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Pedal Bypass Surgery Prevents Amputation in Patients with Critical Lower Limb Ischemia - A Single Center Experience of 99 Pedal Bypass Operations

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Abstract

Background: Bypass surgery below the ankle is now rarely used as prevention of major amputations due to critical limb ischemia. We aimed to investigate results after bypass surgery below the ankle performed at a single center in Denmark. The study was designed as a retrospective, single centre study and endpoints were major amputations, overall survival as well as amputation-free and intervention-free survival.

Methods: We included all patients undergoing pedal bypass surgery at a single vascular centre in Denmark. Baseline was set as date of surgery and patients were followed until amputation, death or end of study. The mean amputation-free and overall survival as well as primary and secondary patency was calculated using Kaplan Meier survival analysis. Cox regression analysis was performed to investigate possible significant co-variables.

Results: We included 93 patients with 99 bypasses. 16 patients (16.5%) experienced one or more open and/or endovascular bypass revisions and 26 (28%) experienced major amputation. Mean patency, primary as well as secondary, was 2.6 years. Mean amputation-free survival was 2.9 years and mean overall survival 3.9 years.

Conclusion: This study shows that in many cases bypass surgery to a pedal artery can prevent major amputation in patients with critical limb ischemia and that patients undergoing this kind of surgery have an expected amputation-free survival comparable to patients undergoing crural bypass operations above the ankle reported in earlier studies. Therefore, this type of operation should be considered as treatment to prevent amputation in patients with no graftable arteries on the lower leg above the ankle.

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Introduction

Patients with critical limb ischemia are often of high age, have multiple comorbidities and face a high risk of major amputation, which further increases their morbidity and mortality [1,2]. Distal bypass surgery to the infra-popliteal arteries is considered a reliable and effective treatment of these patients; however, in some cases the crural arteries are not suitable for bypass surgery [3,4]. As the pedal arteries often are patent even in cases with severe infra-popliteal atherosclerosis, bypass surgery to an artery below the ankle can be the last resort in preventing amputation [5]. This type of operation is however despite good results internationally still controversial and many surgeons are reluctant to perform it [6,7]. In Denmark, this kind of operation has in the past been performed on a regular basis, but during the last decade, the number of pedal bypasses has declined, and now only very few institutions perform this procedure (Figure 1). In Denmark it has often been stated that the reason for the decline in the use of pedal bypass operations is due to poor patency and high amputation rates, but results from centers in Denmark have so far not been investigated. The aim of this study was to investigate whether bypass surgery to an artery below the ankle can prevent major amputation in patients with critical limb ischemia.

Materials and Methods

This study includes patients treated at a single vascular center in Denmark. All patients, who had bypass surgery performed to an artery below the ankle, were identified using operation codes for surgery to a pedal artery registered in the national vascular registry Karbase [8,9]. In Karbase all vascular procedures in Denmark are prospectively registered with information on patient

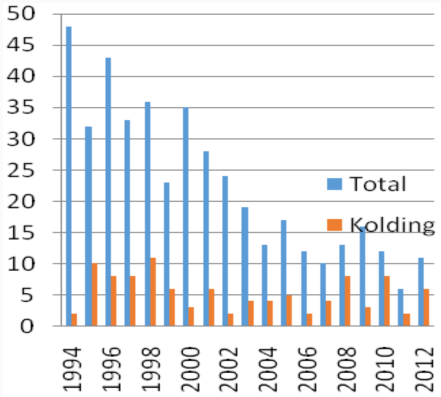

Figure 1: Number of pedal bypasses performed in Denmark from 1994-2012.

characteristics, comorbidities, operation-specific information as well as follow up including patency of reconstruction.

Baseline was set as date of surgery and patients were followed until amputation, death or end of study set as September 19th, 2013. Intervention-free and overall patency was calculated for each bypass. Intervention-free patency was calculated as time to first endovascular intervention, surgical bypass revision or re-do bypass. All analyses were carried out at bypass level, except for mortality analyses, which were calculated at patient level. Median amputation-free and overall survival, as well as intervention-free and overall patency, was calculated using Kaplan Meier survival analysis and Kaplan Meier survival curves were used to give an overview of the results. Cox regression analysis was performed to investigate possible significant co-variables. In the analysis of amputation-free survival and major amputations, patients with two bypasses were censored after the first event and analysis of total mortality survival time was calculated from date of the first bypass operation.

Information regarding operations was retrieved via medical records: Out- and inflow artery, bypass material (*in situ* great saphenous vein, reversed vein or PTFE) and whether the bypass was performed as primary vascular reconstruction or revision of an existing bypass. All vein bypasses were routinely examined clinically including duplex ultrasound scans at six weeks, 3, 6 and 12 months and after two years. In cases where a patient had additional visits at the department or out-patient clinic, the status of the bypass was recorded. The bypass was considered patent if there was palpable pulse distally, if the patient had sufficient ankle-brachial index and/or if the bypass was deemed to be functioning after examination by Doppler or duplex ultrasound.

Most patients had diagnostic scans performed before the bypass operation; MRI-angiography, CT-angiography or digital subtraction angiography. In cases where the distal blood vessels were difficult or impossible to visualize on the angiographies, the patient underwent ultrasound or Doppler examination to identify possible outflow arteries on the foot. These were then explored in the operation theatre. No patients were considered inoperable based on angiography alone.

Information regarding comorbidities (diabetes, kidney function, and hypertension, Congestive Heart Failure (CHF), Chronic Obstructive Pulmonary Disease (COPD) as well as a history of stroke or coronary disease) was retrieved using medical records. Patients were registered as having impaired kidney function if they had creatinine levels above their sex- and age-adjusted reference level. Results from

Table 1: Patient characteristics and comorbidity.

Age, years	72.3 (42.9-92.3)
Mean (range)	
Gender	
Woman n (%)	26 (28)
Man, n (%)	67 (72)
Diabetes	
Type I, n (%)	9 (10)
Type II, n (%)	48 (52)
Smoking	
Current	
Former	36 (39)
Never	
	9 (10)
	48 (51)
Heart disease	
CABG/AMI/PCI, n (%)	
CHF, n (%)	20 (27)
AF, n (%)	
	11 (15)
	17 (23)
Pulmonary disease	
COPD, n (%)	
	13 (17)
Kidney function	
Elevated creatinine	29 (38)
Dialysis	6 (6)

CABG: Coronary Artery Bypass Grafting, AMI: Acute Myocardial Infarction; PCI: Percutaneous Coronary Intervention; CHF: Congestive Heart Failure; AF: Atrial Fibrillation; COPD: Chronic Obstructive Pulmonary Disease

up to a year before operation were eligible and only pre-operative results were included. Regarding smoking, patients were divided into three groups: Ongoing, former or never smokers. Patients were considered former smokers if they stopped smoking at least 6 weeks before surgery. Hypertension was registered as no hypertension, untreated/poorly regulated or well treated hypertension and diabetes as either type 1, type 2 or no known diabetes.

Information on patients' vital status and date of death was retrieved via the National Central Person Registry [10]. Information on major amputations was retrieved *via* Karbase and medical records.

Results

In all 93 patients (26 women and 67 men) with 99 bypasses were included. One patient had two consecutive bypasses done on the same leg and five patients had bilateral pedal bypasses.

Mean age was 72.3 years (range 42.9 to 92.3 years), with a generally higher age among females compared to males (77.4 *vs.* 70.2 years). All patients had critical limb ischemia (rest pain, non-healing ulcers or gangrene) and a high level of comorbidity. For details regarding patient characteristics, see Table 1.

At the end of the study 21 (23%) patients were alive, 70 (75%) had died and 2 (2%) had unknown vital status (lost to follow-up). Mean follow-up time was 3.8 years (range 0 to 17.1 years).

Table 2: Bypass characteristics.

Indication	
Rest pain, n (%)	18 (18)
Non-healing ulcers, n (%)	34 (34)
Gangrene, n (%)	30 (30)
Non-specified critical ischemia, n (%)	17 (17)
Outflow artery	
CFA, n (%)	43 (43)
SFA, n (%)	23 (23)
Supragen a. poplitea, n (%)	6 (6)
Infragen. a. poplitea, n (%)	7 (7)
Other bypass, n (%)	3 (3)
Inflow artery	
Arteria dorsalis pedis, n (%)	78 (79)
Arteria plantaris, n (%)	21 (21)
Bypass material	
In situ great saphenous vein, n (%)	88 (89)
Reversed autologue vein, n(%)	10 (10)
PTFE, n (%)	1 (1)
Patency at discharge	
Patent, n (%)	86 (87)
Occluded, n (%)	13 (13)

CFA: Common Femoral Artery; SFA: Superficial Femoral Artery; PTFE: Polytetrafluoroethylene graft

Table 3: Patency rates, limb salvage and survival with standard errors.

	1 year (%)	5 years (%)	10 years (%)
Primary patency	72.1 ± 5.1	64.8 ± 5.8	54.7 ± 8.2
Secondary patency	79.7 ± 4.6	70.0 ± 5.7	65.4 ± 7.0
Limb salvation	79.9 ± 4.3	65.8 ± 6.1	60.3 ± 7.7
Amputation-free survival	62.9 ± 4.9	27.2 ± 4.8	5.9 ± 3.0
Overall survival	77.3 ± 4.3	37.8 ± 5.3	10.6 ± 4.2

Regarding early failure, 13 bypasses were occluded before discharge. Of those seven patients had major amputation and four patients died. Only two patients with occluded bypass at discharge were alive at the end of the study. One had resting pain, but no tissue loss and one underwent successful endovascular treatment of the crural arteries.

Primary patency

Fifteen patients (16.1%) experienced one or more surgical and/or endovascular bypass revisions; 11 had endovascular and four surgical revisions. Only two patients underwent both endovascular and surgical intervention. Mean primary patency was 2.6 years (range 0 to 12.6 years, median 1.2 years). For patency rates at 1, 5 and 10 years, see Table 3. See Figure 2 for Kaplan-Meier graph.

No significant confounders for primary patency were found using regression analysis. See Table 4 for details.

Secondary patency

We registered occlusion of 22 bypasses (22.2%) during the study. Mean secondary patency was 2.6 years (range 0 to 12.6 years, Median 1.4 years). For patency rates at 1, 5 and 10 years, see Table 3. See Figure 3 for Kaplan-Meier graph.

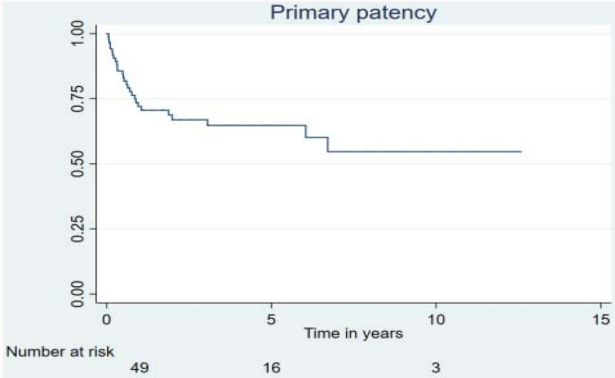

Figure 2: Primary patency.

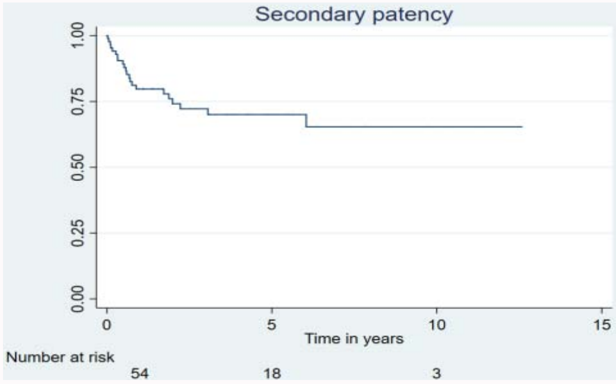

Figure 3: Secondary patency.

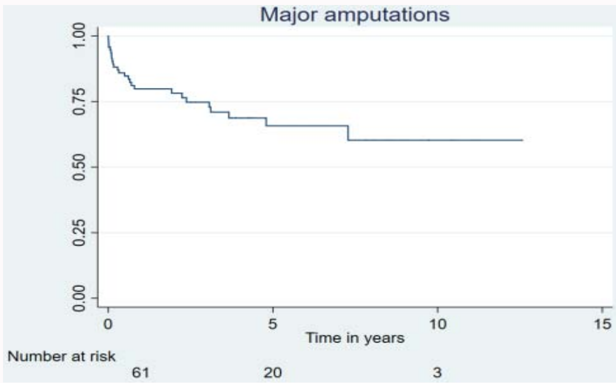

Figure 4: Major amputations.

Using multivariate regression analysis, we found elevated creatinine levels to be associated with a higher risk of occlusion (HR 4.99, p=0.034). See Table 4 for details.

Major amputations

In all 26 patients (28%) experienced major amputation.

Amputation rates at 1, 5 and 10 years can be seen in Table 3. See Figure 4 for Kaplan-Meier graph for major amputations.

Because of very few events in the analysis of major amputations, no regression model could be fitted [11].

Amputation-free survival

Mean amputation free survival was 2.9 years (range 0 to 12.5 y, median 1.8 y). See Table 3 for amputation rates at 1, 5 and 10 years.

Table 4: Multivariate regression analysis – primary and secondary patency.

	Primary patency			Secondary Patency		
	HR	p-value	95% CI	HR	p-value	95% CI
Age						
Age (years)	0.98	0.54	0.931;1.038	0.94	0.074	0.881;1.006
Sex						
Man	Ref	Ref	Ref	Ref	Ref	Ref
Woman	2.12	0.297	0.517;8.695	1.83	0.438	0.396;8.487
History of stroke						
Yes	0.23	0.094	0.041;1.288	0.28	0.194	0.042;1.906
AMI/CABG/PCI						
Yes	1.5	0.633	0.286;7.809	0.92	0.929	0.149;5.676
Atrial fibrillation						
Yes	2.14	0.349	0.437;10.466	0.72	0.764	0.084;6.147
CHF						
Yes	0.12	0.163	0.006;2.395	0.28	0.428	0.012;6.554
Diabetes						
No	Ref	Ref	Ref	Ref	Ref	Ref
Type 1	0.51	0.611	0.036;6.672	0.12	0.152	0.006;2.203
Type 2	0.85	0.861	0.143;5.086	0.75	0.775	0.103;5.455
COPD						
Yes	1.37	0.718	0.244;7.724	0.81	0.847	0.101;6.549
Smoking						
Never	Ref	Ref	Ref	Ref	Ref	Ref
Former	0.5	0.35	0.114;2.156	0.46	0.351	0.090;2.355
Current	0.86	0.841	0.205;3.635	0.26	0.15	0.043;1.614
Kidney function						
Impaired	1.92	0.242	0.643;5.747	4.99	0.034*	1.131;22.063
Hypertension						
None	Ref	Ref	Ref	Ref	Ref	Ref
Well regulated	1.85	0.388	0.457;7.493	1.52	0.577	0.347;6.707
Poorly regulated	5.19	0.28	0.261;103.087	6.5	0.249	0.270;156.540
Diagnosis						
Resting pain	Ref	Ref	Ref	Ref	Ref	Ref
Non-healing ulcers						
Gangrene	0.6	0.597	0.088;4.049	0.23	0.197	0.026;2.130
	0.59	0.666	0.547;6.399	0.47	0.552	0.038;5.746
Inflow						
Femoral	Ref	Ref	Ref	Ref	Ref	Ref
Supragenicular	0.94	0.938	0.213;4.178	0.79	0.79	0.134;4.619
Infragenicular	3.44	0.257	0.406;29.147	1.25	0.864	0.100;15.583
Outflow						
Dorsal pedal artery						
Plantar artery	Ref	Ref	Ref	Ref	Ref	Ref
	0.47	0.277	0.119;1.841	0.59	0.502	0.130;2.714
Redo operation						
Yes	3.04	0.473	0.146	1.97	0.675	0.0828;46.939

HR: Hazard Ratio; CABG: Coronary Artery Bypass Grafting; AMI: Acute Myocardial Infarction; PCI: Percutaneous Coronary Intervention; COPD: Chronic Obstructive Pulmonary Disease; CI: Confidence Interval

*: Statistical significant at 95% CI level

Table 5: Multivariate regression analysis - survival.

	Amputation-free survival				Overall survival			
	HR	p-value	95% CI	HR		p-value		95% CI
Age								
1	0.896	0.964;1.032	1		0.965		0.965;1.038	
Sex								
Ref	Ref	Ref	Ref		Ref		Ref	
Woman	1.39	0.365	0.682;2.829	1.26		0.553		0.592;2.662
History of stroke								
1.39	0.418	0.624;3.118	1.78		0.145		0.821;3.843	
AMI/CABG/PCI								
0.79	0.614	0.314;1.982	1.31		0.596		0.485;3.522	
Atrial fibrillation								
1.79	0.296	0.601;5.300	0.95		0.938		0.296;3.076	
CHF								
2.23	0.146	0.756;6.571	2.1		0.172		0.724;6.094	
Diabetes								
Type 1	0.49	0.327	0.117;2.048	0.59		0.47		0.138;2.495
Type 2	0.91	0.818	0.400;2.062	0.44		0.050*		0.194;1.002
COPD								
1.4	0.461	0.570;3.459	1.56		0.404		0.548;4.457	
Smoking								
Ref	Ref	Ref	Ref		Ref		Ref	
Former	0.36	0.016*	0.158;0.829	0.49		0.092		0.216;1.121
Current	0.44	0.078	0.174;1.096	0.71		0.453		0.295;1.725
Kidney function								
1..30	0.468	0.644;2.608	1.72		0.15		0.820;3.624	
Hypertension								
Ref	Ref	Ref	Ref		Ref		Ref	
Well regulated	0.86	0.7	0.387;1.892	2.22		0.094		0.872;5.675
Poorly regulated	0.81	0.799	0.157;4.157	2.05		0.47		0.291;14.475
Diagnosis								
Non-healing ulcers	0.62	0.304	0.250;1.541	1.28		0.616		0.492;3.300
Gangrene	0.45	0.142	0.158;1.303	1.78		0.281		0.469;4.970
Redo operation				Not included in analysis				
4.08	0.044*	1.041;16.001						
Early failure				Not included in analysis				
5.43	<0.0005*	2.181;13.535						
Amputation	Not included in analysis							
Yes					0.96		0.909	0.469;1.962

CABG: Coronary Artery Bypass Grafting; AMI: Acute Myocardial Infarction; PCI: Percutaneous Coronary Intervention; CHF: Congestive Heart Failure; COPD: Chronic Obstructive Pulmonary Disease

*: Statistical significance at 95% CI level

See Figure 4 for Kaplan-Meier graph for amputation-free survival.

Using multivariate regression analysis, we found that former smokers performed better than both current and never smokers (HR 0.36, p=0.016). We also found both early failure (occlusion of bypass before discharge) and redo operations to be associated with worse outcome (HR 5.43, p<0.0005 and HR 4.08, p=0.044 respectively). See Table 5 for details.

Overall survival

Mean overall survival was 3.8 years (range 0 to 17 years, median 3.2 years). Amputation rates at 1, 5 and 10 years can be seen in Table

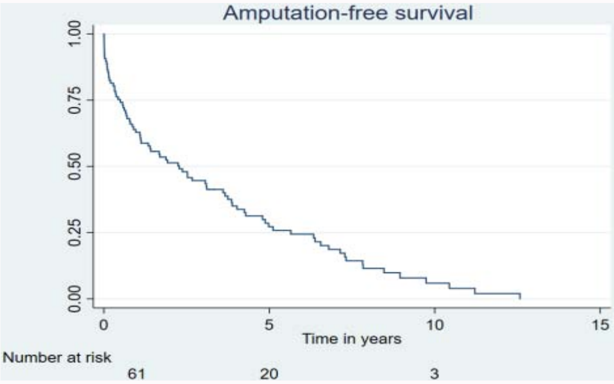

Figure 5: Amputation-free survival.

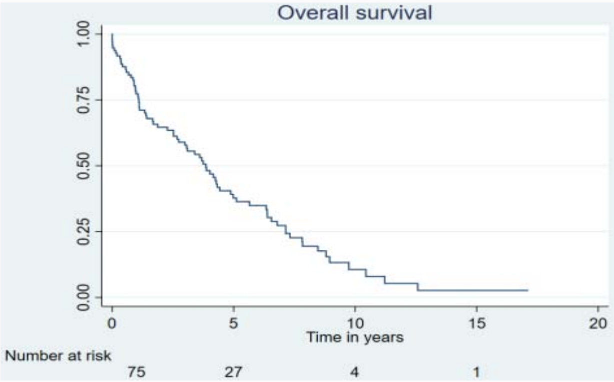

Figure 6: Overall survival.

3. See Figure 5 for Kaplan-Meier survival graph.

Using multivariate regression analysis, we found that patients with type 2 diabetes had a better outcome (HR 0.44, p=0.050). No other significant risk factors or covariates were found.

Discussion

Pedal bypass surgery is still a controversial treatment but in this study we found that this kind of surgery in many cases can prevent major amputation in patients with critical lower limb ischemia.

More than half of the patients in this study had diabetes. This is however not surprising, as the pattern of how arteriosclerosis affects these patients in many cases make crural bypass surgery impossible [5].

In this study we also found, that former smokers did better than never smokers in the analysis of amputation-free survival. This can in part be caused by other life style changes in patients who quit smoking. It is however also quite possible, that genetics play a role: If a patient develops critical lower limb ischemia despite never smoking, it may be due to a more aggressive genetic predisposition for the disease.

Surprisingly patients with type 2 diabetes had better survival than patients without diabetes, although this result was only borderline significant.

Limitations

As mentioned before, we did unfortunately not have any information on the level of regulation of diabetes (measured by the level of glycated hemoglobin, HbA1c), which is known to be an important factor for mortality and morbidity in both type 1 and type 2 diabetics [12]. In our experience, patients with severe arteriosclerosis however, rarely have well-regulated diabetes. We also only had information on current smoking status and not the total number of cigarettes smoked, which is a more accurate estimate of the effect of smoking. Another possible confounder, we did not include, is use of medication. All patients are generally treated with at least one kind of anti-thrombotic medication as well as medication against hypercholesterolemia, but there are of course exceptions: Some patients have difficulties tolerating different kinds of medications and others for various reasons do not want the treatment.

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