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Outcome After Occlusion of Infrainguinal Bypasses in the Dutch BOA Study: Comparison of Amputation Rate in Venous and Prosthetic Grafts

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Objective. *To compare the consequences of occlusion of infrainguinal venous and prosthetic grafts.*
Methods. *In total, 2690 patients were included in the Dutch BOA study, a multicenter randomised trial that compared the effectiveness of oral anticoagulants with aspirin in the prevention of infrainguinal bypass graft occlusion. Two thousand four hundred and four patients received a femoropopliteal or femorodistal bypass with a venous (64%) or prosthetic (36%) graft. The incidence of occlusion and amputation was calculated according to graft material and the incidence of amputation after occlusion was compared with Cox regression to adjust for differences in prognostic factors.*
Results. *The indication for operation was claudication in 51%, rest pain in 20% and tissue loss in 28% of patients. The mean follow up was 21 months.*
After venous bypass grafting 171 (15%) femoropopliteal and 96 (24%) femorodistal grafts occluded. After prosthetic bypass grafting 234 (30%) femoropopliteal and 25 (38%) femorodistal grafts occluded. Patients with occlusions in the venous group had more severe ischemia, less runoff vessels and were older than the patients with prosthetic grafts. In the venous occlusion group 54 (20%) amputations were performed compared to 42 (16%) in the prosthetic occlusion group; crude hazard ratio 1.17 (95% CI 0.78–1.75). After adjustment for above mentioned differences in patient characteristics the hazard ratio was 0.86 (95% CI 0.56–1.32).
Conclusion. *The need for amputation after occlusion is not influenced by graft material in infrainguinal bypass surgery.*

Keywords: Peripheral vascular disease; Vascular surgical procedures; Vascular graft occlusion; Amputation; Femoral artery; Popliteal artery; Tibial arteries; Intermittent claudication; Ischemia; Gangrene; Saphenous vein; Blood vessel prosthesis; Polytetrafluoroethylene (PTFE); Polyethylene terephtalate (Dacron).

Introduction

In the assessment of bypass graft surgery the main outcome is often patency rate. An emerging focus is functional outcome such as adequate relief of symptoms, including relief of pain, healing of ischemic lesions, return to unrestricted ambulation, maintenance of independent living, and general level of patient satisfaction or quality of life. Most of these parameters are heavily influenced by a major amputation, mainly due to restricted mobility. Only 12–13% of patients who had a limb amputation will walk with an artificial leg.[1] Five years after a below knee amputation, 50% will be dead, 30% will have had a major contralateral amputation, and only 20% will be alive with one intact leg.[1] The rate of amputation after bypass surgery is influenced by the indication for operation, with a worse outcome for critical limb ischemia (CLI) than for intermittent claudication (IC). For CLI a more aggressive approach in revascularisation over the years has resulted in a decreasing amputation rate. IC is regarded only a relative indication for surgical treatment and then only after an adequate trial of conservative therapy.

The patency of infrainguinal saphenous vein grafts is better than that for prosthetic grafts.[2–5] However,

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prosthetic material may offer several advantages over autologous grafts such as reduced operative time and limited dissection causing lower morbidity. The purpose of this study is to assess whether the graft material influences the immediate and late amputation rate after infrainguinal bypass graft occlusion.

Patients and Methods

This study was part of the Dutch Bypass, Oral anticoagulants or Aspirin (BOA) study; a multicentre, open, randomised trial, to compare the effectiveness of oral anticoagulants with that of aspirin in the prevention of infrainguinal bypass-graft occlusion. Between April 1995 and March 1998, 2690 patients from 77 centres received an infrainguinal bypass graft for occlusive arterial disease. A total of 40 patients were excluded or withdrawn from the study. Demographic information, medical history, vascular risk factors, indication for surgery, brachial and ankle blood pressures, status of arterial outflow vessels, site of distal anastomosis, graft material used, and concomitant antithrombotic medication were recorded. Randomisation was performed for treatment with oral anticoagulants, with a target international normalised ratio (INR) range of 3.0–4.5, or with 100 mg daily pulverised carbasalate calcium (metabolised to acetylsalicylic acid, equivalent to 80 mg). The choice for autologous saphenous vein or prosthetic grafts was left to the judgement of the vascular surgeon. The primary outcome event was graft occlusion, with the following secondary outcome events: (vascular) death, myocardial infarction, stroke, major amputation, vascular intervention, and major haemorrhage. Follow up was performed 3 and 6 months after surgery and every 6 months thereafter, and consisted of clinical examination with Doppler or duplex scanning, and by arteriography if indicated. The full study protocol and results of the Dutch BOA study have been described previously.[6]

For our study purpose all patients with autologous saphenous venous, PTFE (polytetrafluoroethylene), and Dacron (polyethylene terephtalate) bypass grafts were selected from the BOA database. Amputation rate after occlusion, time interval between occlusion and amputation, and patient survival were determined.

Statistics

The incidence of occlusion and amputation was calculated according to graft material and the incidence of amputation after occlusion was compared with Cox proportional hazards regression. Results are expressed as hazard ratios, with corresponding 95% confidence intervals. Differences in prognostic factors between the patients with a venous or a prosthetic graft were taken into account by the calculation of adjusted hazard ratios. Patient survival was determined by life table analysis. Significance was determined at a P value less than .05.

Results

From the total BOA population we excluded 246 patients with 169 biografts and 77 composite grafts. The remaining 2404 patients were categorised into two groups (Fig. 1). The venous group consisted of 1546 patients with saphenous venous grafts, of which 1140 (74%) were femoropopliteal and 406 (26%) were femorodistal. The prosthetic group (858) consisted of 374 (44%) patients with Dacron and 484 (56%) patients with PTFE grafts; 793 (92%) bypasses were femoropopliteal and 65 (8%) femorodistal. The mean duration of follow up was 21 months for both groups.

Occlusion was verified by Doppler or duplex scanning or angiography in 92% of patients in whom this event occurred (Fig. 1). Table 1 shows the patient characteristics for the two groups. Overall, the indication for operation was claudication in 51%, rest pain in 20% and tissue loss in 28% of patients. The groups were similar with respect to gender and prevalence of diabetes. However, patients with occlusions in the venous group had more severe ischemia, less runoff vessels and were older than the patients with prosthetic grafts.

After venous bypass grafting 267 (17%) occlusions occurred. In this occluded group 171 (15%) grafts were femoropopliteal and 96 (24%) were femorodistal, leading to amputations in 28 (16%) and 26 (27%) patients, respectively. A total of 259 (30%) prosthetic bypass grafts occluded of which 234 (30%) were femoropopliteal and 25 (38%) were femorodistal grafts. This resulted in an amputation in 35 (15%) and 7 (28%) patients, respectively (Fig. 1). Thus, in the venous occlusion group 54 (20%) amputations were performed compared to 42 (16%) in the prosthetic occlusion group. The crude hazard ratio was 1.17 (95% CI 0.78–1.75) (Table 2). Fig. 2 shows the time interval between occlusion and amputation for the two groups. After adjustment for age, Rutherford classification and number of runoff vessels the hazard ratio was 0.86 (95% CI 0.56–1.32). Adjustment for trial medication had no effect on the hazard ratio estimate. Table 3 shows the amputation according to indication for operation and graft material. When the analysis was

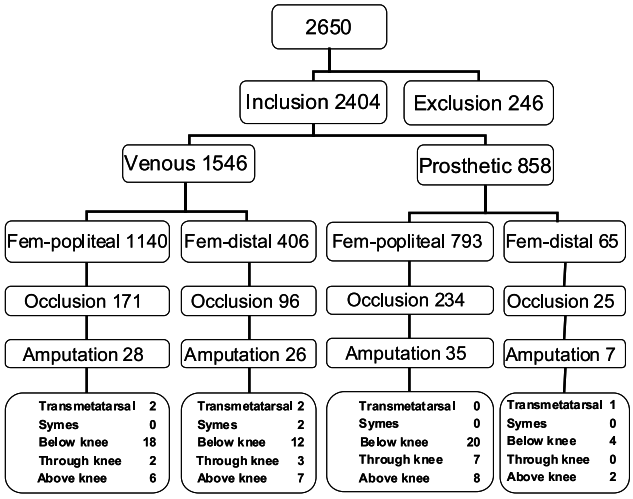

Fig. 1. Two thousand six hundred and fifty Dutch BOA patients and amputations after occlusions.

restricted to patients with femoropopliteal bypasses only, the results were essentially the same.

Discussion

In this study, we found that infrainguinal bypass graft occlusion was associated with an equal risk of immediate and late amputation for saphenous venous and prosthetic (Dacron and PTFE) grafts. Off course from baseline more bypasses occluded in the prosthetic group than in the venous group (30 *versus* 17%). So overall there were relatively more occlusions and, therefore, more amputations in the prosthetic group.

Table 2. Crude and adjusted hazard ratios of venous *versus* prosthetic bypass material for ipsilateral amputation after graft occlusion

Adjustments	Hazard ratio	95% CI
Crude	1.17	0.78–1.75
Age	1.07	0.71–1.61
Sex	1.16	0.78–1.74
Diabetes mellitus	1.16	0.77–1.73
Rutherford classification	0.98	0.66–1.47
Runoff vessels	0.90	0.60–1.37
Site distal anastomosis	0.96	0.63–1.48
All of these but sex and diabetes	0.86	0.56–1.32

We used the data of the Dutch BOA study in which patients were not randomised for graft material but for treatment with aspirin or oral anticoagulants. Ideally, our study question should be investigated in a randomised controlled trial. However, the prospective study population with 2405 patients is large and allows for additional analysis as described in this paper. Our results are supported by John *et al.* in a prospective study on 290 above-knee femoropopliteal bypass grafts. A total of 99 bypasses occluded with no difference in amputation rate between saphenous vein and PTFE after a median follow up of 20 months.[7] A more recent retrospective study by Jackson *et al.* of 189 femoropopliteal bypass grafts, described 57 occlusions. In this study, the ischemic consequences of femoropopliteal bypass graft occlusion were more severe with PTFE than with saphenous vein resulting in a higher amputation rate.[8] No effect was seen of oral anticoagulants and aspirin in terms of the amputation rate after bypass failure.

Our findings are supported by a recent prospective study describing 402 patients with femoropopliteal

Table 1. Baseline characteristics of all patients and those who developed an occlusion of their bypass

	Graft material			
	Venous		Prosthetic	
	All ($n=1546$)	Occluded ($n=267$)	All ($n=858$)	Occluded ($n=259$)
Age (years)	69±10	69±10	68±10	67±10
Male	1020 (66.0)	160 (59.9)	534 (62.2)	163 (62.9)
Rutherford category				
III	706 (45.7)	97 (36.3)	534 (62.2)	154 (59.5)
IV	348 (22.5)	85 (31.8)	141 (16.4)	44 (17.0)
V	492 (31.8)	85 (31.8)	183 (21.4)	61 (23.5)
Site of distal anastomosis				
Femoro-popliteal	1133 (73.7)	171 (64.0)	793 (92.4)	235 (90.3)
Femoro-distal	413 (26.3)	96 (36.0)	65 (7.6)	25 (9.7)
Runoff				
0	62 (4.0)	14 (5.4)	19 (2.2)	8 (3.1)
1	500 (32.4)	118 (44.0)	191 (22.3)	66 (25.6)
2	510 (33.0)	69 (25.9)	301 (35.1)	90 (34.5)
3	475 (30.7)	66 (24.7)	347 (40.4)	95 (36.8)
History				
Diabetes mellitus	413 (26.7)	77 (28.8)	224 (26.1)	69 (26.6)
Myocardial infarction	271 (17.5)	47 (17.6)	152 (17.7)	46 (17.8)
Allocated to trial aspirin	762 (49.3)	155 (58.1)	446 (52.0)	125 (48.3)

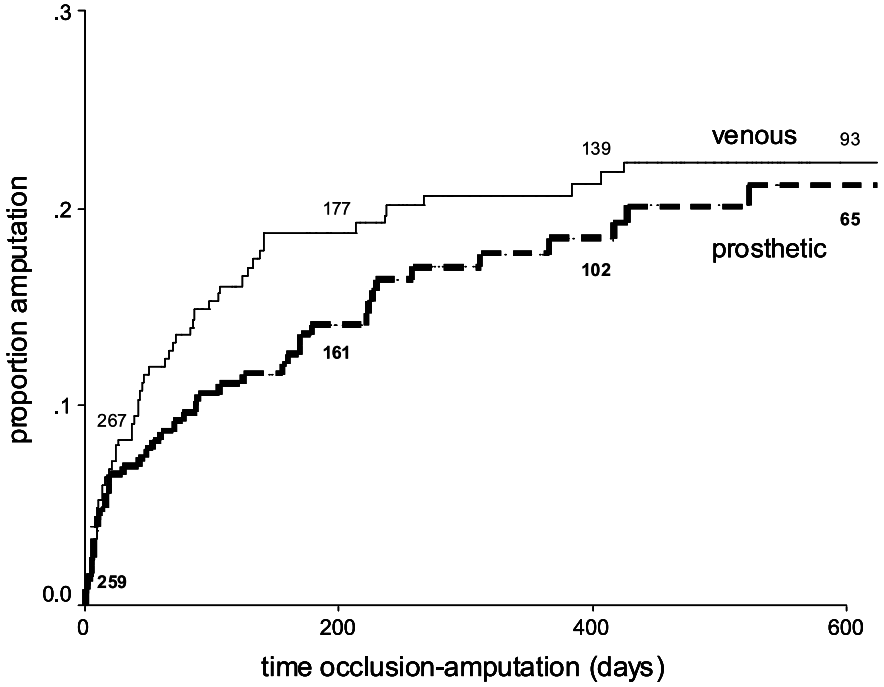

Fig. 2. Time interval between occlusion and amputation with number of patients at risk.

bypasses, randomised to oral anticoagulants (target INR of 1.4–2.8) and aspirin or aspirin only. The indication for surgery was limb salvage in 66% of the patients and 100 occlusions were reported. Although oral anticoagulants and aspirin gave less ischemia than aspirin after PTFE graft occlusion, the incidence of major amputation after occlusion was the same after a median follow up of 36 months. There was no difference between these two medication groups after vein graft occlusion.[9]

A recently published randomised trial showed that PTFE was associated with a higher incidence of amputation after graft occlusion when compared to Dacron.[10] In our study, the rate of amputation was similar in the patients with a Dacron (16.7%) and PTFE (16%) graft, however, due to the low numbers of patients and amputations in these subgroups, firm conclusions cannot be drawn.

A total of 82 amputations were performed in 1164 patients with CLI, giving an amputation rate of 7% over a mean follow up of 21 months. In contrast, John *et al.* and Jackson *et al.* reported an overall amputation rate of 22 and 18%, respectively, at 20 months. There is general agreement that surgical revascularisation provides durable results for critical ischemic limbs in 85–90% of cases with less mortality, shorter hospital stay and longer survival than primary amputation.[11–13] However, there is no consensus regarding the use of operative treatment for claudicants. In a recently presented study, the health utility outcome scores in claudicants were similar or worse than for patients with osteoarthritis undergoing arthroplasty.[14] In spite of a rather modest increase in walking distance these patients experienced a substantial improvement in quality of life (QoL) scores after intervention, which also proved to be cost effective, at least short term. Up to 5% of men and 2.5% of women aged 60 years or older have symptoms of intermittent claudication. Without revascularisation, every year about 0.3–1% of these patients require an amputation.[15,16] Only one fourth of all claudicants deteriorate progressively and an intervention is needed in approximately

Table 3. Occlusions and amputations according to indication for operation and graft material

	Graft material					
	Venous			Prosthetic		
	All (1546)	Occluded (267)	Amputation (54)	All (858)	Occluded (259)	Amputation (42)
Claudication	706	97	4	534	154	10
Rest pain	348	85	18	141	44	11
Tissue loss	492	85	32	183	61	21

0.5% per annum.[17–19] Previous studies describing femoropopliteal bypass grafting in claudicants report an overall amputation rate of 0.5–1.4% per year.[20,21] In our study, 14 amputations were performed in a total of 1240 patients with IC giving an amputation rate of 1.1% over 21 months. Several studies report that failed revascularisation attempts adversely affect the ultimate level of amputation, resulting in more knee-joint loss, whereas other studies report no difference.[22–26] In the event of an amputation after failure of a bypass graft a below knee amputation is performed in about 60% and an above knee amputation in around 40%.[26,27] In this study, a below, through and above knee amputation occurred in 56, 13 and 24%, respectively.

The choice of which material to use in infrainguinal bypass graft surgery is mostly based on the site of the distal anastomosis, availability of adequate autologous saphenous vein, and if it is the first revascularisation attempt or not. There are arguments why prosthetic grafts could be inferior to venous grafts in the outcome after occlusion. Occlusion in prosthetic grafts is mostly acute without a (symptomatic) stenosis as a warning sign. This provides less time for development of collaterals and metabolic adaptation of ischemic muscle. Flow in prosthetic grafts is considered as an all-or-none situation between high velocity flow and occlusion. Also, prosthetic grafts are more thrombogenic than venous grafts and could cause crural artery thromboembolism. On the other hand, venous grafts are more susceptible to compression forces compared to the (ring-enforced) prosthetic grafts.

In spite of all these hypothetical arguments we found no difference between venous and prosthetic graft material in the risk of amputation after infrainguinal bypass occlusion.

Acknowledgements

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