombectomy of the crural arteries and additional femoro-popliteal or femorocrural bypass grafting were the treatments of choice. In the 1980s, however, intra-arterial catheter-directed thrombolysis was successfully attempted to improve arterial runoff before surgical re-vascularisation to increase patency rates of peripheral bypass surgery.[12] During recent years, complete endovascular treatment (thrombolysis and stent grafting) has become an alternative to open surgery.

This study conducts a systematic review of patients presenting with acute thrombosed popliteal artery aneurysms with ischaemia and compares different strategies of treatment; preoperative thrombolysis followed by exclusion of the PAA with bypass surgery (group A) and surgery alone (crural thrombectomy and bypass surgery, group B), using as primary outcome limb loss and as secondary outcomes mortality rate and primary patency of the bypasses.

Methods

Literature search

To identify relevant literature, a systematic search was performed in the medical databases of Medline (January 1990—June 2008), EMBASE (January 1990—June 2008) and Cochrane Library, comprising the Database of Systematic Reviews (January 1990—June 2008).

The keywords 'acute ischemia,' OR 'leg ischemia,' OR 'acute thrombosis,' AND 'popliteal artery aneurysm,' OR 'thrombosed popliteal artery aneurysm' were used along with synonyms. For endovascular or surgical treatment, we used the terms 'thrombolysis,' OR 'thrombosuction,' OR 'endovascular treatment,' OR 'surgical treatment,' OR 'open repair,' OR 'bypass' OR 'peripheral bypass.' There was no language restriction.

Criteria for inclusion

Titles and abstracts were screened by two reviewers (R.K. and J.V.) independently to identify potentially relevant articles, using the inclusion and exclusion criteria. Discrepancies in judgement were resolved after discussion and, when necessary, after mediation of a third reviewer (F.M.). First, for inclusion, patients had to be treated for an acute thrombosed popliteal artery aneurysm with either thrombolysis followed by bypass surgery, including intra-operative thrombolysis (group A) or surgery alone (crural thrombectomy followed by bypass, group B). In some articles, patients with acute thrombosed PAAs were not the main subject of the manuscript, but a subpopulation, and no detailed information was given of this subgroup. Data were included in this review only if there was a separate description of the acute PAAs in the article. Second, at least one of the outcome parameters — that is, limb salvages, mortality or primary graft patency — had to be reported. Third, the study should include a minimum of five patients. Fourth, it should be an original patient series (studies containing duplicate material were excluded and the ones with the best-documented material were included for analysis).

Data extraction

The following data were recorded per study: method of data collection (prospective or retrospective), selection of patients for the study (consecutive or selected and, if selected, inclusion and exclusion criteria). Furthermore, patient characteristics (number of patients, sex, age and grade of acute ischaemia), relevant risk factors, (i.e., diabetes, smoking, hypertension and renal failure) and characteristics of the arterial tree (diameter PAA and number of outflow arteries) were recorded. Finally, data about the procedure such as technique (medial/dorsal approach, venous/PTFE bypass and endovascular repair) and follow-up data were collected. The following outcomes were recorded and analysed: technical success, primary patency, limb salvage, complications and survival. Technical success was defined as restored outflow through at least one patent crural artery in continuation with the pedal arch. Primary patency was defined as uninterrupted flow (<50% stenosis) in the bypass with neither an additional procedure performed nor an intervention to solve disease progression in the adjacent native vessel.

Data extraction was done by two reviewers (R.K. and J.V.) independently. Discrepancies in judgement were resolved after discussion and, when necessary, after mediation of a third reviewer (F.M.). The full text of these articles was retrieved for further analysis.

Data analysis

Continuous values will be described as means ± standard deviation. Trial heterogeneity was estimated using the Cochrane Q statistic. The I^2 statistic, which is the proportion of total variation among studies that is likely to be

explained by between-study heterogeneity rather than chance, is reported. Substantial heterogeneity exists when I^2 exceeds 50%. Data were pooled using a fixed-effect model if heterogeneity was limited; a random-effect model was used when there was significant heterogeneity among the studies. The conventional 0.05 level of significance was employed.

Thrombolytic treatment

In 28% of patients, a PAA was diagnosed due to acute symptoms of thrombosis.[8] Patients with acute limb ischaemia usually present with limb-threatening ischaemia with minimal or no sensory loss, which, in the absence of paralysis is defined as grade IIa or, in the presence of sensory loss extending beyond the toes, grade IIb, according to Rutherford acute limb ischaemia classification.[14] Rutherford grade III limb ischaemia presents with muscle paralysis extending above the foot, profound sensory loss and inaudible arterial and venous Doppler signals.[14] This classification of acute ischaemia is very important, because it determines the urgency of the treatment. Thrombolysis, with or without additional surgery, has been advised for the treatment of acute ischaemia Rutherford class I–IIa.[14] When sensory loss or motor deficit is present (class IIb–III), there is no time for thrombolysis and surgery has to be performed immediately.

In recent years, a combination of thrombolysis followed by surgery, or sole endovascular treatment consisting of thrombolysis of the PAA and crural arteries and additional exclusion of the PAA with use of a covered stent, has been proposed for treatment of acute thrombosed PAA. Lysis can clear the thrombosed PAA as well as runoff arteries effectively and might improve inflow and outflow and, therefore, relieve persistent ischaemia. However, thrombolysis-related complications might occur; the limb must be capable of withstanding an additional period of ischaemia, and the patient must tolerate the administration of a fibrinolytic agent. In the included studies, no patients were treated with intravenous thrombolysis. Of the 313 patients treated with intra-arterial thrombolysis, 255 were treated with preoperative thrombolysis, the remaining 58 were treated with intra-operative thrombolysis. Of note is that only 4 out of 22 studies used intra-operative thrombolysis.

Results

The initial search yielded 135 articles. After screening of titles and abstract, 101 articles were excluded. The most frequent reasons for exclusion were study design (review, case report with fewer than five patients), location of aneurysms and no acute thrombosed PAAs. One study was excluded after reading the full text.

Results were collected from 33 series containing data from 895 acute thrombosed PAAs.[3–5,7,9–11,13,18–20,21,23–43] Of those 895 patients, intra-arterial thrombolysis was used in 313 (35%)[3,4,7,10,11,18–20,21,25–27,30–32,34–37,42,43] (Fig. 1). In 223 of 313 PAAs, the thrombolytic treatment was successful, defined as restored outflow through at least one patent crural artery in continuation with the pedal arch, resulting in 71% success. In 52 (17%) patients, the thrombolytic treatment was unsuccessful; all of those patients were treated with thrombectomy followed by bypass surgery and were included in the preoperative thrombolysis group. In 38 patients results of the thrombolytic therapy were not recorded. Details of complications during thrombolytic treatment were published for only 142 of the 313 acute thrombosed PAAs treated with thrombolysis (Table 1). Minor bleeding occurred in 14 patients (9.9%), but none required surgical intervention. No major bleedings or cerebral vascular accidents were recorded. Most of the retrieved articles lacked detailed information regarding Rutherford grade of ischaemia, time, total dose of thrombolytic treatment and the number of patent crural arteries.

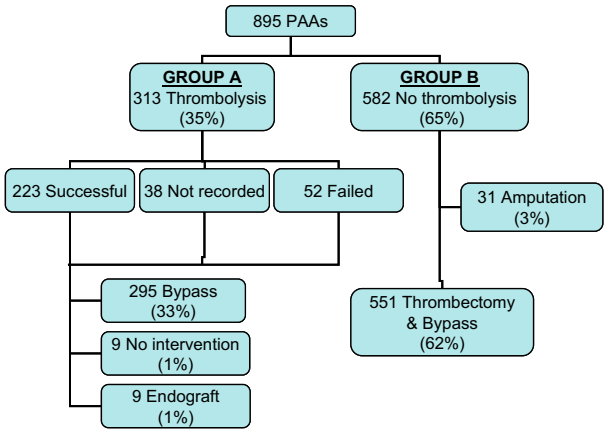

Figure 1 Flow chart of the treatment modalities of patient group A and B.

Of the 895 patients whose data were collected, the acute ischaemia classification was only noted in 122 patients (17%). Of these 122 patients, 101 (83%) presented with marginally threatened limb ischaemia grade IIa, 18 (15%) patients presented with grade IIb and three (3%) presented with irreversible limb ischaemia grade III. A description of the method of treatment for each patient was provided only in few of these 122 patients.

Surgical vascular repair was performed in 846/895 patients (95%). A primary amputation was necessary in 31 patients. Thrombolysis was followed by surgical repair in 295 of 313 patients. After thrombolysis, 18 patients did not undergo surgery, nine (3%) were considered unfit for any surgery and nine (3%) received an endograft.

Data on the surgical approach were available for 372 of the 846 patients (44%). A medial approach was used in 312

Table 1 Complications due to thrombolysis in 142 PAA.[3,4,7,10,11,15–17,20,22,24,27,29,32–34,36,39,40]

	%	SD (%)
Haematoma	2.8	16.5
Minor bleeding	9.9	29.8
Major bleeding	0.0	
Acute leg deterioration	3.5	18.4
Foot drop	2.1	14.4
Pneumonia	0.7	8.4
Mortality	0.0	

PAAs (84%) and the posterior approach in 60 (16%). Type of conduit was recorded in only 402 patients and comprised a vein graft in 318 patients (79%) and a prosthetic graft in 84 (21%). No detailed information was given concerning the type of prosthetic material used.

Early outcome (< 30 days) of acute thrombosed PAA

A 30-day fixed-effect pooled mortality rate of 3.2% (95% (C.I.) 1.8—4.6) was determined in 564 of 895 patients. There are limited data on mortality rates between groups. The major amputation rate within 30 days was 14.1% [95% C.I. 11.8—16.4] ($I^2 = 27\%$) of the 895 acute thrombosed PAAs because of irreversible ischaemia. Of these amputations, 31 (20%) were performed without previous thrombolysis or bypass surgery. Thrombolysis before surgery resulted in a non-significant − 2.3% [95% C.I. −12.7 to 8.2; $P = 0.688$] − absolute reduction of the number of amputations compared with thrombectomy followed by bypass (Fig. 2).

Long-term results of acute thrombosed PAAs

The mean primary patency rates at 1, 3 and 5 years after the bypass of the acute thrombosed PAAs were, respectively, 79% ± 19.0 ($n = 57$), 77% ± 6.3 ($n = 36$) and 74% ± 6.3 ($n = 7$) in group A and 71% ± 12.8 ($n = 88$) ($P = 0.026$), 54% ± 26.0 ($n = 37$) ($P = 0.164$) and 45% ± 28.4 ($n = 16$) ($P = 0.249$) in group B (Table 2). Because of the small group size, no distinction between the different approaches and the different types of conduit could be made.

Owing to lack of data in the included studies, no distinction between group A and group B could be made regarding mean secondary patency and limb-salvage rates. The mean secondary patency and limb-salvages rates at 1 year were 82% ± 24.6 ($n = 74$) and 85% ± 10.4 ($n = 94$), respectively, and at 5 years, 80% ± 14.0 ($n = 26$) and 76% ± 13.1 ($n = 41$), respectively.

Discussion

Thrombolysis before surgery results in a significant improvement in 1-year primary graft patency rates compared with surgery alone. There is no effect on reduction in amputation rate.

No level 1 evidence can be obtained concerning this limb- and life-threatening subject. Remarkably, most published studies are conducted with retrospective data, and almost every study lacks important characteristics (e.g., grade of ischaemia, type of graft material, outflow crural arteries, conduction of dermatofasciotomy and surgical approach) or long follow-up.

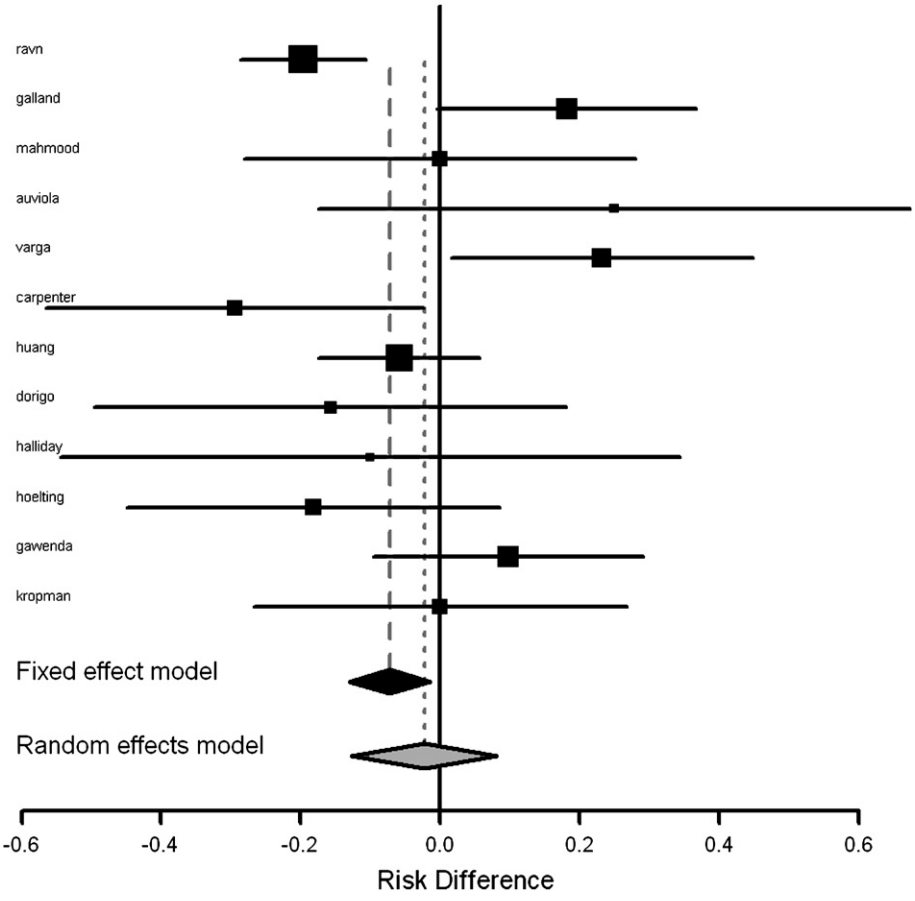

Figure 2 Amputation rate with or without preoperative thrombolysis in acute thrombosed popliteal artery aneurysms. Q-test: $P = 0.0009$, $I^2 = 65\%$ [95% C.I. 35.3-81.1].

Table 2 Primary patency rate for surgical repair of acute thrombosed PAA.

Reference (Year)	Procedures (N)	Primary patency (%)				
		1 year	2 years	3 years	4 years	5 years
Shortell et al. (1991)	22[b]	69[b]	60[b]	39[b]	39[b]	39[b]
Carpenter et al. (1994)	7[a] 17[b]	100[a] 66[b]	78[a] 48[b]	78[a] 38[b]	78[a] 38[b]	78[a] 38[b]
Hoelting et al. (1994)	9[a] 11[b]	100[a] 66[b]	—	—	—	—
Sarcina et al. (1997)	17[b]	88[b]	82[b]	76[b]	67[b]	67[b]
Steinmetz et al. (2000)	15[a]	80[a]	80[a]	80[a]	—	—
Dorigo et al. (2002)	14[a] 10[b]	74[a] 56[b]	—	—	—	—
Galland et al. (2002)	22[a] 14[b]	—	—	76[a] 67[b]	—	—
Marty et al. (2002)	11[a]	46[a]	—	—	—	—
Aulivola et al. (2004)	4[a] 9[b]	67[a] 85[b]	67[a] 85[b]	67[a] 85[b]	67[a] 85[b]	67[a] 85[b]
Huang et al. (2007)	24[a] 50[b]	84[a] 62[b]	—	—	—	—

[a] With thrombolytic therapy.
[b] Without thrombolytic therapy.

The reported overall 5-year primary patency rates for elective surgical repair of non-acute symptomatic PAA are 66–86%.[8] In this review, primary patency rates for acute symptomatic PAAs were 74% in group A and 45% in group B ($P = 0.249$) at 5 years. As in elective femoro-popliteal occlusions, the additional value of thrombolysis prior to bypass surgery remains to be proven.[44–46]

The major amputation rate was 14% because of irreversible ischaemia. Thrombolysis before surgery resulted in a small absolute reduction of the number of amputations compared with surgery alone; however, this effect is not significant because of the high heterogenicity among the studies and the small numbers of the subgroups.

Endovascular stenting has been successfully used in the management of aortic aneurysms; however, its utility in the treatment of PAAs remains questionable. Unfortunately, endovascular treatment of PAAs lacks long-term follow-up. Conversely, endovascular graft repair has the advantage of being minimally invasive, which is important in the treatment of unfit patients. The disadvantage of an all-endovascular treatment of PAA thrombosis could be the fact that the restored flow is often in one crural artery, and that the flow is unlikely to be sufficient to sustain a prosthetic stent. However, it is remarkable that after successful thrombolysis, with at least one patent crural artery, only nine patients received an endograft in this systematic analysis.

Operative results concerning repair of PAA are closely related to the status of the distal outflow and the type of graft material.[8] Unfortunately, only a few studies reported the status of the distal outflow and the grade of ischaemia. Therefore, the patencies between groups cannot be statistically compared without considering bias.

Nevertheless, acute repair of PAAs must be avoided.

Conclusion

Preoperative and intra-operative thrombolyses do not result in a significant reduction for amputations. One-year primary patency rates of surgical interventions after thrombolysis are significantly different compared with surgery alone; 3- and 5-year primary patency rates are not significantly different. No distinction could be made between groups regarding secondary patency and limb-salvage rates. Data on complete endovascular approach of thrombosed PAAs are scarce.

Conflict of interest/funding

None.

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