HAEMODYNAMICS IN AXILLOBIFEMORAL BYPASS GRAFTS

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HAEMODYNAMICS IN AXILLOBIFEMORAL BYPASS GRAFTS

HAEMODYNAMIEK IN AXILLOBIFEMORALE PROTHESEN

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CHAPTER 1

INTRODUCTION

1.1 History of the axillobifemoral bypass

Extra-anatomic bypass is a term used by vascular surgeons for the past 30 years, referring to bypasses with a routing not normally taken by an artery. Most extra-anatomic bypasses are subcutaneous through much of their course. The most common examples of these bypasses have been the axillofemoral and the femorofemoral cross-over bypass, although many other versions of extra-anatomic bypasses have gained popularity. Freeman, in 1952, reported on what appeared to be the first extra-anatomic bypass (1). This procedure was a femorofemoral bypass using an endarterectomized superficial femoral artery. In 1960, McGaughan reported upon an iliac cross-over popliteal artery bypass using a Dacron graft (2). In 1961, Blaisdell reported upon the use of a Dacron bypass from the descending thoracic aorta to a femorofemoral graft to supply distal circulation after removal of an infected aortic graft (3). In 1962, Vetto reported a series of ten femorofemoral bypasses using prosthetic (Dacron) grafts (4), an article which popularized this procedure.
Lewis documented in 1961 the merit of the subclavian artery as an inflow source for the lower extremities when he operated on a patient with a ruptured abdominal aortic aneurysm which had dissected upward toward the arch. He implied that the subclavian artery is able to nourish both lower extremities with acceptable limitations (5).
In 1962, Blaisdell reported the first axillofemoral bypass (6). It was placed in a patient who suffered a cardiac arrest while being anaesthetized for reoperation for thrombosis of an aortic aneurysm prosthesis. After the patient had been resuscitated, the operation was continued with the patient under local anaesthesia using a technique of extra-anatomic axillofemoral bypass. This technique has changed very little over the last three decades. Louw reported in 1963 (7) the independent development of an axillofemoral bypass procedure, which was similar to the Blaisdell procedure, but using a vein instead of prosthetic material. Since these early publications several case reports have been published on the use of prosthetic axillofemoral bypasses (8-20). Reports on axillofemoral bypasses using vein as a conduit are scarce and are sometimes mentioned incidently in larger series. Only Stipa in 1971 (21) discussed the use of veins more extensively in a case report, but its use has never gained popularity.

1.2 Patency

The first reported series on axillounifemoral grafting by Mannick in 1968 (22) in 15 high risk patients with severe ischemia of both legs secondary to aortoiliac occlusive disease and two patients with a septic aortic graft showed a successful revascularisation in 14 patients. During the seventies end eighties several series were published on the primary and secondary patency rates of axillobifemoral bypasses, summarized in table 1. The range for primary patency varied between 37 and 95 percent after two years (23-40). A recent large series reported by Harris et al (40) showed a primary patency after 3 years of 85 percent using PTFE

axillobifemoral prostheses. Published data on secondary patency are also listed in table 1, ranging from disappointing patency rates of only 60 percent after 4 years (30) to promising results with secondary patency rates of up to 97 percent after 2.5 years (29).
There are a number of other reports on primary and secondary patency rates of axillofemoral bypasses but these series did not distinguish between axillounifemoral or axillobifemoral bypass grafts and therefore are not listed in table 1 (22, 41-50).
No conclusions can be drawn from such an overview of the literature, but a few remarks can be made. The overall primary patency rate in these published data is 63 percent after 3.6 years. The data suggest that PTFE has a better primary patency rate (71 % after 3.7 years) than Dacron in axillobifemoral grafts (56% after 3 years). A prospective randomized trial comparing PTFE and Dacron would be necessary to evaluate these inconclusive data. The secondary patency rate is nearly the same for both types of prosthetics. The overall secondary patency in this literature survey is 73 percent after 3.6 years, which is markedly lower than the primary patency rates for aortobifemoral bypasses ranging between 89 and 95 percent after 3 years (51-53).

1.3 Mortality

Table 1 shows an acceptable overall postoperative mortality rate of 8.1 percent. This rate is relative high due to the fact that all indications are included. Beside patients treated electively for atherosclerotic occlusive disease, with mortality rates of 4-6 percent, also patients treated as an emergency for aortoenteric fistulae or infected abdominal grafts are included, with a mortality rate of about 40 percent.

1.4 Factors influencing patency

The lower patency rates for axillo(bi)femoral grafts were thought to be caused by impaired inflow or outflow, the length and diameter of the graft, the configuration of the graft, and compression of the graft.

1.4.1 Inflow

Ascer reported that 16 percent of the failed axillofemoral grafts were associated with haemodynamically significant stenosis of the donor subclavian artery (35). Calligaro prospectively determined the incidence of unsuspected inflow stenosis with arteriography in 40 consecutive candidates for primary or secondary axillofemoral bypass surgery (54). Ten of the 40 patients exhibited inflow stenosis greater than 50 percent of luminal diameter in 12 subclavian arteries. Upper extremity arterial pressure measurements suggested potential inflow artery stenosis in only three of the 12 instances. This low detection rate of inflow stenoses in subclavian arteries by non-invasive upper extremity pressure measurements was also reported

Table 1. List of published reports on axillobifemoral (ABF) bypasses.

Author	Year	Material	ABF n	Death (%)	ABF PPR (%)	ABF SPR (%)	Follow-up (years)
Mannick (23)	1970	Dacron	9	5.0		89	1
Johnson (24)	1977	Dacron	56	1.8		76	5
Ray (25)	1979	Dacron	21	3.7		77	5
Alexander (26)	1980	PTFE	21	20.7		79	1
Broomè (27)	1980	Dacron	20	15.0	55		2
		PTFE	24	15.0	95		2
Hepp (28)	1982	both	17	6.3		77	5
Burrell (29)	1982	Dacron	38	8.0	37	97	2.5
Lüdtke (30)	1983	Dacron	25	14.7		60	4
Corbett (31)	1984	Dacron	13	0.0		38	2
Hepp (32)	1985	both	20	5.0	65	73	5
Ascer (33)	1985	PTFE	28	5.3	47	77	5
Allison (34)	1985	both	25	6.4	45	58	5
Ascer (35)	1985	PTFE	22	5.3	50	77	5
Chang (36)	1986	PTFE	26	2.0	75		5
Donaldson (37)	1986	both	72	7.9	54	72	3
Savrin (38)	1986	PTFE	28	18.0	75		5
Kalman (39)	1987	Dacron	59	9.0	77		3
Harris (40)	1990	PTFE	76	4.5	85		3
		Dacron	241	7.2	56	73	3
		PTFE	225	10.1	71	78	3.7
		both	134	6.4	55	70	4.5
		Total	600	8.1	63	73	3.6

PTFE = polytetrafluoroethylene; PPR = primary patency rates; SPR = secundary patency rates

by Whelan (55) and Crawford (56). However, in hardly any reported series on axillofemoral bypass grafting routine preoperative analysis of the inflow tract by angiography was performed. Consequently the quality of the inflow tract can not be ruled out as a factor influencing patency rates.

1.4.2 Outflow

Ray suggested in 1979 that outflow has a major influence on the patency rates. He reported a patency of 74.4 percent after 5 years when the superficial femoral artery was occluded, and 85.3 percent when the artery was patent (25). O'Donnel came to the same conclusion after performing non-invasive haemodynamical outflow measurements in patients treated with an axillobifemoral bypass (57). Burrell reported in his ten year review only one occlusion in 20 patients with patent superficial femoral arteries and nine occlusions in 44 patients with occluded superficial femoral arteries (29). Several other publications reported similar results (24,58,59). In contrast, Ascer was not able to show a significant influence of outflow on the patency rates of axillofemoral bypasses (35).

1.4.3 Length and diameter

Specific analyses of graft length in axillobifemoral bypasses are not published, nevertheless it is logical to anticipate a significant influence of the length on graft patency, but unfortunately the surgeon can not influence this aspect.

The influence of graft diameter as a factor for patency has been a point of debate because it influences flow velocity. Sauvage suggested that flow velocity is closely related to graft patency (60). He demonstrated with grafts implanted into canine carotid arteries that thrombus accretion on a synthetic flow surface occurs in an inverse relationship to the velocity of blood flow, and he concluded that there was a minimal "critical" velocity of flow, below which graft occlusions would occur. This "critical" velocity varied depending on the graft material studied; for Dacron it was 8-9 cm/sec. Furthermore, it has been suggested that flow velocity in axillobifemoral grafts needs to be above this value for the graft to remain patent (25). Based on this theory, thrombus accretion would be expected to occur on the flow surface of an 8 mm Dacron graft with a flow of less than approximately 240 ml/min. Ray (25) measured a mean flow rate during operation for 25 axillounifemoral grafts of 313 ml/min, and the mean flow rate in the main limb of axillobifemoral bypass grafts was 912 ml/min. The increase in flow -and therefore also the flow velocity- observed in the main limb of axillobifemoral bypass grafts was cited by LoGerfo (61) as the main reason for his significantly better 5 year patency results for bilateral grafts (74 %) compared to unilateral grafts (37 %). Similar differences in patency were observed by Delaurentis (46) and Johnson (24), but were not found in the series of 59 axillofemoral grafts reported by Eugene (59) and in 56 axillofemoral grafts reported by Ascer (35). The latter suggests that they did not find a significant difference, because they used 6 mm PTFE grafts, in which they achieved higher flow velocities, thereby decreasing the probability of thrombus formation within these long grafts. They chose this graft because previous mean flow measurements performed in patients with an axillobifemoral graft showed flow rates of 621 to 912 ml/min, which is easily managed by a 6 mm graft according to Sanders (62), who showed a flow capacity for 6 mm diameter grafts exceeding 1200 ml/min. Because the neointima will reduce the inner diameter to about 5 mm, the flow capacity will be reduced below the minimal capacity necessary for the stem branch of an axillobifemoral graft. Graham (63) did confirm that there was a significant difference both in basal and maximal (after papaverine) peroperative flow rates between the axillounifemoral and axillobifemoral grafts that remained patent and those with an early occlusion. All 8 mm grafts with basal flow rates of less than 120 ml/min and maximal flow rates of less than 210 ml/min failed, compared to only 2 out of 31 grafts with flow rates higher than these levels. Chang (36) was not able to show any significant difference in patency for axillofemoral bypasses which ranged in size from 8 to 10 mm in diameter. During the last decade nearly all reported axillobifemoral bypasses have parent and distal branches of 8 mm in diameter, from which one can expect that the flow velocity normally exceeds the critical velocity of 8-9 ml/min.

1.4.4 Configuration

Today controversy still exists about the ideal (anatomic) configuration of the femorofemoral limb, some authors favouring the "lazy S" configuration (25) and others the "inverted C" configuration (61). The "inverted C" configuration has the advantage of carrying a high flow rate in the segment of the axillobifemoral graft that supplies both legs practically all the way down to the ipsilateral femoral artery, but has the disadvantage of a retrograde end-to-side anastomosis for the cross-over graft. On the other hand, the "lazy S" configuration, although leaving a distal segment of the axillofemoral stem with a lower flow has the advantage of a more streamlined antegrade anastomosis between the axillofemoral and the femorofemoral grafts, probably resulting in less flow disturbance.

Szilagyi (64) found that, while simple end-to-end anastomosis did not decrease flow, end-to-side anastomosis decreased flow by as much as 50 percent and that the efficiency of volume flow could be improved by decreasing the angle of the anastomosis.

Although Ray (25) performed all their axillobifemoral grafts in the "lazy S" (Fig. 1) manner they changed their policy to the "inverted C" (Fig. 2) because they had two ipsilateral occlusions in their series. Pasternak (65) (Fig. 3) in 1980 tried to solve two problems, namely the compression at the rib cage and the bifurcation configuration, by sewing the parent branch to a femorofemoral cross-over in the midline, creating a symmetrical bifurcation configuration. This technique has not been reported eversince.

Ward (66) (Fig. 4) also changed the geometry of axillobifemoral bypass grafts by constructing an axillounifemoral graft followed by a cross-over branch not sutured to the prosthesis but more proximally to the common femoral artery. By doing this he expected to find a patency rate for axillobifemoral bypass grafts equal to the patency rate for femorofemoral cross-over grafts (56-86 % after 5 years) (25,58,63,67-70). Unfortunately no further investigations were published. Rutherford made a modification with the advantages that it provides more streamlined antegrade anastomoses and also preserves the higher flow rate all the way to the anastomosis to the ipsilateral femoral artery (71) (Fig. 5).

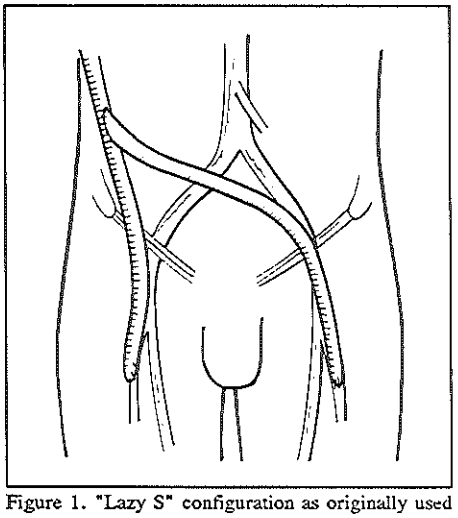

Figure 1. "Lazy S" configuration as originally used by Ray (25).

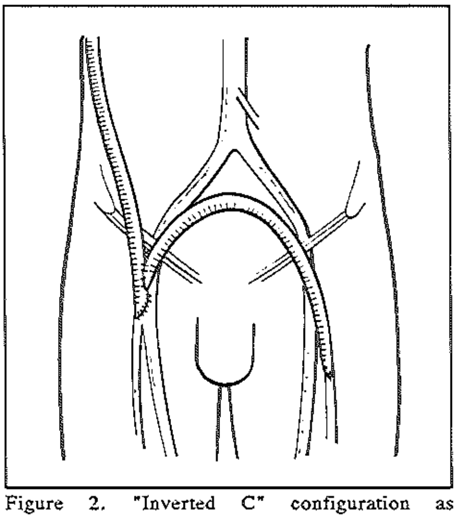

Figure 2. "Inverted C" configuration as recommended by LoGerfo (61).

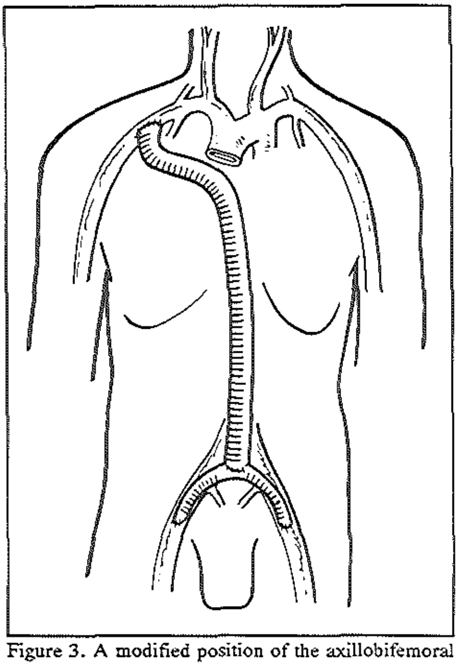

Figure 3. A modified position of the axillobifemoral graft according to Pasternak (65).

1.4.5 Compression

Besides the controversy about the configuration there have also been widespread discussions on graft failure due to compression. Mannick reported in 1970 (23) his late results on axillofemoral grafting and mentioned that it was his impression that an axillofemoral graft was much more susceptible to thrombosis early in the postoperative period than several months after implantation, probably due to a relatively stiff fibrous capsule which is formed around the graft during this period. He found that the majority of acute graft thromboses were noted when the patient wakes up in the morning and it seems likely that compression of the graft when sleeping represented a major cause of early graft failure. He therefore recommended a lateral path of the subcutaneous tunnel. Tangpraphaphorn (72) proposed an alternative intrapleural route for tunneling the axillofemoral bypass to the groin in order to prevent compression against the bony chest wall during sleep, a technique

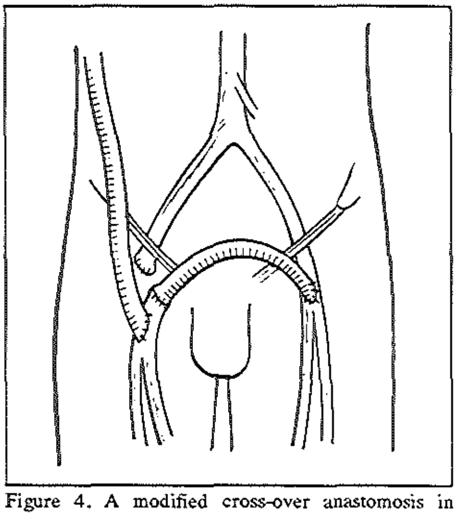

Figure 4. A modified cross-over anastomosis in axillobifemoral grafting according to Ward (66).

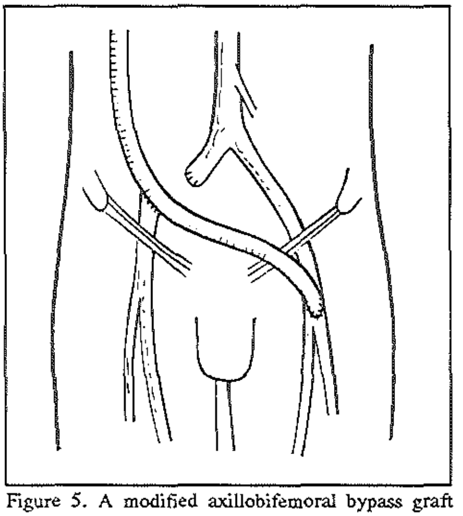

Figure 5. A modified axillobifemoral bypass graft according to Rutherford (71).

that did not gain much popularity. Pasternak rerouted the main stem of the axillobifemoral graft to the midline in order to prevent compression (65) (Fig. 3). Alexander (26) reported one occlusion after 24 weeks due to compression during sleep in his series of 21 axillobifemoral bypasses with PTFE. Jarowenko performed a non-invasive analysis to demonstrate, whether graft compression during sleep really occurred (73). He showed that external compression by body weight did not alter the pulse volume recordings and segmental Doppler pressures in the distal circulation. Therefore, these data suggest that external compression by body weight may not be an important cause of graft failure. Then it was suggested that graft occlusion might be caused be a low flow state during sleep. Despite the convincing results reported by Jarowenko, Kenney reported in 1982 (48) that the use of externally supported axillofemoral Dacron grafts increased the 3 year patency rate from 68 percent up to 100 percent. He theorized that his results were improved because the new prosthesis did not kink and was incompressible, and therefore he recommended the use of externally supported axillofemoral grafts.
Since his publication nearly all implanted axillobifemoral grafts (Dacron as well as PTFE) have been externally supported.

1.5 Complications

During the last two decades many publications reported common and uncommon complications after axillofemoral grafting.

1.5.1 Anastomotic aneurysms

The occurrence of false aneurysm formation at the proximal or distal anastomoses has been reported (25,42,74), but this complication is not unique for this bypass procedure.

1.5.2 Non-anastomotic aneurysms

Orringer reported the formation of an aneurysm in the midportion of an axillofemoral Dacron graft, probably due to a flaw in the graft fabric or fabric erosion by the constant motion of the graft as it crosses over a bony prominence (74). This was also observed by Mii (75) in 1990. Histological examination and the clinical course suggested that a graft versus host reaction might have been the main cause of these aneurysms, an observation and conclusion also made by Bak (76) and Trippestad (77) in 1986. Midportion aneurysms in axillofemoral bypass grafts have not been reported since.
Specific complications due to the implantation of an axillofemoral bypass graft are cervical plexus lesions, proximal anastomotic problems, as rupture or emboli into the brachial artery, or thrombosis of the subclavian artery.

1.5.3. Plexus lesions

Krüger in 1971 (44) and Kempczinski in 1978 (78) reported injuries to the trunks of the brachial plexus, which lie in close proximity to the axillary artery, probably due to traction on the nerves during exposure of the vessel. They recommended to avoid hyperabduction in the shoulder and gentle handling of the nerve trunks during exposure.

1.5.4 Proximal anastomosis

Complications of the proximal anastomosis are quite rare. In a review of literature, Bunt and Moore (79) found a 1.6 percent complication rate of the axillary anastomosis. Reported complications include thrombosis of the axillary artery (27,29,42,78,80,81), embolization (26,80,82,83), and arterial steal syndrome (78,84). Sullivan reported in 1989 (85) two patients suffering proximal anastomotic suture dehiscence several weeks after surgery when they fully extended and raised the affected arm. Disruptions of the proximal anastomosis were also reported by Daar (86), Alexander (26) and White (87). Therefore it is recommended to make the proximal anastomosis at the first or second portion of the axillary artery, medial to the insertion of the pectoralis minor muscle, to allow a full range of arm motion, not resulting in tension at the anastomosis and not altering the course of the artery (42,79,80,88).

1.5.5 Seromas

Perigraft seroma formation is repetitively reported in literature (25,82,89,90), but probably due to the usually retrospective analysis in most reports, the exact incidence is not known. Gooding in 1984 (91) prospectively studied axillofemoral bypasses with sonography and found a 100 percent incidence of perigraft fluid collections. Blumenberg in 1985 reviewed the cause and treatment of perigraft fluid collections and gave recommendations to reduce the incidence of perigraft fluid collections (90). He recommended meticulous tunneling techniques with an atraumatic tunneler that comfortably accommodates the graft, but does not create too large a tunnel. Pollit (92) constructed a long tunneling device to avoid the need for a help incision.

1.6 Indications

The indications for axillobifemoral grafting have not changed much during the last decades. After an enthusiastic start for axillobifemoral bypasses as an alternative to aortobifemoral bypasses, the indications became more and more restricted, due to disappointing patency rates compared to aortobifemoral bypass grafting. Generally accepted indications are now: Poor risk patients with atherosclerotic occlusive disease or patients with an aortoenteric fistula and/or an infected abdominal aorto-distal bypass graft. Abdominal aneurysmal disease has also been an indication for axillobifemoral bypass grafting in poor risk patients (37,66,93-95), but this indication has lost interest, due to incomplete thrombosis of abdominal aneurysms and ensuing rupture.

1.7 Outline of the thesis

This thesis is based on four publications on the subject of graft configuration and haemodynamics in axillobifemoral bypass grafts:

1. A clinical evaluation of 17 patients with axillobifemoral bypass graft operations, performed for various indications. Two important observations were made: an asymmetrical blood flow distribution between the two distal branches, in favour of the ipsilateral branch, and turbulent flow at the site of the bifurcation, as observed with duplex scanning. These observations, described in chapter 2, led to the development of a new design for an axillobifemoral bypass graft.
2. The second publication is a report of the results of an in-vitro study, performed to analyse the haemodynamical properties of three currently used axillobifemoral bypass graft configurations (with contralateral branches at angles of 30°,90° and 150°) and the newly designed axillobifemoral bypass graft. The pressure drops across the four different axillobifemoral bypass bifurcation configurations under sinusoidal flow of a Newtonian fluid were analysed at four different flow rates at three different systemic mean pressures. This in-vitro experiment is described in chapter 3.
3. The third publication reports on the haemodynamical in-vivo properties of two different axillobifemoral bypass graft configurations (one with a contralateral branch at an angle of 90° and one with a symmetrical bifurcation and flowsplitter). This in-vivo study was conducted, because the in-vitro study was performed with a sinusoidal pulsatile flow of a Newtonian fluid, which has a different impact on flow profiles and flow disturbances than the in-vivo physiological pulsatile flow of a non-Newtonian fluid, namely blood. All pressure losses across the bifurcation, ipsilateral and contralateral, were measured at different flow rates. The results are discussed in chapter 4.
4. In order to evaluate the clinical relevance of these findings, an international multicenter prospective randomized trial was conducted. The patency rates and clinical behaviour of the two different axillobifemoral bypass grafts, differing only in configuration of the bifurcation (one with a contralateral branch at an angle of 90° and one with a flowsplitter), were analysed in this trial. In 19 centers in Germany, Belgium, France and the Netherlands 117 patients were randomized, 59 receiving a prosthesis with a flowsplitter and 58 a prosthesis with a 90° bifurcation. Analysis of the results after 3 years with a mean follow up of 12 months is discussed in chapter 5.

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CHAPTER 2

EXPERIENCES WITH THE AXILLOBIFEMORAL BYPASS AS A LAST RESORT

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2.1 Abstract

The axillobifemoral bypass is a vascular operation by which the arterial blood flow is diverted from one of the upper extremities to both lower extremities. If an abdominal vascular reconstruction is not possible or not allowed this alternative is chosen in patients with severe vascular disease in both legs.
The results of the first 17 patients who received an axillo-bifemoral bypass at the 'De Wever Hospital' in Heerlen are reviewed. Postoperative investigation showed that after exercise the brachial blood pressure was lower on the side where the bypass was anastomosed than in the other arm. However, continous wave Doppler registrations revealed no alterations of the blood flow velocity of both the upper extremities and the cerebral arteries before and after exercise. There was an asymmetric blood flow through both distal branches of the vascular graft which might influence the patency rate. In patients with severe vascular disease of the lower extremities, for whom an intra-abdominal vascular reconstruction constitutes an excessive risk, we now prefer to create an axillobifemoral bypass.

2.2 Introduction

The axillobifemoral bypass is a vascular operation in which the blood flow is diverted from the right or left axillary artery to both femoral arteries (Fig. 1). In contrast to e.g. the aortic bifurcation graft and the femoropopliteal bypass, it is considered an extra-anatomical bypass, because the arterial blood flow is not diverted parallel to existing anatomical pathways but along a surgically created one.
The technique of axillobifemoral bypass graft was first reported in 1963 (1). In 1966, its use was reported in patients who could not be exposed to general anaesthesia or had an infected aortic bifurcation graft (2).

The indications for axillobifemoral bypass are:

1. infected abdominal vascular graft.
2. inaccessibility of the abdomen.
3. severe cardiopulmonary disease.

In case of an infected aortic bifurcation graft, an axillobifemoral bypass allows for a good blood supply to the legs via a 'clean' road. The infected graft is then removed. Abdominal infections, massive adhesions, intra-abdominal malignant tumors, or strongly calcified abdominal arteries may impede an intra-abdominal operation. Some patients with severe cardiac or pulmonary disease may be at too high a risk for an abdominal operation. It is a major benefit that the axillobifemoral bypass need not be created under general anaesthesia; it is possible to apply local anaesthesia in combination with intravenous sedation for the operation of the axillary artery. An additional benefit is that potency defects through nerve damage cannot occur, in contrast to abdominal vascular operations, in the small pelvis. In some cases potency may even recover when the ischemia, causing the potency defect, is terminated by improved blood flow in the small pelvis resulting from the axillobifemoral bypass (3).

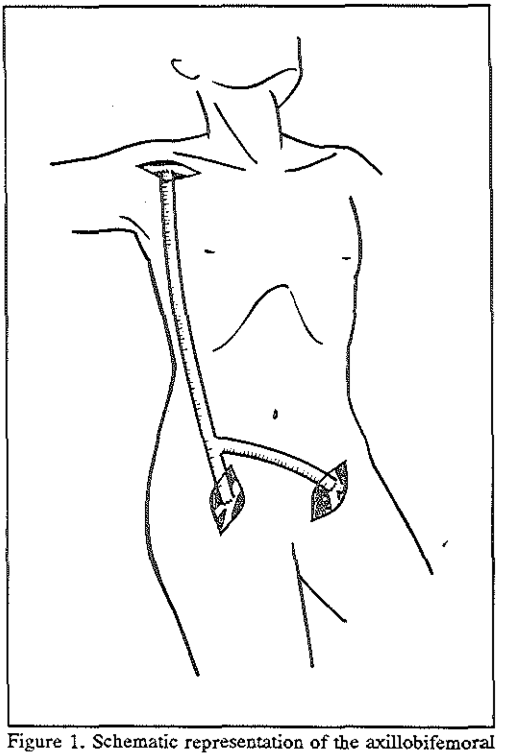

Figure 1. Schematic representation of the axillobifemoral bypass graft.

The operation results mainly depend on whether the graft will occlude or not. Thrombus formation is a major cause of graft occlusion and mainly occurs within the first 6 months. The graft bifurcation appears to be a preferred site. Intima proliferation at the anastomoses is observed in the long run; it may also cause obstruction of the graft. External compression by constrictive clothing or by sleeping on the side of the graft has been suggested as a cause for graft thrombosis. Jarowenko et al. however, report that Doppler pressure measurements did not reveal changes in haemodynamics when patients were lying on the graft (4). The different studies cannot be compared as to patency of the grafts. The long-term results are calculated on the basis of the few patients who survived for 5 or 10 years. Several authors have calculated that the axillobifemoral bypass may be patent after 5 years in 76 to 90% of the patients (5-7).

The results are also influenced by the condition of the arteries before the operation. In claudicants the results appeared to be better than in patients with limb threatening ischemia (80% versus 50%) (8). Although promising results have been obtained with the axillobifemoral bypass, it remains a second-choice procedure. In aorto-iliac vascular disease the aortic bifurcation graft is still preferred. First, because it usually has a better outcome, and secondly, after the axillobifemoral bypass the number of reoperations for thrombosed graft is very large (4 to 50%) compared to the aortic bifurcation graft (less than 5%) (8).

Table 1. Survey of 17 patients in whom an axillobifemoral bypass was performed.

patient (years)	sex	age risk factors	indication	preoperative (months)	anaesthesia	follow-up
A	m	70	night pain	calcified aorta	general	43
B	f	82	pregangrenous	cardiopulmonary	epidural	31
C	m	77	night pain	cardiac	spinal	30
D	m	61	night pain	pulmonary	general	27
E	m	62	night pain	adhesions	general	26
F	f	53	pregangrenous	cardiac	general	23
G	m	68	aortoduodenal fistula	infected graft	general	18*
H	m	66	night pain	cardiopulmonary, diabetis mellitis	general	15
J	m	66	night pain	cardiac	general	12
K	m	81	night pain	cardiac	general	6
L	m	70	pregangrenous	cardiopulmonary	general	2*
M	m	72	pregangrenous	cardiopulmonary	general	2*
N	f	65	night pain	cardiac	general	2
O	f	71	night pain	cardiac	general	2
P	f	78	night pain	cardiac, diabetis mellitis	spinal	1*
Q	m	75	pregangrenous	cardiac, diabetis mellitis	general	1*
R	m	58	night pain	lung cancer	epidural	1*

m = male; f = female; * = death

2.3 Patients and Methods

From 1983 to mid-1986 17 patients operated for an axillobifemoral bypass. Table 1 presents a survey of patient characteristics, indications, and risk factors. Cardiac risk factors were: valvular defect, recent infarction or imminent decompensatio cordis. Pulmonary risk factors were: severe Chronic Non Specific Lung Disease, or pulmonary silicosis (diseases still presenting frequently in older people in the south-eastern part of the Netherlands). Preoperative angiography showed that in 12 patients the distal part of the aorta was obstructed; in 5 patients the obstruction was located in the iliac arteries to the common femoral arteries. The surgical technique applied did not deviate from the methods described in the vascular surgical handbooks. A externally supported 8 mm knitted dacron-graft with a cross-over branch at an angle of 90° was used. The externally supported part reached beyond the costal arch in order to prevent compression.

In 11 patients who were still alive at follow-up, flow velocity was measured bidirectionally, using a 5 MHz continuous wave Doppler instrument at the sites indicated in Figure 2. In addition, systolic blood pressure in arm and ankle on both sides was measured before and after exercise. The exercise consisted of walking on a treadmill with a 10 degree gradient at a speed of 3.5 km/h during 5 minutes. Statistical analysis of the data was done with the paired t-test on the basis of normal distribution.

2.4 Results

Two patients (P and R) required a reoperation immediately after the operation due to an occluded graft. Trombectomy could be performed successfully.

Three of the six non-survivors died from a myocardial infarction (L. M, and P), and one due to lung cancer (R). Patient G died from ruptured aneurysm on closed aortic stump 18 months after implantation. Patient Q died from sepsis due to decubitus resulting from diabetes mellitus. In these six non-survivors, good pulsations at the graft were felt until shortly before their deaths. Good patency of the graft was confirmed in the two patients in whom autopsy was performed.

The 11 patients evaluated completed the 5 minutes' walking exertion. In two of them (C and D) the graft was thrombosed after 12 and 27 months respectively. Nevertheless, both patients were content with the distance they were able to walk; therefore, reoperation was not performed. From measurements in the nine other patients it appeared that the difference between the results at rest and those obtained after exercise were maximal immediately after exercise. This is why only these results have been compared.

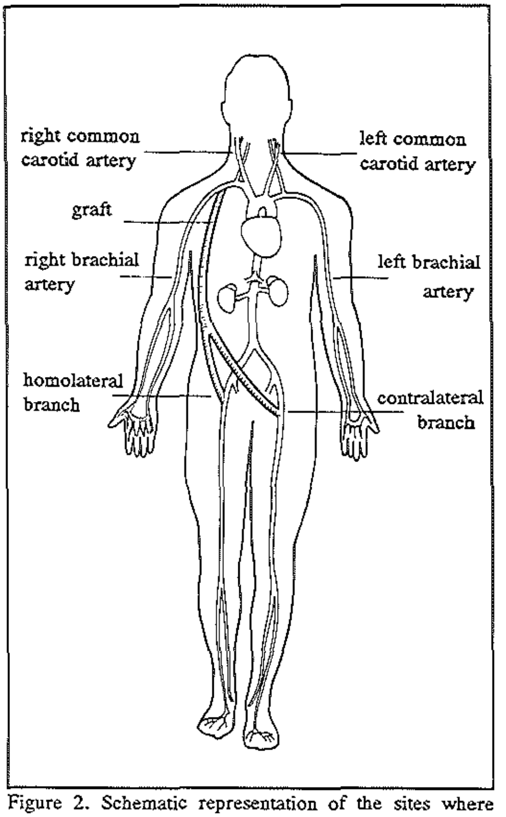

Figure 2. Schematic representation of the sites where Doppler measurements were performed.

After the operation there was no significant decrease of flow velocity in the ipsilateral common carotid artery compared to the contralateral common carotid artery, both before and after exercise. This also applied to both brachial arteries (Table 2).

The flow velocity in the ipsilateral branch of the axillobifemoral bypass was significantly higher ($p < 0.05$) than that in the contralateral branch (Table 2).

After exercise the blood pressure in the ipsilateral arm decreased in constrast to the unaltered blood pressure in the contralateral arm (Fig. 3).

Six patients underwent additional investigations using a Duplex-scanner (Kretz). Good patency of the graft was confirmed. The internal diameter of the graft was 7 ± 1 mm. Spectral broadening resembling turbulence in the blood flow was observed at the graft bifurcation.

Table 2. Survey of the blood flow velocities at the ipsilateral side, i.e. the side of the axillary anastomosis, and the contralateral side measured before and after exercise using Doppler measurements. The Doppler measurements are expressed in mean amplitude corresponding to mean flow velocity.

		patients																	
		A		B		C		D		E		F		G		H		J	
		BE	AE	BE	AE	BE	AE	BE	AE	BE	AE	BE	AE	BE	AE	BE	AE	BE	AE
Common carotid	IL	10	8	19	15	9	9	8	8	11	12	10	8	8	8	8	9	8	6
artery	CL	10	8	19	19	10	9	8	8	12	13	10	10	8	8	10	11	9	7
Brachial artery	IL	10	7	7	5	7	9	7	4	12	11	14	12	4	4	7	6	4	4
	CL	10	7	7	6	6	8	7	4	12	11	12	11	4	4	9	7	4	4
distal branch of	IL	9	13	14	38	18	30	9	20	14	18	12	10	22	40	12	32	7	8
bypass	CL	4	7	7	20	10	14	7	8	9	12	10	10	6	5	10	8	7	8

BE = before exercise; AE = after exercise; IL = ipsilateral; CL = contralateral

2.5 Discussion

The high mortality after this operation in our group of patients can be explained by the high mean age (69 years) and the poor condition before the operation. They were not eligible for an intra-abdominal vascular operation. The patients included in this study had severe ischemia of the legs and consequently rest pain. In all cases ischemic pain was relieved without performing an amputation. Most patients reached a satisfactory walking distance. At follow-up examination of the 9 patients with a patent graft, a decrease of the systolic blood pressure was observed, especially after walking exercise, in the arm on the side where the bypass was anastomosed compared to the other arm. Doppler investigation did not reveal any differences in blood flow through both brachial arteries before and after exercise. This is in accordance with the absence of subjective complaints such as tingling in the arm or loss of strength. The axillary artery appears to be able to sufficiently supply blood to the arm and the legs. Also the cerebral blood flow is not clearly influenced by exercise of the legs. None of the patients complained of vertigo during walking. In the ipsilateral branch of the axillobifemoral bypass the flow velocity was higher than in the contralateral branch. This may be explained in two ways. First, the ipsilateral branch of the graft is almost in line with the

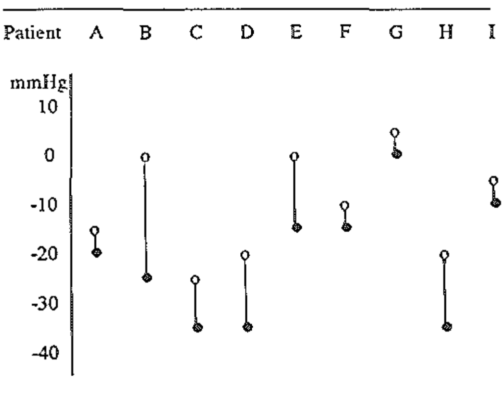

Figure 3. Difference in blood pressure between the ipsilateral brachial artery and the contralateral brachial artery before (○) and after (●) excercise respectively.

main branch from the axillary artery. This is caused by the fact that the graft is placed lateral to thorax and abdomen. The contralateral branch is at an angle of 90° to the ipsilateral branch. Consequently, the ipsilateral branch has a more favourable position in relation to the main branch than the contralateral branch. Secondly, turbulence, observed with the Duplex scanner near the bifurcation, may enhance these differences in flow velocity. Notably, the latter phenomenon may have a momentous impact on the patency of the graft.
In our clinic the axillobifemoral bypass has been established in the treatment of patients with severe vascular disease of the distal part of the aorta or both iliac arteries, for whom an intra-abdominal vascular reconstruction constitutes an excessive risk.

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CHAPTER 3

HAEMODYNAMICS IN AXILLOBIFEMORAL PROSTHESES: an in-vitro study

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3.1 Abstract

An in-vitro study was conducted to measure intraluminal pressure distributions in different axillobifemoral bypass graft configurations under pulsatile flow in a Newtonian fluid.
At the site of the bifurcation of currently used axillobifemoral (ABF) prostheses (Fig. 1) a pressure drop was measured, which was more profound in the contralateral distal branch. The pressure drop increased significantly with increasing flow rate and increasing angle between the distal branches. Within the physiological flow range this pressure drop could be as high as 30 mmHg. No pressure drop was measured in a new experimental design of an axillobifemoral prosthesis with a bifurcation and flowsplitter (Fig. 2). Neither changing flow rates nor varying angles between the distal branches produced a significant pressure drop in this type of graft. It is theorized that this favourable haemodynamical property as observed in an in-vitro experiment, will lead to an improved clinical performance as measured by graft patency rates.

Key words: axillobifemoral, bifurcation geometry, haemodynamics

3.2 Introduction

A clinical study (1) performed by Go and Wittens in 1987 to look at a possible steal phenomenon caused by axillobifemoral bypasses, which could have been expected according to experimental studies (2,3), revealed no steal phenomenon, but instead some unexpected results: Continuous wave Doppler analysis showed in patients with an ABF prosthesis a significantly ($p < 0.05$) higher bloodflow in the ipsilateral distal branch compared to the - at

90° angle connected - contralateral cross-over branch. This difference which increased after exercise was also confirmed by duplex studies. Moreover duplex examination showed turbulent flow after exercise at the bifurcation site, especially in the first 2 cm of the contralateral cross-over branch. Turbulent flow, causing an asymmetrical flowdistribution, might be the result of the asymmetrical configuration of the bifurcation of the ABF bypasses that were used in these experiments. Today controversy still exists about the ideal anatomic configuration of the femorofemoral limb, some authors favouring the "lazy S" configuration and others the "inverted C" configuration. The "inverted C" configuration has the advantage of carrying a high flow rate in the segment of the axillobifemoral graft that supplies both legs practically all the way down to the ipsilateral femoral artery, but has the disadvantage of a retrograde end-to-side anastomosis for the cross-over graft. On the other hand, the "lazy S" configuration, although leaving a distal segment of the axillofemoral stem with a lower flow has the advantage of a more streamlined antegrade anastomosis between the axillofemoral and the femorofemoral grafts, probably resulting in less flow disturbance.
No comparative haemodynamical studies of the currently used configurations, namely at angles of 30° ("lazy S"), 90° or 150° ("inverted C") have been published (Fig. 1). We therefore decided to perform an in-vitro study with the three ABF bypass graft configurations, currently in use, and one experimental graft. This experimental graft has a symmetrical bifurcation and a membrane, that cleaves the blood column in two blood columns, called a flowsplitter (Fig. 2). The aim of this study was to study the haemodynamical properties of the different configurations and their possible clinical relevance.

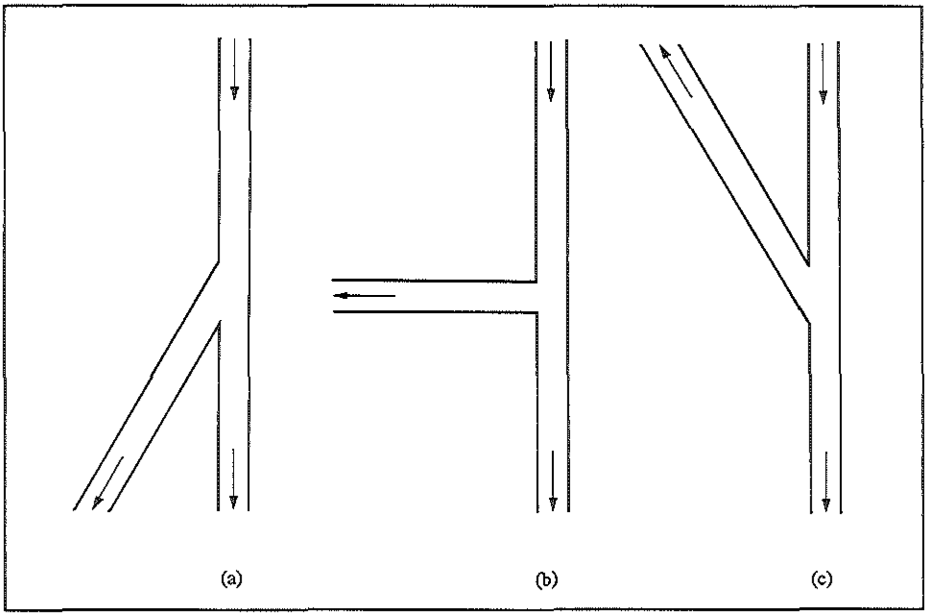

Figure 1. Three conventional ABF prostheses (8 mm PTFE) with femorofemoral cross-over branches at angles of 30° (a), 90° (b) and 150° (c).

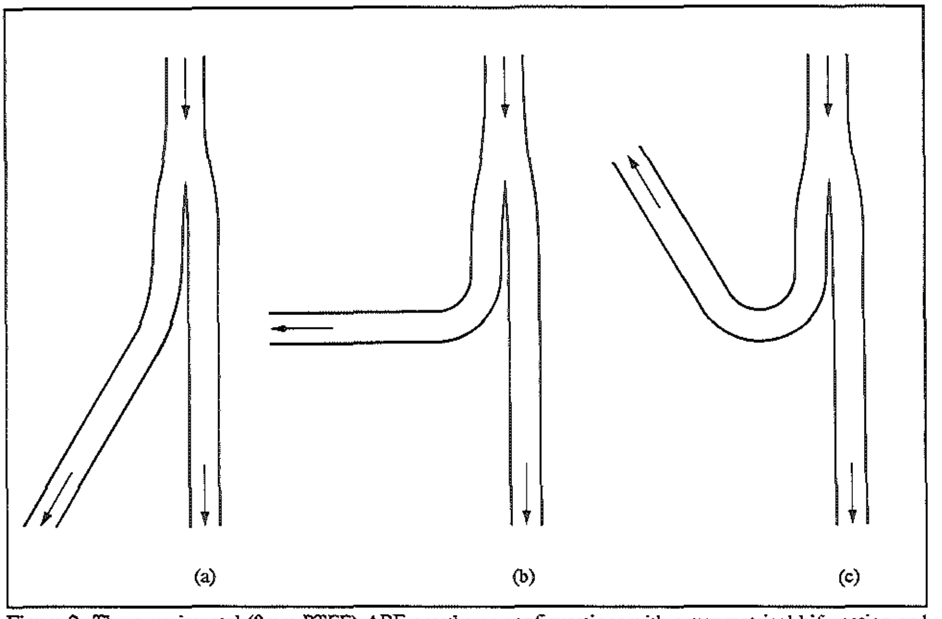

Figure 2. Three expimental (8mm PTFE) ABF prostheses configurations with a symmetrical bifurcation and a flowsplitter and contralateral branches at angles of 30° (a), 90° (b), and 150° (c).

3.3 Materials

Eight mm. thinwalled polytetrafluoroethylene (PTFE) grafts from W.L. Gore & Associates were used. Three currently used configurations of ABF prostheses were made (Fig. 1). One with the contralateral branch at an angle of 30° to the parent branch, simulating the "lazy S" configuration. One with the contralateral branch at an angle of 90° to the parent branch, a configuration made by several prosthetic graft manufacturers and one with an angle of 150° to the parent branch, a configuration favoured by surgeons who make an axillo-unifemoral bypass combined with a femoro-femoral cross-over ("inverted C"). Finally, an ABF bypass with a symmetrical bifurcation and flowsplitter was constructed by using a 16x8 mm PTFE ("aortobifemoral") bifurcation prosthesis with flowsplitter. After tapering the proximal ("aortic") part of the prosthesis to 8mm, the bifurcation was extended at the proximal end and both distal ends with 8 mm PTFE grafts (Fig. 2). One of the distal branches was positioned at angles of 30°, 90° and 150° to the other branch simulating the conventional configurations used (Fig. 1). This resulted in a total of 6 different configurations that could be tested.

3.4 Methods

A rollerpump was used to create a pulsatile flow pattern (4), producing flow rates of 420, 740, 940 and 1200 ml/min (Fig. 3). By varying the peripheral outflow resistance 3 systemic mean pressures were created with the use of 3 pairs of needles with different lumen sizes. The

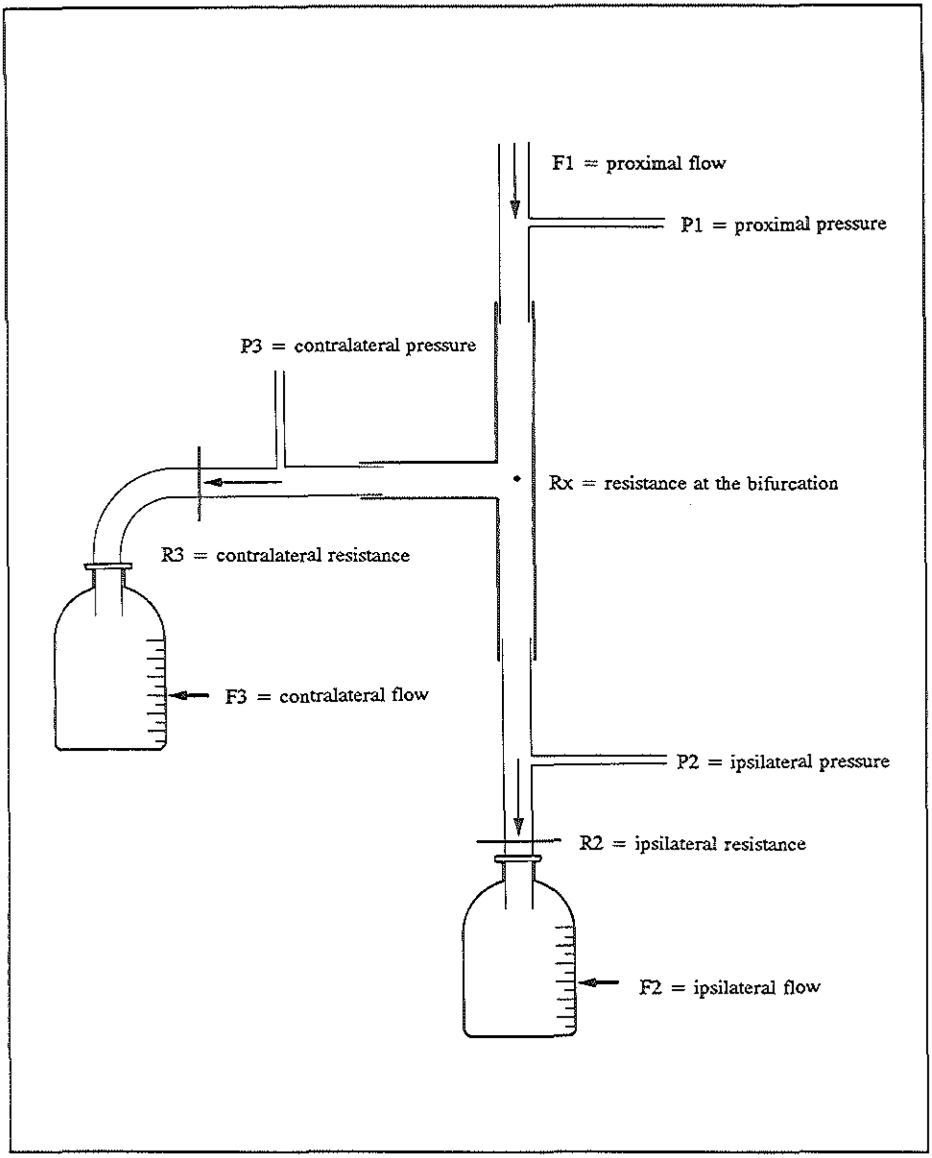

Figure 3. A diagram of the experimental set-up.

needles were placed at the same distance from the bifurcation. Each pair of resistances was of the same diameter for both distal branches (Fig. 3). The measurements were repeated after exchanging the left and right resistances.

Using the three different outflow resistances proximal, (systemic) mean pressures were created of 62.5, 92.5 and 132.5 mmHg respectively.

A Newtonian fluid - dextran solution - with a viscosity of 2.0 cPoise was used. This is

somewhat lower than the viscosity of bloodplasma (2.2-2.5 cPoise). The viscosity of blood - being a non-Newtonian fluid - varies from 2.5 to 5.0 cPoise, mainly dependent on the haematocrit (5).
After creating 3 proximal (systemic) mean pressures, each at 4 different flow rates, the flow and pressure was measured at equal distances to the bifurcation in both distal branches (Fig. 3). By positioning the tubes horizontally, the influence of gravity was ruled out. All tubing and prostheses were of the same length during all measurements. The proximal branch of the prostheses was 20 cm., to allow laminar flow to have developed before reaching the bifurcation, and both distal braches were 10 cm in length. The pressure losses due to the tubing were also investigated by measuring the pressure losses across a straight 8 mm PTFE graft of 30 cm. By subtracting the pressure drop across the straight tube from the pressure drop across an axillobifemoral graft configuration, the pressure loss due to the bifurcation of that particular axillobifemoral graft configuration could be calculated.
All 6 bifurcation configurations and one straight control graft were put in one framing and were subjected to three consecutive measurements under 12 different conditions (3 proximal "systemic" mean pressures, at 4 different flow rates).

3.5 Statistical analysis

Analysis of variance was used to compare the "conventional" prostheses with respect to the pressure drops between the proximal and distal side of the bifurcation, and to evaluate the effects of the flow distribution and the changes in pressure between the ipsilateral and contralateral branch for all applied flows and pressures. Only second order interactions were considered. Random effects were taken for the experiments, while the other factors were considered fixed. For each conventional prosthesis configuration (30°, 90° and 150°), differences with the correspondingly angled flowsplitter prosthesis at the same experiment were assessed using the paired t-test. The same was done in the comparison of the flow and pressure distribution between the ipsilateral and contralateral sides.
P-values of <0.01 were considered to be statistically significant.

3.6 Results

Control measurements, performed after exchanging the resistances, confirmed that both the ipsilateral and the contralateral resistances did not differ significantly.
Analysis of variance (Table 1) showed that the different outcomes between the conventional prostheses were significantly influenced by the flow rates, the proximal (systemic) mean pressure and the ipsilateral or contralateral distal branch. The 3 consecutively performed experiments did not differ significantly.
All measurements performed on the 3 flowsplitter configurations with one distal branch positioned at an angle of 30°, 90° or 150° to the other branch were not significantly different (Fig. 4). The maximal pressure drop between the proximal branch and the distal branches was less than 1 mmHg and was regarded as being negligible.
All pressure drops were corrected for the pressure loss, found across the control straight 8 mm graft. The resulting corrected pressure drop was considered to be caused by the geometry of the bifurcation. The pressure drops across the bifurcation of the three conventional prostheses and the experimental prosthesis are shown in figure 5. The pressure drops across the ipsilateral distal side at three different proximal (systemic) mean pressures (62.5, 92.5 and 132.5 mmHg.) are shown in figure 5 a,b,and c. The pressure drops across the

Table 1. Analysis of variance with respect to pressure drops, taking into account the influence of the bifurcation configurations of 3 different conventional prostheses, 4 different flow-rates, 3 different proximal (systemic) mean pressures, the ipsilateral and contralateral distal branches and the 3 consecutively performed experiments.

Source of variation	DF	Mean square	F-value	P-value
MAIN EFFECTS				
prostheses	2	758.5	1039.1	<.001
flow rates	3	2719.5	13396.3	<.001
proximal pressures	2	37.2	161.8	<.001
distal branches	1	239.6	7047.1	<.001
experiments	2	2.0	4.6	NS
2-WAY INTERACTIONS				
prosth * flow	6	43.1	98.0	<.001
prosth * pressure	4	5.9	13.4	<.001
prosth * branch	2	37.3	85.0	<.001
prosth * exper.	4	.7	1.6	NS
flow * pressure	6	13.1	29.8	<.001
flow * branch	3	5.3	12.1	<.001
flow * exper.	6	.2	.5	NS
pressure * branch	2	2.5	5.8	<.001
pressure * exper.	4	.2	.5	NS
branch * exper.	2	.0	.1	NS
RESIDUAL VARIATION	166	.4		

DF = degrees of freedom.

contralateral distal side are shown in figure 5 d,e,and f. The figures show that the pressure drops increase markedly with increasing flow rate for all levels of the applied proximal (systemic) mean pressure. Pressure drops generally increased with increasing angle between the parent and cross-over branch of the conventional prostheses.

Even at high flow rates no pressure drops were measured across the bifurcation of the flowsplitter prostheses.

All pressure drops observed for the conventional configurations were significantly greater as compared to the corresponding flowsplitter configuration (P<0.01). This applied to the ipsilateral as well as the contralateral side, except for the ipsilateral and contralateral side of the 30° angled conventional configuration at flow rates of 400 and 700 ml/min. Within the physiological range of flow rates (400 - 1200 ml/min) pressure drops as high as 30 mmHg were observed.

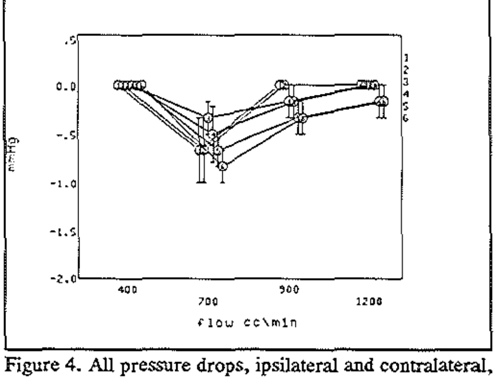

Figure 4. All pressure drops, ipsilateral and contralateral, of all three flowsplitter configurations at a mean pressure of 132.5 mmHg. Bars indicate the standard deviation.

At all mean pressures no significantly different pressure losses were found between the ipsilateral and contralateral side for the 30° angled conventional prosthesis. For the

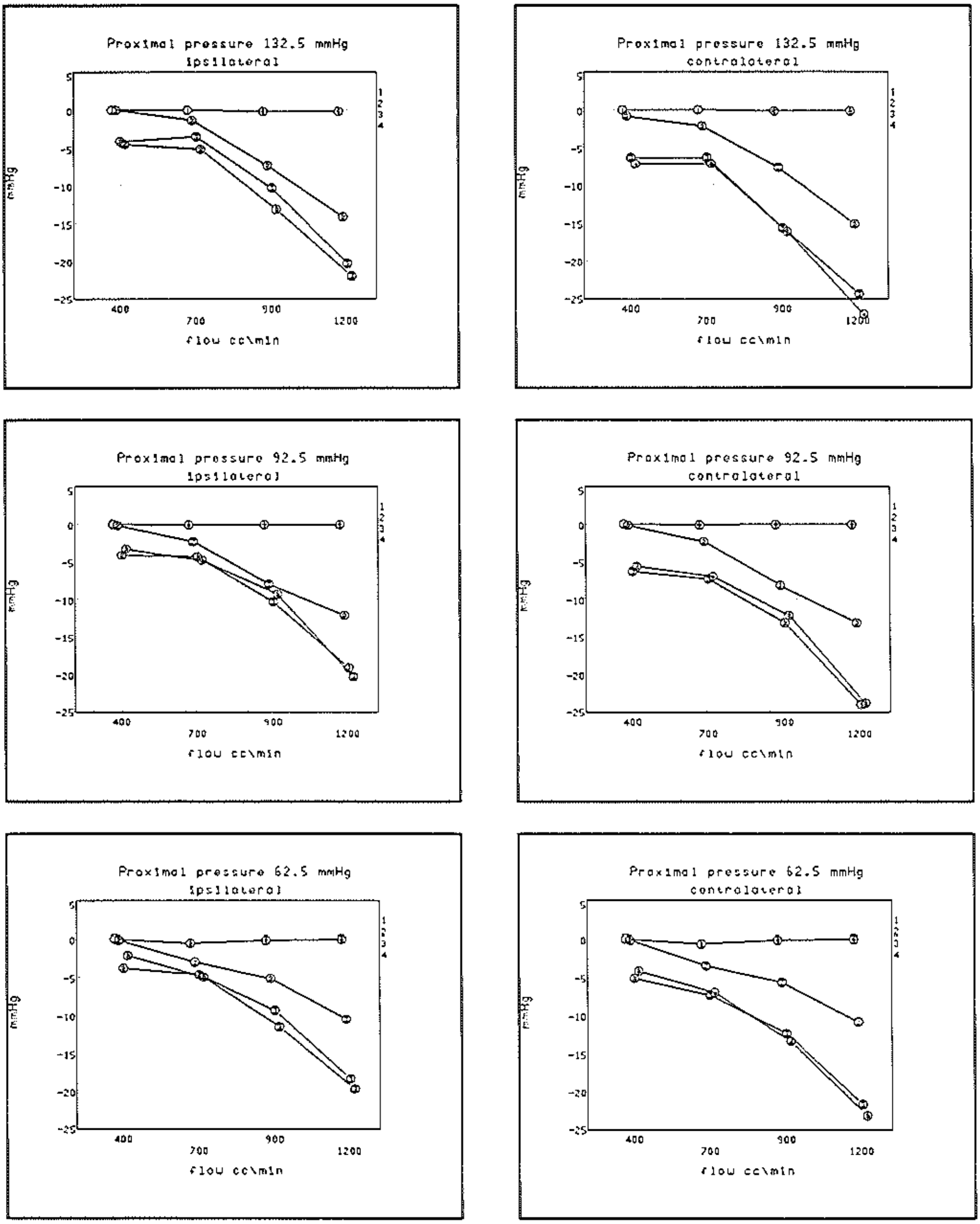

Figure 5. Pressure drops (means of 3 experiments) due to the bifurcation geometry of the experimental prosthesis with the flowsplitter (1) and 3 conventional ABF prostheses with a 30° angle (2), a 90° angle (3) and a 150° angle (4) on the ipsilateral and contralateral side at three different proximal (systemic) mean pressures and 4 different flow rates. For the experimental prostheses (1) the mean of all three configurations is shown.

two other conventional configurations (90° and 150°) the pressure drop measured at the contralateral side was generally greater as compared to the ipsilateral side ($P<0.01$). The negligible pressure losses at the flowsplitter bifurcation were symmetrically distributed between both distal branches.
The flow distribution between both distal branches was in complete accordance with the pressure distribution between both distal branches for all prostheses.

3.7 Discussion

When blood flows at a steady rate through a long smooth and straight vessel, it flows in streamlines and also in concentric layers within the vessel, with each layer remaining the same distance from the wall and the central portion of the blood staying in the centre of the vessel. This phenomenon is called laminar flow. However, when blood flow becomes too high, when it passes by an obstruction in a vessel, when it makes a sharp turn, or when it passes over a rough surface, the flow may become turbulent rather than streamlined. Turbulent flow means that the blood flows crosswise in the vessel as well as along it, usually forming whirls in the blood called eddy currents (6,7). When eddy currents are present, there is much higher resistance than when the flow is laminar, because eddies add to the overall friction of blood flow within a vessel.
The tendency for turbulent flow increases in direct proportion to the velocity (v) of the blood, in direct proportion to the diameter (d) of the blood vessel, but is inversely proportional to the viscosity (n) of the blood, devided by its density (r), in accordance with the following equation:

$$Re = \frac{v \cdot d}{n/r}$$

Reynolds number (Re) is the measure of the tendency for turbulence to occur. When Reynolds number rises above a certain value, turbulent flow will occur at the branches of vessels. This turbulent flow will die out along the ensuing straight portion of the vessel. When Reynolds number rises above approximately 2000, turbulence can occur even in a straight smooth vessel. Each vessel or bifurcation configuration has its own critical Reynolds number, depending on its geometry, at which turbulence will occur. Ferguson et al. (8) demonstrated that bifurcations in the circulation can be expected to have a lower critical Reynolds number at which turbulence occurs than straight tubes.
Bifurcations cause a geometrical disturbance of flow which increases with increasing bifurcation angle (Fig. 6). These flow disturbances, shown by several flow visualization studies (6,7,9,10), represent

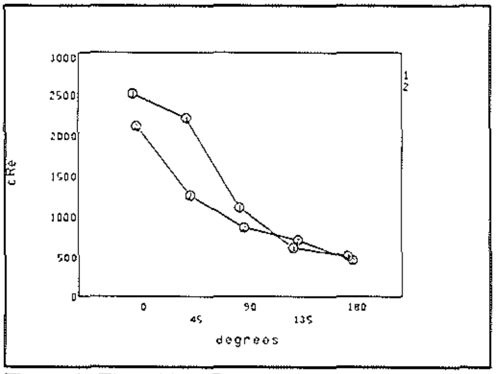

Figure 6. The critical Reynolds numbers for different bifurcation angles under steady (1) and pulsatile (2) flow conditions in glass models according to Ferguson and Roach.

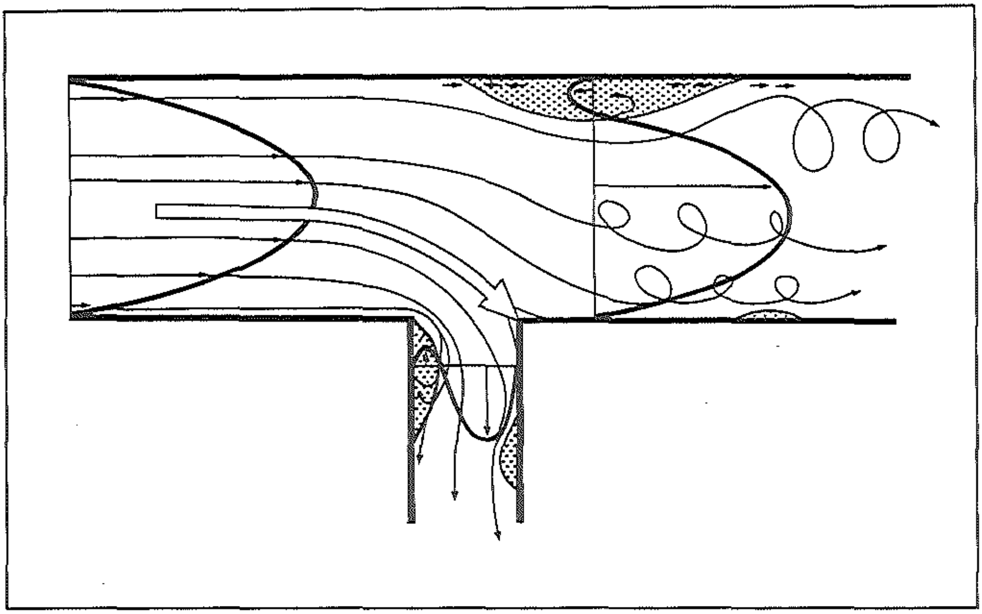

Figure 7. Flow separation zones (grey) in a 90° angled bifurcation with secondary flows. The arrows marks shear forces along the wall according to Liepsch.

"secondary flow", which is flow with another direction than the main flow in areas of flow separation. When the flow increases real turbulence is created, in which there is a random distribution of flow direction throughout the lumen of the vessel and areas of flow separation are not recognized anymore.

Because turbulence acts as a resistance being a functional stenosis within the vessel it will cause a pressure drop. Figure 7 shows a flow velocity profile at a 90° angled bifurcation with 2 large and 2 small areas of separation. Flow separation areas cause, just as turbulence, a functional stenosis. Real turbulence in the normal vascular tree in the human body never occurs because the critical Reynolds numbers are only reached during systole, which is too little time to create a full turbulence, but separation phenomena occur quite often (6). The flow rate in flow separation areas is decreased and can even become zero. Such a low flow state is known to increase the coagulability. Higher coagulability could lead to clot formation and eventually occlusion in prostheses aligned with a pseudoendothelium, a sequence of events unlikely to occur, when there is a normal endothelial wall with normal prostacyclin production and normal compliance of the vessel wall.

Considering these facts, we wanted to know the critical Reynolds numbers for the bifurcation geometries used. Injecting a small amount of ink into the fluid stream is a frequently used method to visualise turbulence at certain flow rates (8). We could not use this method, because PTFE grafts are not transparent. However, because turbulent flow causes a functional stenosis (6,7,11) and therefore a pressure drop, we were able to calculate the critical Reynolds number for each prosthesis. The assumption was made that a pressure drop of at least 5 mmHg was caused by turbulence at the bifurcation. The flow rate that caused a 5 mmHg pressure drop across the bifurcation at a proximal mean pressure of 62.5 mmHg was calculated for each bifurcation geometry. Knowing the flow rate, the diameter of the vessel, the density and the viscosity of the fluid, the critical Reynolds numbers were calculated (Table 2).

Flow measurements at rest in axillo-bifemoral bypasses were performed by LoGerfo et al.(12) and found to be about 600 ml/min. When a prosthesis with a diameter of 8 mm. was used and the was haematocrit between 0.35 to 0.40, the Reynolds number was between 200 and 350. When Reynolds number becomes lower than the critical Reynolds number (cRe) turbulence is created. Using the Reynolds numbers, as calculated out of the data from LoGerfo, turbulence will occur, when the 150° angled axillobifemoral prosthesis (cRe=330) is inserted, and at least areas of flow separation are to be expected, when the 90° angled axillobifemoral prosthesis (cRe=400) is inserted. In walking the increased flow (up to 1200 ml/min) creates increased Reynolds numbers (up to 700), which will also cause turbulent flow or flow separation areas in the axillobifemoral prosthesis with a bifurcation with a 30° angle (cRe=560).

Table 2. The critical Reynolds numbers for the different axillobifemoral configurations.

			Critical Reynolds number
bifurcation	150° angle	:	330
	90° angle	:	400
	30° angle	:	560
	flowsplitter	:	>1000

The results in our in-vitro study did show an asymmetrical pressure loss and flow distribution between the two distal branches in the 90° and 150° angled conventional prostheses, which is similar to what we found in our clinical study in 1987 (1). The flow disturbances at the bifurcation site, leading to the pressure loss in both distal branches, might also be responsible for clot formation (13,14) and stenosis at the bifurcation, which eventually causes a more profound asymmetrical flow distribution in favour of the ipsilateral branch or an occlusion of the contralateral branch.

The pressure drop at the bifurcation site, caused by flow disturbances, was significantly higher, when conventional configurations were used compared to the experimental flowsplitter prosthesis. This pressure drop increased significantly with increasing flow rate.

Pressure drops due to flow disturbances at the bifurcation site were not seen in the experimental prosthesis, neither in relation to changing flow rates nor in relation to changing angles between the distal branches.

The arterial pressure in each part of the systemic circulation is directly proportional to the vascular resistance (15). The resistance in large arteries is very low, so that the mean arterial pressure in arteries as small as 3 mm in diameter is still 97 - 95% of the aortic mean pressure. Therefore, the ideal axillobifemoral bypass graft should have as little resistance as possible. Our experimental axillobifemoral prosthesis showed superior haemodynamic properties in this in-vitro study, because the flowsplitter devided the flow for each branch without induction of flow disturbances at the bifurcation, acting as a resistance.

3.8 Summary

At the bifurcation site of currently used axillobifemoral prostheses a pressure drop was measured, and found to be generally higher in the contralateral distal branch. The pressure drop increased significantly with increasing flow rate and increasing angle between the distal branches. Within the physiological range of flow rates a pressure drop as high as 30 mmHg was measured. No pressure drop was measured in our experimental axillobifemoral prosthesis

with a bifurcation and flowsplitter, neither with changing flow rates nor with varying angles between the distal branches. It is theorized that this favourable haemodynamical property, as observed in this in-vitro experiment, will lead to an improved clinical performance as measured by graft patency rates.

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CHAPTER 4

HEMODYNAMICS IN AXILLOBIFEMORAL PROSTHESES: an in-vivo study

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4.1 Abstract

An in-vitro study (1) revealed significantly better haemodynamical properties for a newly designed axillobifemoral bypass graft, with a flowsplitter at the bifurcation, when compared to the currently used axillobifemoral bypass graft configurations. In order to evaluate these results in-vivo a study on pigs was performed. The haemodynamical properties of two different axillobifemoral bypass grafts (Vascutek Limited), differing only in configuration of the bifurcation: one with a contralateral branch at an angle of 90° and one with a symmetrical bifurcation and flowsplitter, were analyzed in an animal experiment using pigs.
The prostheses were interpositioned between the aorta and the common iliac arteries. At different flow rates pressure measurements were performed 3 cm proximal to, and 5 and 12 cm distal to the bifurcation.
The 90° angled prostheses showed a significant pressure drop across the bifurcation under all flow conditions. The pressure drops increased significantly with increasing flow rate. No pressure drop was measured across the bifurcation of the flowsplitter prosthesis. Consequently all ipsilateral and contralateral pressure drops at 5 and 12 cm of the 90° angled bifurcation were significantly ($P<0.001$) greater as compared to the pressure drops found in the flowsplitter prostheses.
Conclusion: The newly designed axillobifemoral prosthesis with a flowsplitter showed highly significant better haemodynamical properties in-vivo compared with the 90° angled axillobifemoral prostheses due to the difference in bifurcation geometry.

Key words: axillobifemoral, bifurcation geometry, haemodynamics

4.2 Introduction

A haemodynamical in-vitro study (1) revealed significantly better haemodynamical properties for a newly designed axillobifemoral bypass graft, with a flowsplitter at the bifurcation, when compared to the currently used axillobifemoral bypass grafts with femorofemoral cross-over branches at angles of 30°,90° and 150° to the parent branch. These results were obtained with a sinusoidal pulsatile flow and a Newtonian fluid. In order to evaluate these results under physiological conditions with a real pulsatile (systolic and diastolic) flow and normal blood being a non-Newtonian fluid an in-vivo study on pigs was performed.
The haemodynamical properties were analyzed of two different axillobifemoral bypass grafts, differing only in configuration of the bifurcation: one with a contralateral branch at an angle of 90° and one with a symmetrical bifurcation and flowsplitter (Fig. 1.).

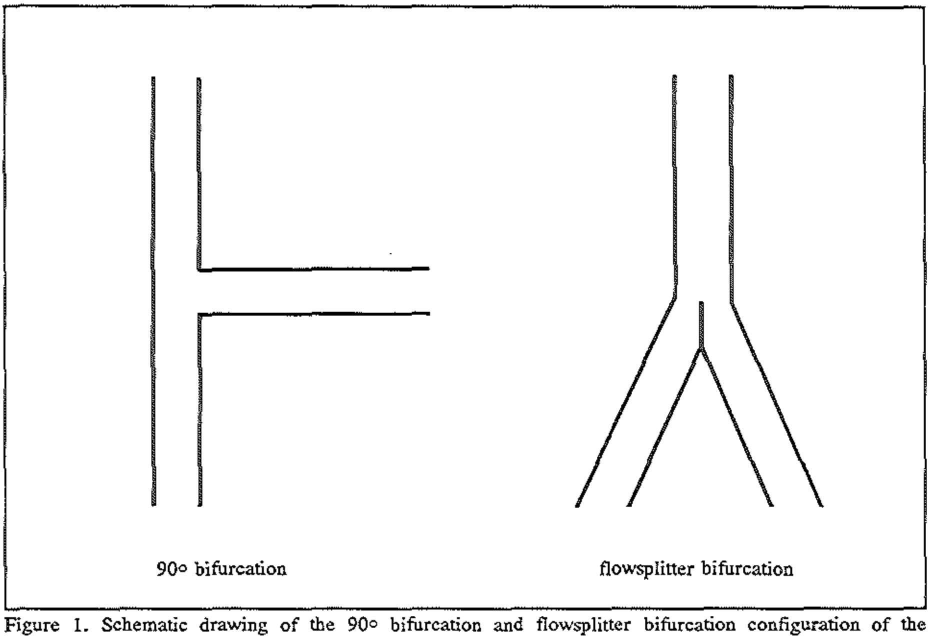

Figure 1. Schematic drawing of the 90° bifurcation and flowsplitter bifurcation configuration of the axillobifemoral bypass grafts.

4.3 Materials and Methods

All prostheses used were made of externally supported gelatine coated knitted Dacron (Vascutek Limited). The diameter of the parent branch and both distal outflow branches was 8 mm in the 90° prosthesis, while the specially designed flowsplitter prosthesis had 10 mm parent branches and distal outflow branches of 8 mm. The length of the proximal branch was 5 cm in both bypass configurations and all distal branches were 15 cm in length. These

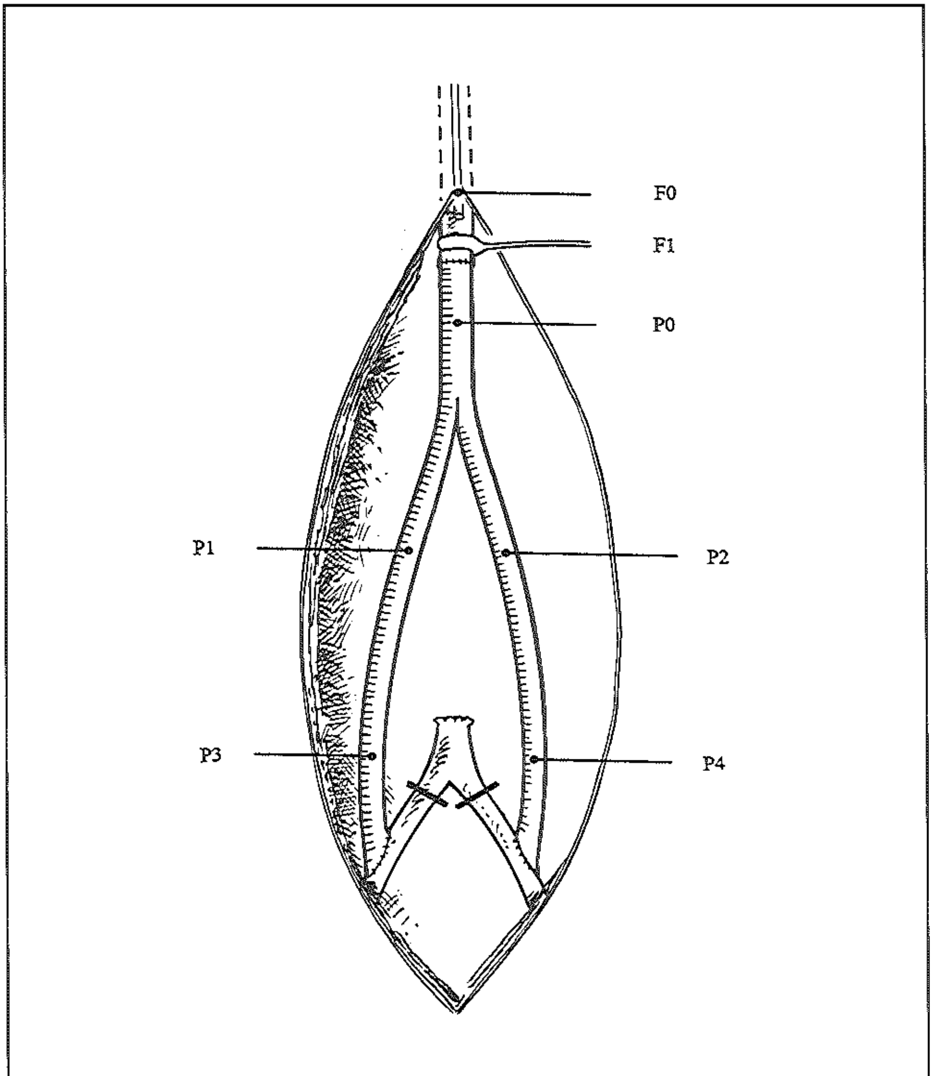

Figure 2. Diagram of the in-vivo experiment. The pressure measurements (P0-P4) and flow measurements (F0-F1) locations are shown.

prostheses were specially designed and manufactured by Vascutek Limited for the purpose of this study.

Five adult Landrace pigs with a mean body weight of 90 kg (± 5 kg) were sedated with Ketalar, anaesthetized with Fentanyl, ethraan and nitrous oxide and paralysed with Pavulon, which was augmented intermittently to maintain adequate surgical anaesthesia. The pigs were ventilated with a volume-controlled ventilator via an endotracheal tube. Central venous, pulmonary artery, and wedge pressures were measured by using a Swan-Ganz catheter introduced through the left jugular vein, allowing cardiac output measurements. Through the left carotid artery a catheter was placed in the descending aorta to continuously measure the intra-aortic pressure.

At laparotomy the suprarenal aorta down to the iliac arteries was dissected. The aorta was chosen to be the inflow artery because of its diameter (10 mm) and the flow rates that could be established. Before insertion of the graft 5000 U of heparin was administered intravenously in order to prevent clot formation, and was repeated every 30 min. The bypass graft was interpositioned between the suprarenal aorta and the common iliac arteries. The proximal anastomosis was end-to-end and distal anastomoses were end-to-side with a length of 2 cm. The back flow to the aorta was interrupted on both sides by ligating the proximal common iliac arteries (Fig. 2).

Intra-arterial pressure measurements were performed at 3 cm proximal and at 5 and 12 cm distal to the bifurcation in both legs. Just proximal to the proximal end-to-end anastomosis a 10 mm electromagnetic flow probe was installed over the aorta. All pressures, bloodflow and heart rate were continuously recorded on an 8 channel recorder. Cardiac output measurements at intervals of 15 minutes using the thermodilution technique were used to check for flow measurement irregularities. During the measurements the flow was manipulated by intravenous isoprenaline infusion in the left jugular vein (0.5-3.0 ugr/min) and intra-arterial administration of papaverine (50 mgr in each leg) through the distal pressure measurement catheters. The low flow rates were created by gradual compression of the suprarenal abdominal aorta, at least 20 cm proximal to the graft anastomosis. By using these techniques the flow through the parent branch could be manipulated to be between 500 and 1500 ml/min. The hematocrit was measured every hour and kept between 0.30 and 0.35 throughout the experiment by dilution or blood transfusion.

After recording of the measurements the distal branches were cut, about 1 cm proximal to the distal anastomoses, and connected again crosswise. This was done in order to eliminate an asymmetrical outflow or distal anastomotic asymmetry. All measurements were performed again after which the total bypass was removed and another type inserted, after which the whole procedure was repeated with the distal branches in a normal position and crosswise. At random the 90° angled bypass was inserted first and the flowsplitter prosthesis secondly in 3 pigs and in the other two pigs vice versa.

4.4 Statistical analysis

Pressure drops (calculated as the pressure proximal to the bifurcation minus the pressure distal to the bifurcation) at 5 and 12 cm distal to the bifurcation at all different flow rates and different distal branches were compared using the paired T-test. The same test was used to compare the ipsilateral versus the contralateral pressure drops. P-values given are two-sided; $P < 0.05$ was considered to be the level of statistical significance.

4.5 Results

No significant difference was found in the results of the measurements with the prostheses in a normal position compared to the crosswise position of the legs of the prostheses. This was found for both types of prostheses and under all flow conditions, confirming the symmetrical outflow in all experiments.

The 90° angled prostheses did show a significant pressure drop at 5 and 12 cm across the bifurcation under all flow conditions. The pressure drops increased significantly with increasing flow rate. All pressure drops ipsilateral and contralateral at 5 and 12 cm of the 90° angled bifurcation were significantly ($P<0.001$) greater as compared to the pressure drops found in the flowsplitter prostheses (Fig. 3).

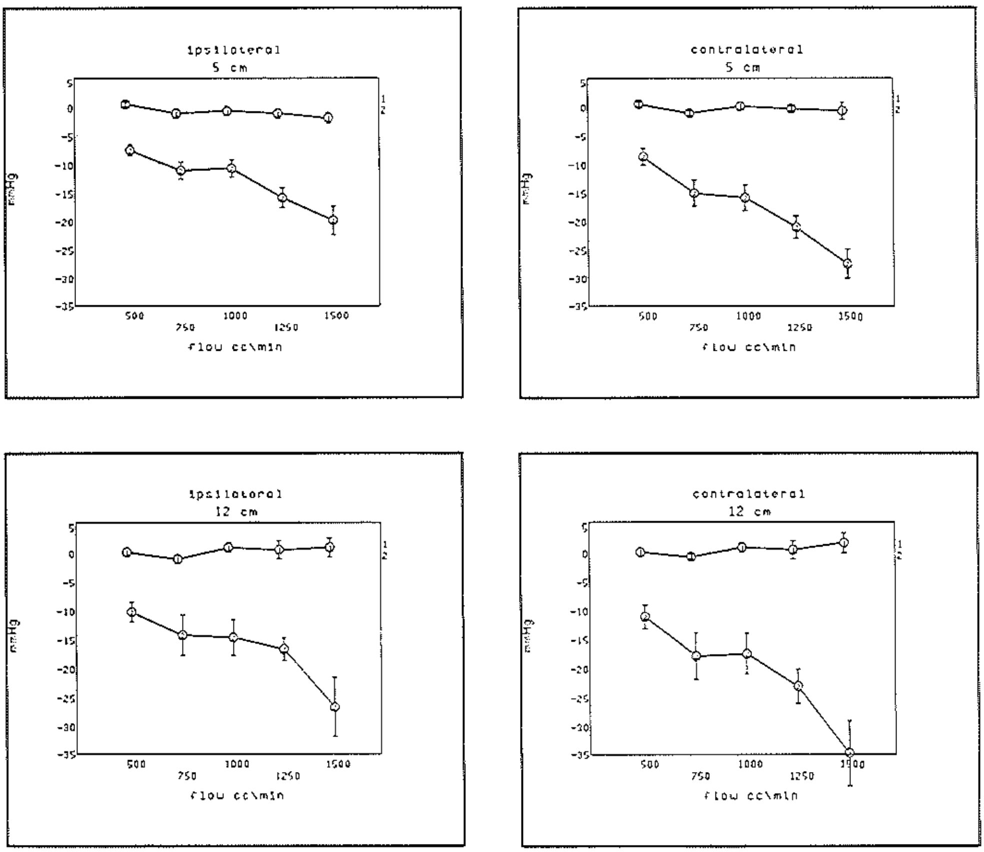

Figure 3. Pressure drops measured 5 and 12 cm distal to the bifurcation of the flowsplitter prosthesis (1) and the 90° angled prosthesis (2) on the ipsilateral side and the contralateral side. Data given are mean ± SD of 5 experiments.

Neither at 5, nor at 12 cm across the flowsplitter bifurcation did the mean ipsilateral pressure drop significantly differ from zero mmHg. The same applied to the contralateral side.
In comparing the ipsilateral and contralateral pressure drops at 5 cm of the 90° angled bifurcation no significant difference could be found at a flow rate of 500 ml/min, but all higher flow rates did show a significantly higher mean pressure drop at the contralateral side ($P < 0.05$). The corresponding difference at 12 cm distal to the bifurcation was significant only at flow rates of 1250 and 1500 ml/min ($P < 0.05$) (Fig. 3). The pressure drops measured could be as high as 35 mmHg.
There were no significant differences in mean pressure drop between the two distal branches in the flowsplitter prostheses both at 5 and 12 cm (Fig. 3).

4.6 Discussion

Since its introduction in 1963 (2,3), the axillobifemoral bypass graft has been used increasingly in the management of lower limb ischemia in poor-risk patients because of the low mortality rate compared with conventional central bypass techniques. Controversy exists about the ideal (anatomic) configuration of the femorofemoral limb some authors favouring the "lazy S" configuration and others the "inverted C" configuration. The "inverted C" configuration has the advantage of carrying the high flow rate that exists in the segment of the axillobifemoral graft that supplies both legs practically all the way down to the ipsilateral femoral artery, but the disadvantage of a retrograde end-to-side anastomosis for the cross-over graft (4,5). On the other hand, the "lazy S" configuration (6), although leaving a distal segment of the axillofemoral stem with a lower flow has a more streamlined antegrade anastomosis between the axillofemoral and the femorofemoral grafts causing less flow disturbance.
Flow patterns at arterial branches and bifurcations have been intensively investigated because of the possible role of haemodynamics in the development of atherosclerosis. These flow patterns display complex three-dimensional patterns characterized by flow separation and helical recirculating flow (7). When Reynolds number rises above a certain value, turbulent flow will appear and this phenomenon is mainly dependent of the geometry of the tubing. Every particular tubing geometry has its own critical Reynolds number at which turbulence will occur. It is known that the critical Reynolds number at bifurcations is much lower than in straight tubes (8). The pressure drop across a bifurcation is due to the presence of these vortical flow patterns and turbulent flow at higher Reynold numbers. Like in experimental tubing each vessel or bifurcation configuration has its own critical Reynolds number depending on its geometry. Because we were not able to visualize the turbulent flow at certain flow rates during our experiment we calculated the critical Reynolds numbers for the bifurcation geometries used. Turbulent flow causes a functional stenosis (9,10,11) and therefore causes a pressure drop. The assumption was made that a pressure drop of 5 mmHg was caused by at least flow separation or turbulence. Pressure drops < 5 mmHg were concidered to be a possible artefact or due to energy loss caused by the shear stress forces alone. The flow rates that caused a 5 mmHg pressure drop were used to calculate the critical Reynolds number. The critical Reynolds number for the 90° angled and flowsplitter bifurcation were respectively 165 and > 1000.
Turbulence in the vascular tree in the healthy human body rarely occurs, because the critical

Reynolds numbers are only reached during systole, which is too little time to create a full turbulence, but flow separation phenomena occur quite often at tributaries of the larger arteries (11).

In this study, pressure was measured through pressure taps inserted into the graftlumen at 5 and 12 cm distal to the bifurcation. Due to the disturbances in the flow profile, especially at short distances to the bifurcation, the pressure taps (at 5 cm) may not provide an accurate measure of the mean cross-sectional pressure at that level. However, these flow disturbances become less apparent with increasing distance from the junction and we can reasonably assume that the more distally measured pressures are more representative of the mean cross-sectional pressure. Although the pressure taps extend into the lumen their effect on the actual pressure is small because of their small diameter in comparison with the graft diameter. The error due to this effect was calculated to be maximally 1 mmHg.

Our earlier clinical study (12), performed to evaluate, by continuous wave doppler analysis and duplex scanning, the haemodynamical properties of axillobifemoral bypasses with a contralateral branch at an angle of 90°, showed a significantly higher blood flow in the distal ipsilateral branch and turbulent blood flow at the end-to-side anastomosis between the parent branch and the cross-over branch. Based on this finding, we performed an in-vitro study to analyse all currently used axillobifemoral graft configurations with cross-over anastomoses at angles of 30° ("lazy S"), 90° (manufactured by several industries) and 150° ("inverted C"). We simultaneously analysed the haemodynamical properties of a newly developed axillobifemoral prosthesis with a symmetrical bifurcation and a midstream flowsplitter as in aortobifemoral bypasses. This study (1) revealed no clinically significant asymmetrical flow distribution between the two distal branches in the currently used axillobifemoral bypass configurations but it showed a highly significant symmetrical pressure drop between the proximal branch and both distal branches. These pressure drops increased significantly with increasing flow rate and also with increasing angle between the two distal branches. The results were obtained with a simulated pulsatile flow and a Newtonian fluid with a viscosity of 2.0 cPoise.

This in-vivo study was conducted to evaluate the haemodynamical properties of two axillobifemoral bypass grafts under physiologic conditions. For that purpose we now performed the measurements in blood, being a non-Newtonian fluid and in a real physiological pulsatile (systolic and diastolic) flow.

In order to further improve the haemodynamical properties of the newly designed axillobifemoral bypass graft used in the in-vitro study, the parent branch diameter was changed from 8 to 10 mm, as a result of which the cross-sectional area increase across the bifurcation was reduced from 200 % to 128 %. The physiological increase in cross-sectional area is 116 %, and considered ideal (13,14). This reduced increase in cross-sectional area will decrease the velocity changes at the site of the bifurcation and probably decrease the induced flow disturbances.

The impact of the difference in "mechanic" sinusoidal pulsatile flow as in the in-vitro study compared to a physiologic pulsatile systolic and diastolic flow is not known. LoGerfo showed that the flow separation areas visualized in a continuous and pulsatile flow pattern did not significantly change, but physiological pulsatile flow patterns were not studied (10). He and others (15,16) found only small pressure drops across the bifurcation due to these flow separation areas, a finding we can not confirm. In contrast we found in this in-vivo study relatively high pressure drops both in the ipsilateral and contralateral branch of the 90° angled axillobifemoral prostheses. No pressure drop was measured in the new axillobifemoral prostheses with a symmetrical bifurcation and flowsplitter.

The measurements in the in-vitro study were made using a Newtonian dextran solution with a viscosity of 2.0 cPoise. Since the viscosity of blood is about 4.0 cPoise when the heamatocrit is between 0.30 and 0.35 the in-vivo pressure drops would be higher and may be estimated by dimensional analysis. The pressure drop difference between the in-vitro and in-vivo experiments under the same haemodynamical circumstances (the same Reynolds number) can be calculated and are expected to increase 2 times the measured in-vitro values. This high increase was not found and might be influenced by the different pulsatile flow patterns between the in-vitro and in-vivo experiment.
Because the bifurcation configuration was the only variable in this experiment we theorized that these pressure drops were caused by a resistance at the bifurcation site due to flow separation or turbulence. These areas of flow separation causing areas with relatively low shear stresses are likely to be the local haemodynamic factor that initiates intimal hyperplasia (17) and therefore might be responsible for reduced patency rates.
No pressure drop was measured in the new axillobifemoral prosthesis with a symmetrical bifurcation and flowsplitter. This prosthesis was therefore considered not to induce flow disturbances and therefore would have the theoretical advantage not to induce intimal hyperplasia, a frequent cause of graft occlusions.
In order to evaluate the clinical relevance of these different haemodynamical properties due to the altered geometry of the bifurcation a prospective randomized clinical trial was performed (18).

4.7 Conclusion

Ninety degrees angled prostheses did show a significant pressure drop at 5 and 12 cm across the bifurcation under different flow conditions. These pressure drops increased significantly with increasing flow rate. No pressure drop across the flowsplitter bifurcation in each leg of the prosthesis was measured neither at 5 cm nor at 12 cm distal to the bifurcation. As a consequence there is also no significant difference in mean pressure drop between the two distal branches in the flowsplitter prosthesis both at 5 and 12 cm.
Especially at high flow rates the contralateral pressure drop across the 90° angled bifurcation was significantly higher compared to the ipsilateral pressure drop.
In conclusion we state that the newly designed axillobifemoral prosthesis with a flowsplitter showed highly significant better haemodynamical properties in an in-vivo experiment compared with the 90° angled axillobifemoral prosthesis due to the difference in bifurcation geometry.

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CHAPTER 5

EUROPEAN AXILLOBIFEMORAL BYPASS TRIAL: a prospective randomized multicenter study

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5.1 Abstract

Haemodynamical in-vitro and in-vivo studies revealed significantly better haemodynamical properties for a newly designed axillobifemoral bypass graft, with a flowsplitter at the bifurcation, when compared to the currently used axillobifemoral bypass graft with a contralateral branch at an angle of 90°. In order to analyse the clinical relevance of these improved haemodynamical properties a prospective randomized clinical trial was performed. The patency rates of two different axillobifemoral bypass grafts, differing only in configuration of the bifurcation: one with a contralateral branch at an angle of 90° and one with a flowsplitter, were analysed.

In 19 centers 117 patients were randomized, 59 receiving a prosthesis with a flowsplitter and 58 a prosthesis with a 90° bifurcation. Indications and risk factors were equally distributed in both groups.

Final analysis after 3 years with a mean follow up of 12 months (range 3-36 months) showed that the prosthesis with a flowsplitter had a significantly better patency rate after 2 years of 84 % compared to the patency rate of the prosthesis with a 90° angled bifurcation of 38 % (P $< 0,0001$; Log-Rank test).

These data were not significantly influenced by indication for operation, associated riskfactors (e.g. diabetes mellitus, hypertension or myocardial infarction), outflow tract or mode of anticoagulant therapy.

Other endpoints like death and graft infection did not differ significantly.

Conclusion: The new axillobifemoral bypass graft with a flowsplitter showed a highly significant ($P<0,0001$) better patency rate of 84% after two years compared to the patency rate of the 90° angled axillobifemoral prosthesis of 38 %, confirming the clinical relevance of the bifurcation geometry.

5.2 Introduction

The unilateral axillofemoral bypass graft as an alternative management for unilateral aortoiliac occlusive disease was described in 1963, independently and nearly simultaneously by Blaisdell and Hall (1), using a Dacron graft, and by Louw (2), who utilized saphenous vein. In 1966, Sauvage and Wood (3) described the axillobifemoral graft and theorized that the addition of a femoral cross-over graft doubled the flow in the parent graft and thereby would improve patency rates. Controversy exists about the ideal anatomic configuration of the femorofemoral limb some authors favouring the "lazy S" configuration and others the "inverted C" configuration. The "inverted C" configuration has the advantage of carrying the high flow rate that exists in the segment of the axillobifemoral graft that supplies both legs practically all the way down to the ipsilateral femoral artery, but the disadvantage of a retrograde end-to-side anastomosis for the cross-over graft. On the other hand, the "lazy S" configuration, although leaving a distal segment of the axillofemoral stem with a lower flow has a more streamlined antegrade anastomosis between the axillofemoral and the femorofemoral grafts causing less flow disturbance. Our earlier clinical study (4), performed to evaluate the haemodynamical properties by continuous wave Doppler analysis and duplex scanning of axillobifemoral bypasses with a "lazy S" configuration showed a significantly higher blood flow in the distal ipsilateral branch and turbulent blood flow at the end-to-side anastomosis between the parent branch and the cross-over branch. Based on this finding, we than performed an in-vitro study to analyse all currently used axillobifemoral graft configurations with cross-over anastomoses at angles of 30° ("lazy S"), 90° (manufactured by several industries) and 150° ("inverted C"). We simultaneously analysed the haemodynamical properties of a newly developed axillo-bifemoral prosthesis with a symmetrical bifurcation with a midstream flowsplitter as in aortobifemoral bypasses. This study (5) revealed no significant asymmetrical flow distribution between the two distal branches in the currently used axillobifemoral bypass configurations but it showed a highly significant symmetrical pressure drop between the proximal branch and both distal branches. These pressure drops increased significantly with increasing flow rate and also with increasing angle between the two distal branches. Within the physiological range of flow rates this pressure drop could be as high as 30 mmHg. Because the bifurcation configuration was the only variable in this experiment it was theorized that these pressure drops were caused by a resistance at the bifurcation site due to turbulence and flow separation. No pressure drop was measured in the new axillobifemoral prosthesis with a symmetrical bifurcation and flowsplitter, neither with changing flow rates nor with varying angles between the distal branches. These findings were consequently confirmed in an in-vivo study, in which the haemodynamical properties of 90° angled prostheses were compared with the new flowsplitter prostheses (6). The pressure drops shown in these studies might be responsible, as a result of the flow disturbances, for clot formation and graft occlusions. In order to evaluate the clinical relevance of these different haemodynamical properties due to the altered geometry of the bifurcation an international prospective randomized multicenter axillobifemoral trial was started.
The aim of this study was to compare the patency rates and clinical behaviour of two different axillobifemoral prosthetic grafts, that differ only in the configuration of the bifurcation: one with a contralateral branch at an angle of 90° (which is the current standard configuration) and the other with a symmetrical bifurcation and flowsplitter (Fig. 1).

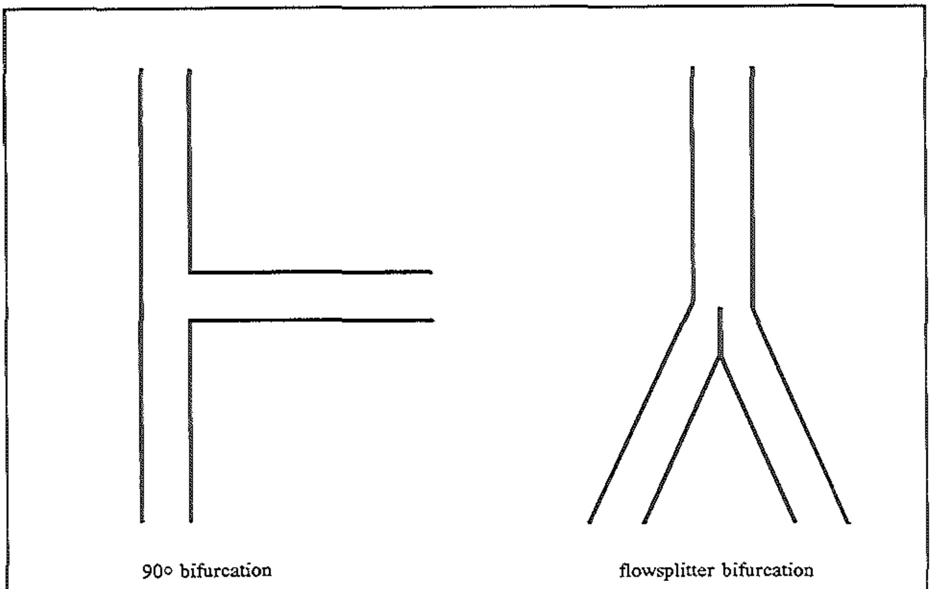

Figure 1. Schematic drawing of the 90° bifurcation and flowsplitter bifurcation configuration of the axillobifemoral bypass grafts.

5.3 Materials and Methods

5.3.1 Materials

All prostheses used were made of externally supported gelatine coated knitted dacron (Vascutek Limited). The diameter of the parent branch and both distal outflow branches was 8 mm in the (commercially available) 90° prostheses, while the specially designed flowsplitter prostheses had 10 mm parent branches and distal outflow branches of 8 mm. These prostheses were specially designed and manufactured by Vascutek Limited for the purpose of this study.

5.3.2 Methods

The study protocol was approved by the ethical committees in 19 participating centers in Belgium, France, Germany and The Netherlands.
Patients selected for axillobifemoral bypass grafting were randomized, by opening sealed envelopes, for each center seperately. Each center was allowed to adhere to their own routine for indications and postoperative management provided this routine remained the same throughout the trial period. Patients with a walking distance of more than 100 meter or a life expectancy of less than 6 months were excluded from the study. Patients with infected abdominal grafts and/or aorto-enteric fistulae were compelling indications for axillobifemoral

bypass grafting and therefore included in the study. High-risk patients suffering atherosclerotic occlusive or aneurysmal disease were also included in the study.
Preoperative data collected included age and sex of the patient, indication for operation, concurrent disease, physical examination, doppler ultrasound study, angiography and duplex examination.
No special investigations were performed to analyse the donor artery except that the bloodpressures of both arms were compared after which the axillary artery with the highest arm bloodpressure was used. When bloodpressures were equal the axillairy artery on the side of the worst circulated leg was used.
The surgical technique used for axillobifemoral graft placement in general is similar to that originally described (1,7).
Postoperative anticoagulant therapy varied in different centers from none, to platelet aggregation inhibitors or coumadine derivatives, but was kept the same for each center throughout the trial period.
Postoperative complications, like thrombosis, bleeding, false aneurysm formation, seroma formation, lymph leakage and wound infections were recorded.
Based on pre- and perioperative angiography, doppler ultrasound and duplex studies and taking into account peroperative additional outflow enhancement procedures, outflow was scored to be; symmetrically good (ipsi- and contralateral patent deep and superficial femoral arteries); symmetrically bad (ipsi- and contralateral patent deep femoral artery) or asymmetrically (an ipsilateral patent deep femoral artery and a contralateral patent deep and superficial femoral artery, or vice versa).
Follow up was performed after 1, 3, 6, 9 and 12 months and 6 monthly thereafter. At each visit patient history and physical examination were recorded. Angiography, doppler ultrasound and duplex studies were performed at 3 and 12 months postoperatively.
Ipsi- or contralateral branch occlusions were recorded as interim events. All occlusions were verified by angiography, doppler ultrasound or duplex studies. Endpoint events were: graft infection, death or total occlusion, afterwhich the follow up was discontinued. Early occlusions within 7 days postoperatively were interpreted as technical failures, not caused by the geometry of the axillobifemoral bypass, and were not considered to be an endpoint.

5.4 Statistical analysis

Proportionate data were compared with the chi-square test and the numeric data (expressed as mean $\pm$ standard error) were compared by means of the Mann-Withney Two Sample test. Statistical analysis of the grouped study interim-event rates and endpoint-event rates in randomized patients was made by a single comparison based on a life-table analysis (Log-rank) technique. Results were also analysed to adjust for any imbalance in prognostic factors between the two groups.

5.5 Results

From May 1988 till August 1990 121 patients were randomized in 19 centers in Belgium (1), Germany (9), France (1) and The Netherlands (8). Four patients were lost to follow up,

Table 1. Distribution of risk factors and indications for operation.

		90° bifurcation		flowsplitter	
		n=58	%	n=59	%
Risk factors					
Age (years)	:	71	(46-86)	70	(45-89)
Sex: male	:	44	(25.9)	49	(83.1)
female	:	14	(24.1)	10	(16.9)
Diabetes mellitus	:	15	(25.9)	15	(25.4)
Hypertension	:	26	(44.8)	24	(40.7)
Angina pectoris	:	30	(51.7)	37	(62.7)
Myocardial infarction	:	22	(37.9)	24	(40.7)
Coronary artery bypass	:	3	(5.2)	8	(13.6)
TIA	:	6	(10.3)	1	(1.7)
CVA	:	11	(19.0)	11	(18.6)
Respiratory disease	:	26	(44.8)	25	(42.4)
Carcinoma	:	5	(8.6)	9	(15.3)
Previous Vasc. operations	:	19	(32.8)	24	(40.7)
Indications for operation					
Claudication (<100m)	:	9	(15.5)	5	(8.5)
Rest pain	:	20	(34.5)	19	(32.2)
Gangrene	:	17	(29.3)	22	(37.2)
Abdominal aneurysm	:	1	(1.7)	2	(3.4)
Infected vasc. prosthesis	:	4	(6.9)	4	(6.8)
Aorto-enteric fistula	:	2	(3.5)	5	(8.5)
Other	:	5	(8.6)	2	(3.4)

TIA = Transient Ischemic Attack; CVA = Cerebro Vascular Accident

leaving 117 patients, 94 men and 23 women with a mean age of 70 years (range 45-89) for analysis. 59 patients received a prosthesis with a flowsplitter and 58 a prosthesis with a 90° bifurcation. Risk factors and indications for operation were equally distributed in both groups as shown in table 1.

Important to notice is the high incidence of cardio-pulmonary disease (81%), which was the main indication for the extra-anatomical bypass. The remaining indications were due to an abdominal infections like an infected prosthesis or an aorto-enteric fistula, or local surgical problems as dense adhesions or iatrogenic lesions of the gut.

Preoperative doppler measurements showed similar mean ankle-brachial resting pressure indices in both groups, namely 44.5% on the left side and 47% on the right in the 90° group (range 0-110) and 44.3% and 46.5% respectively in the flowsplitter group (range 0-114).

5.5.1 Operation

The proximal anastomosis was on the proximal part of the right axillary artery in 66.7 % and on the left in 33.3 %. To enhance outflow that appeared to be restricted by deep femoral artery stenosis or occluded superficial femoral arteries, additional surgical procedures were performed as listed in table 2. In both groups about half of the patients were treated with a bilateral profundaplasty, in which the distal anatomosis reaches at least beyond the proximal part of the deep femoral artery for more than 1 cm. About 5 % of the patients received an additional femoro-popliteal bypass.

Table 2. Distribution and frequency of additional outflow procedures.

	90° bifurcation		flowsplitter	
	n=58	%	n=59	%
Outflow procedure				
ipsilateral profundaplasty :	30	(51.7)	30	(50.8)
ipsilateral fem-pop :	3	(5.2)	4	(6.8)
contralateral profundaplasty :	29	(50.0)	25	(42.4)
contralateral fem-pop :	3	(5.2)	2	(3.4)

5.5.2 Postoperative complications

Postoperative mortality, defined as death within 30 days after surgery or during the same hospital admission was 17.2 % in the 90° group and 6.8 % in the flowsplitter group, which difference is statistically not significant. The only significant influence on the postoperative mortality (Log-rank; $P<0.05$) was the indication for surgery in which - as expected - patients operated for infected grafts and or aorto-enteric fistulae showed much higher mortality rates of 37.5 % and 43 % respectively, while high-risk patients with atherosclerotic obstructive disease showed a postoperative mortality rate of only 5.5 %.
The postoperative complications were equally distributed in both groups. The most frequent postoperative complication was early occlusion, defined as an occlusion within 7 days postoperatively. This occurred in 12 patients (20.7 %) in the 90° bifurcation group and in 18 patients (30.5 %) in the flowsplitter group, a difference that did not reach statistical significance ($P=0.1$). An attempt to reestablish bloodflow was performed in 7 of the 12 cases in the 90° bifurcation group and was successfull in all. In 13 of the 18 cases in the flowsplitter group restoration of flow was successful. One attempt in the flowsplitter group was unsuccessfull. In 13 of all 21 attempts a technical failure appeared to be the cause of the occlusion and in 8 cases no cause could be identified with certainty. In 7 patients no attempt was made due to severe outflow impairment not amenable to further reconstruction, or was not deemed feasible because of cardio-pulmonary and septic problems. All successfully thrombectomized early occlusions were continued to be followed, and considered to be primary patent.
Postoperative bleeding occurred in 3 patients (5.2 %) in the 90° bifurcation group and in 4 patients (6.8 %) in the flowsplitter group. These bleedings were noted to be related to additional surgical procedures performed during axillobifemoral bypass grafting. In 5 of the 7 bleeding complications an operative intervention was necessary to treat the condition, but anticoagulant therapy could be continued in all these cases.
A relatively high incidence of postoperative seroma formation, defined according to

Blumenberg (18) as a perigraft collection of clear, sterile fluid, was found in 10 patients (18.2 %) in the 90° group and in 15 patients (25.4 %) in the flowsplitter group. The palpable collection of fluid around the prosthesis persisted for a mean period of 64 days (range;10-210) in the 90° group and for 51 days (range;7-220) in the flowsplitter group. The majority of these seroma formations were asymptomatic but nevertheless 18 patients were treated with repetitive punctures probably leading to graft infections in three patients.
Postoperative wound infections, defined as delayed wound healing with positive cultures and treated with antibiotics, were seen in 4 patients (6.9 %) in the 90° bifurcation group and also in 4 patients (6.8 %) in the flowsplitter group. Seven of the 8 infections were in the ipsilateral or contralateral groin and 1 was located at the help incision. None were detected at the proximal anastomosis site.
Five graft infections were recorded, 4 during the postoperative period and one after 76 months. Three occurred in the 90° group (5.2%) and 2 in the flowsplitter group (3.4%). Carefull analysis of the cause of these infections showed that in 3 patients repeated punctures for seroma formation caused the graft infections, because the first cultures in these cases were sterile. Graft infection was expected to occur more often in the group of patients treated for abdominal infection (infected aortic graft or aorto-enteric fistula), but this was not confirmed by the study results.
Postoperative anticoagulant therapy was similar in both groups. In the 90° group 28 patients (48.3 %) received coumadine derivatives, 26 patients (44.8 %) received platelet aggregation inhibitors and 4 patients (6.9 %) received no anticoagulant therapy. In the flowsplitter group 28 patients (47.5 %) received coumadine derivatives, 28 (47.5 %) platelet aggregation inhibitors and 3 (5.1 %) no medication.

5.5.3 Follow-up

Mean follow up was 12 months, ranging from 3 to 36 months. During this period Doppler ultrasound studies were performed to analyse the changes in ankle to brachial pressure indices at rest and to check for a possible asymmetrical distribution between ipsilateral and contralateral ratios in relation to the angiographically scored outflow. The data revealed a statistically significant mean increase in ankle-brachial pressure index of 30 % ranging from -40 to 89 % (Mann-Whitney; $P<0.05$) for all patients. No significant difference in ankle-brachial pressure index changes could be identified between both study groups. The ankle-brachial pressure index increase after axillobifemoral bypass grafting was symmetrically distributed between the ipsilateral and contralateral leg in both study groups.
The patency rate of the distal ipsilateral branches of the axillobifemoral bypasses did not show a significant difference between both groups (Log-rank; $P=0.13$) (Fig. 2). There was a highly significant difference in the patency rate of the distal contralateral branch between the two groups in favour of the flowsplitter group (Log-rank; $P< 0.0004$) (Fig. 3).
After 2 years 35.7 % of all 117 patients had died. This high late mortality rate confirms the selection of high-risk patients for this operation. Life table analysis did not show a statistically significant difference in the late mortality rate between the two groups (Fig. 4). The cause of death was in 50 % of the patients cardiac disease, in 8 % pulmonary disease, in 3 % carcinoma, and in the remaining 39 % unidentified. Indication for surgery and other risk factors as listed in table 2 did not significantly influence the late mortality rate in both groups. One late graft infection was observed 76 months after implantation. It was the result of

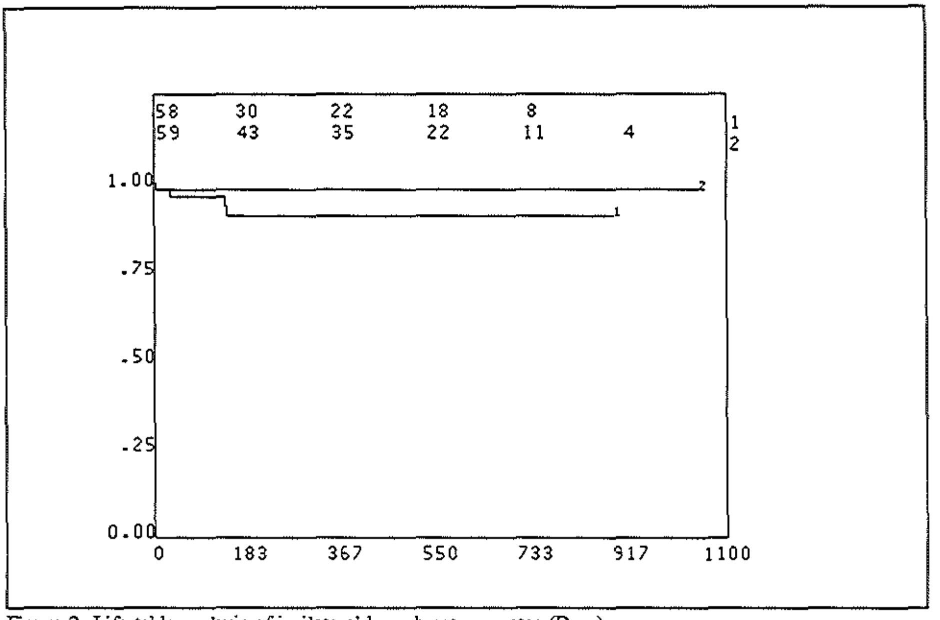

Figure 2. Life table analysis of ipsilateral branch patency rates (Days).
1 = 90° group; 2 = flowsplitter group

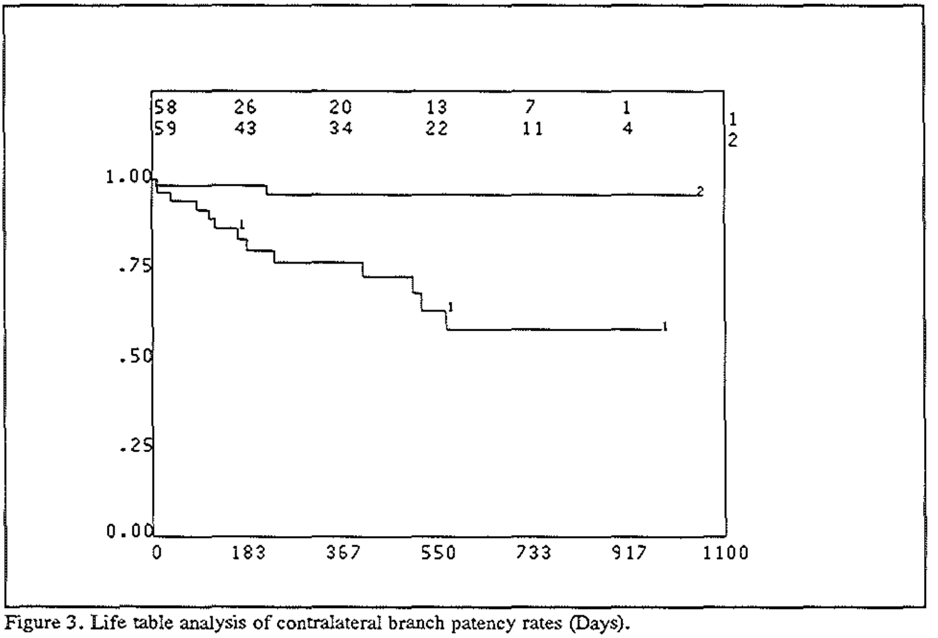

Figure 3. Life table analysis of contralateral branch patency rates (Days).
1 = 90° group; 2 = flowsplitter group

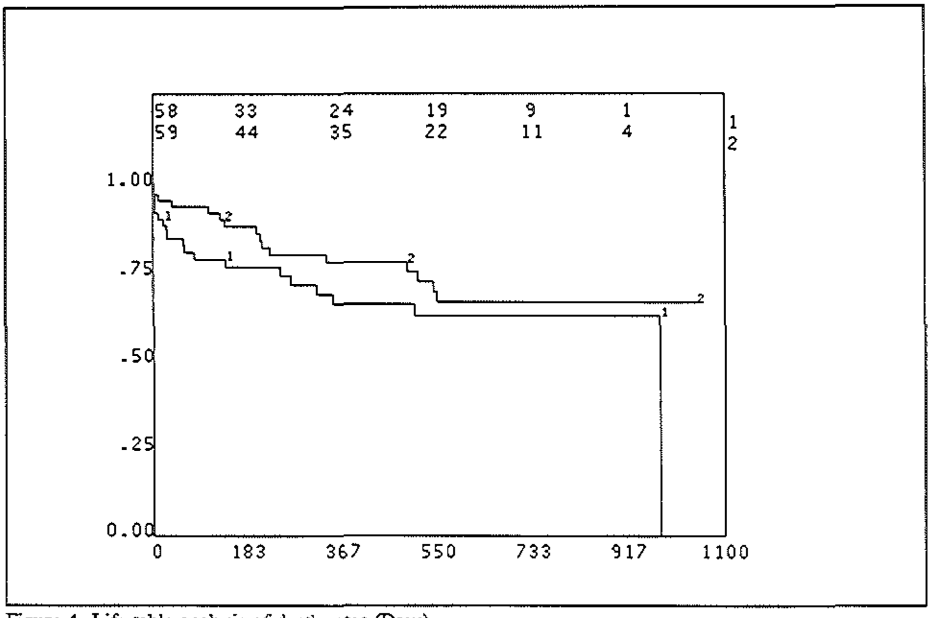

Figure 4. Life table analysis of death rates (Days).
1 = 90° group; 2 = flowsplitter group

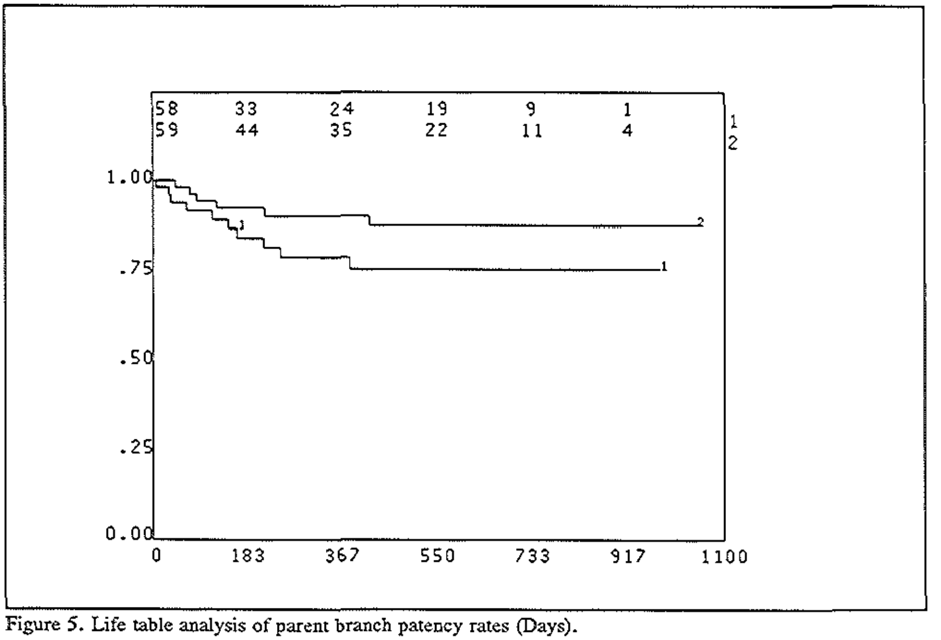

Figure 5. Life table analysis of parent branch patency rates (Days).
1 = 90° group; 2 = flowsplitter group

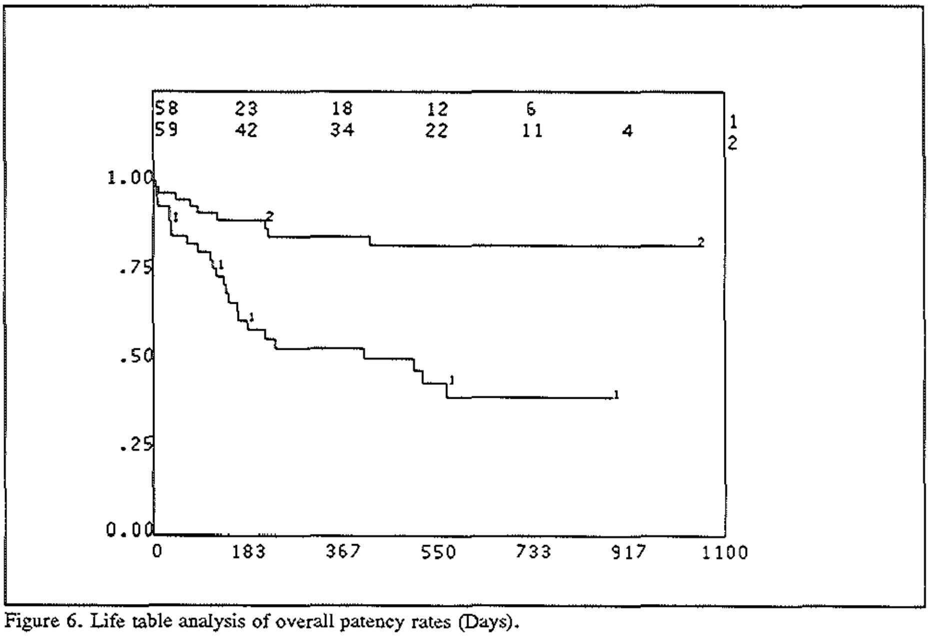

Figure 6. Life table analysis of overall patency rates (Days).
1 = 90° group; 2 = flowsplitter group

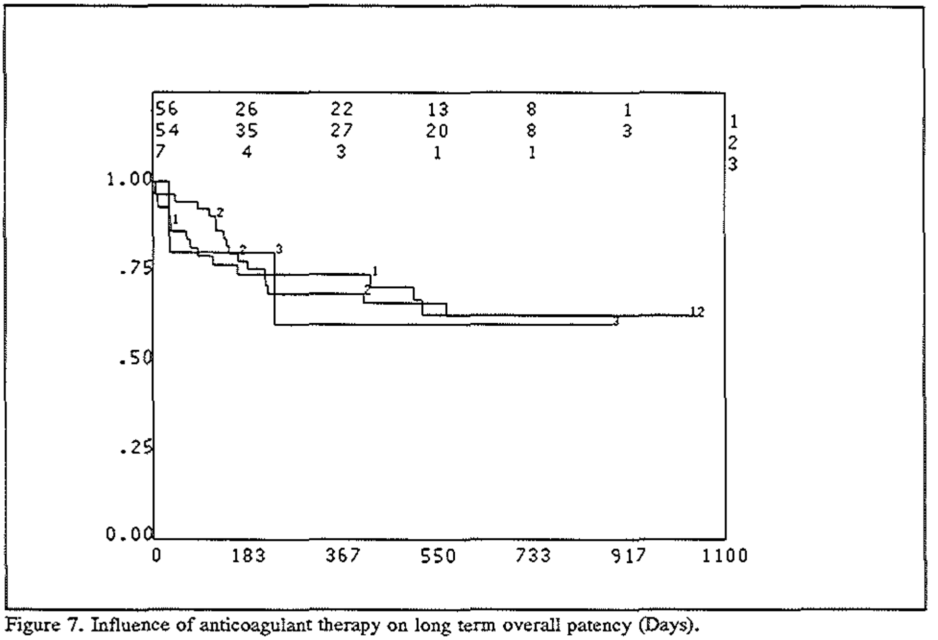

Figure 7. Influence of anticoagulant therapy on long term overall patency (Days).
1 = Coumadine derivatives; 2 = Platelet inhibitors; 3 = No anticoagulant therapy

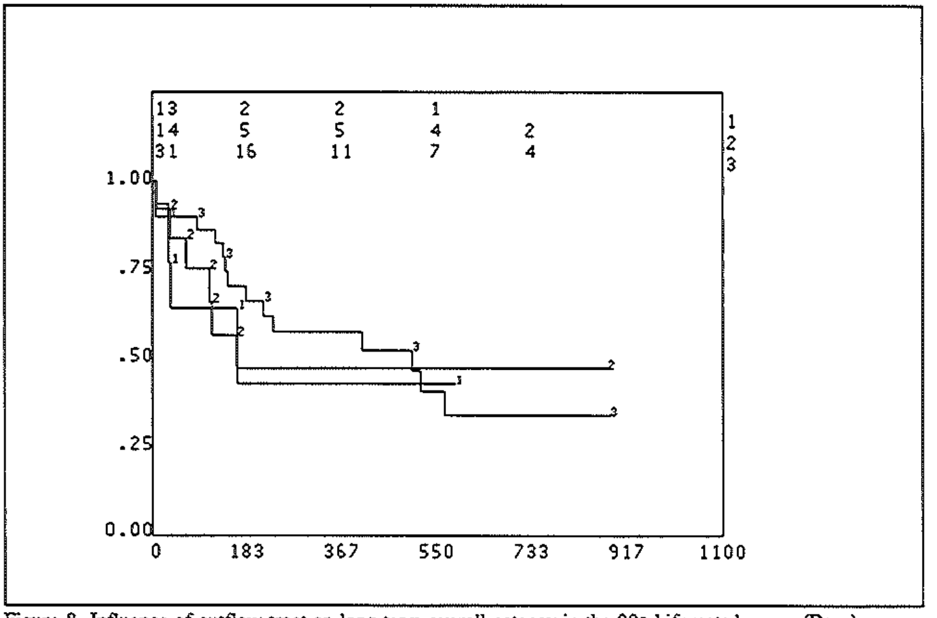

Figure 8. Influence of outflow tract on long term overall patency in the 90° bifurcated group (Days).
1 = Symmetrically good; 2 = Asymmetrically; 3 = Symmetrically bad

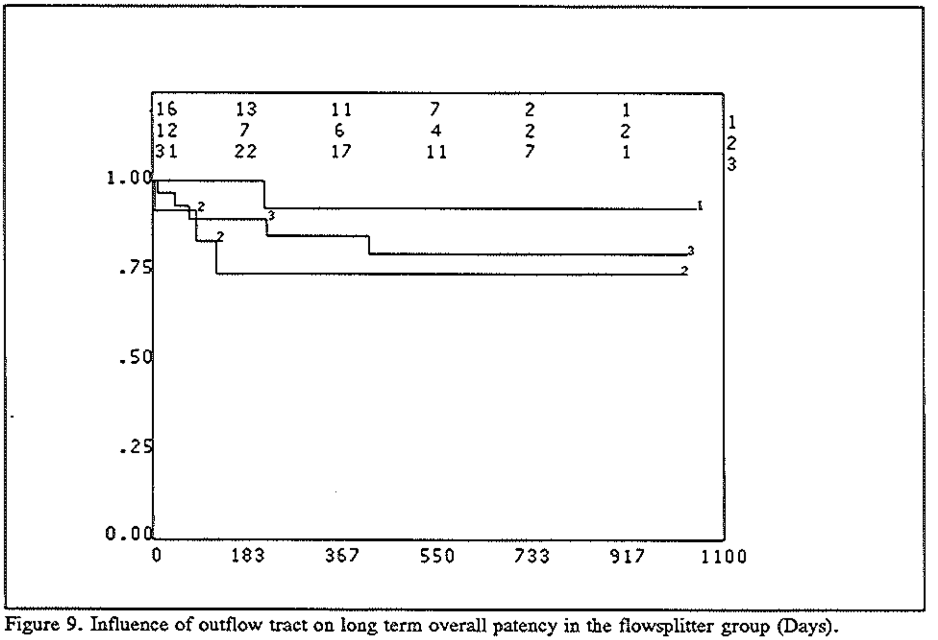

Figure 9. Influence of outflow tract on long term overall patency in the flowsplitter group (Days).
1 = Symmetrically good; 2 = Asymmetrically; 3 = Symmetrically bad

decubitus at the crossing of the costal margin, a complication necessitating a latissimus-dorsi flap transposition and insertion of a new graft.

During follow up there was a smaller number of total graft occlusions as shown by the life table in fig. 5. No statistical significant difference could be identified in this outcome.

Life table analysis for all occlusions, that is total occlusions and ipsilateral or contralateral distal occlusions, showed a two year patency of 38 % for the 90° bifurcated graft in contrast to the patency rate of 84 % for the bypass with a flowsplitter (Log-rank; $P<0.0001$) (Fig. 6)

Risk factors (Table 1), indications for surgery, post operative complications like early thrombosis with successfull thrombectomy, infection, bleeding or seroma formation did not significantly influence the patency rates of the two types of prostheses.

An attempt for thrombectomy was performed in 9 (45 %) of the 20 late occluded grafts in the 90° group of which 4 were successfull. All 3 attempted thrombectomies in the 4 late occluded flowsplitter prostheses were unsuccessfull. Follow up of the successfully embolectomized total occlusion in one patient in the 90° group was discontinued because only primary patency rates were analysed in this study.

The graft failures attributed to a statistically significant different (Log-rank: <0.05) major amputation rate of 13.9 % in the 90° group and 6.8 % in the flowsplitter group. Three occluded flowsplitter prostheses were replaced by aortobifemoral bypasses causing one postoperative death.

Life table analysis did not show any statistically significant difference between the patency rates of all grafts related to the anticoagulant therapy regimen (Fig. 7). The influence of the difference in outflow, shown in fig. 8 and 9, was found to be not statistically significant.

5.6 Discussion

In modern vascular surgery axillobifemoral bypass grafting retains a place as the procedure of choice for the treatment of infected aortic grafts, aorto-enteric fistulae, and in a proportion of high-risk patients with limb threatening ischemia. Results may be influenced by indication for operation, which varies from stringent to rather liberal in published series (8-12). In our series such a variation is also noted, some centres restricted the procedure to cases of aorto-enteric fistula or aortic graft sepsis, others included patients with severe claudication. Because the study was prospectively randomized and the randomization was performed for each center separately, these differences did not affect the aim of the study namely to compare the patency rates and clinical behaviour of two different axillobifemoral bypass grafts. When comparing the absolute patency rates from this series with previously published data, one should pay attention to the percentage of claudicants included, because in these cases the patency rate is allegedly higher than in a limb salvage group (11). In our series only 15 claudicants (12 %) were included, which is a small group when compared to several large series (10-13). Three patients were electively treated for infrarenal abdominal aneurysms by ligation of the common iliac arteries and an axillobifemoral bypass. One of these patients died postoperatively and one died after 7 months due to an unknown cause. Leather and Karmody (14,15) suggested that this technique offers a reasonable alternative to the treatment of abdominal aortic aneurysms when the indication is compelling and the risk of direct graft implantation excessive. A statement which has not been confirmed by later publications. Risk factors like diabetes, hypertension and cardio-pulmonary disease were present in more than 90 % of all patients, which is also reflected in the high mortality rate we encountered.

The severity of the atherosclerotic occlusive disease is expressed by the mean preoperative resting ankle to brachial pressure ratios of less than 47 %.
Postoperative mortality was 17.2 % in the 90° group and 6.8 % in the flowsplitter group and was only influenced by the indication for operation, a finding also observed by Savrin et al.(9) He found a high postoperative mortality rate of 67 % for emergency procedures and only 7 % for elective cases. This is comparable to our results, namely a high postoperative mortality rate in patients operated for infected grafts and or aorto-enteric fistulae of 37.5 % and 43 % respectively, and an acceptably low mortality rate of only 5,5 % in electively treated high-risk patients with atherosclerotic occlusive disease.
Our objective was to analyse the primary patency rates of the prostheses in both groups. Also successfully thrombectomized early thrombosed grafts were considered primary patent. The patency rate of those successfully thrombectomized grafts after 2 years was 0 % in the 90° group and 62 % in the flowsplitter group. Statistical analysis did not reveal a significant difference between thrombectomized and non thrombectomized grafts.
A relatively high incidence of postoperative seroma formation, was found in 18.2 % in the 90° group and in 25.4 % in the flowsplitter group. In other published series (11,12,16,17) this incidence ranged from 2.2 % to 60 %. No high concentrations of gelatine, which was first thought to induce the seroma formation, were found in 3 analysed fluid samples of seromas. Blumenburg et al (18) showed that the fluid accumulations around the grafts were an ultrafiltrate of serum, and occured more often in grafts (Dacron or PTFE) placed in the subcutaneous position. Although repetitive aspirations in 18 of 25 seromas caused 3 graft infections (16.7%), we consider it an acceptable alternative to the more extensive therapy of graft replacement, with respect to the high risk in this group of patients. Blumenburg found an 8 % infection rate after repetitive aspirations.
The overall graft infection rate of 4.3 % in our series compares favourable to the infection rates in other series. Christenson (19) and Parsonnet (20) found infection rates of 9.1 % and 11.1 % respectively.
It has always been stated that patency is ultimately related to outflow. In axillobifemoral bypass grafting this has been confirmed by several reports (13,21,22). However Kalman et al in 1987 (23) was not able to detect a statistically significant difference in patency for axillobifemoral bypass grafts with different outflow tracts. Our series also showed no significant difference in patency rates in both the 90° group and the flowsplitter group in relation to the outflow tract. Nevertheless a patency rate of 91 % after 2 years in the flowsplitter group with a good outflow is extremely good.
No published data are available on the influence of anticoagulant therapy on the patency rate for axillobifemoral bypasses. Although one might anticipate a beneficial effect of anticoagulant therapy in the relatively long extra-anatomical bypasses (24) this series could not reveal any positive influence of anticoagulant therapy on patency rates.
The patency rates reported for axillobifemoral grafting performed in the 1960's and 1970's ranged from 50 % to 80 % at 5 years in most series and were clearly inferior to the patency achieved with standard aortobifemoral bypasses. Moreover, many axillobifemoral grafting series reported secondary patency, the corresponding primary patencies being lower (20,21,25,26). Attempts to explain the decreased patency rates of axillobifemoral grafting, compared to aortobifemoral bypass grafting, have centered on the use of bilateral versus unilateral grafts, the type of prosthetic material and the possible effects of the extraanatomic subcutaneous location of the grafts. Two large series confirmed the increasing opinion that an axillobifemoral configuration results in a better patency rate than the axillounifemoral graft (8,21). However, Ascer et al (27) found in a non randomized study no significant difference

between axillounifemoral grafting and axillobifemoral grafting. Similarly no clear differences in patency have been demonstrated for different materials of unsupported prosthetic axillobifemoral bypass grafts (12,26). In an effort to prevent graft compression Schultz et al (28) introduced externally supported axillobifemoral Dacron prostheses in 1978, and reported a 5 years primary patency rate of 75 %. These results were notable superior to the previously achieved by others for axillobifemoral grafting. In 1990 Harris et al (29) showed a 5 years patency of 85 % utilizing externally supported PTFE.
It is apparent that the majority of grafts fail within the first year after operation (29,30). Therefore 2 year patencies do reflect the performance of an axillobifemoral graft adequately. Moore et al (25) reported his experience of 52 Dacron axillobifemoral grafts with a primary patency rate of 45 % at 2 years. Donaldson et al (26) reported a primary patency rate at 2 years of 58 %.
The performance of a graft that is inserted to function indefinitely, is reflected by all occlusive events. Therefore the life table analysis for all occlusive events, which are the ipsilateral and contralateral occlusions with the total occlusions (Fig. 6), was used to be compared with the data reported in other series.
This series showed a 2 year primary patency of 38 % in the 90° group and 84% in the flowsplitter group. This difference in patency supports our opinion that the graft bifurcation configuration has a major influence on graft patency. In view of the previously performed in-vitro and in-vivo studies (5,6) it can be imagined that the flow disturbances that occur at the bifurcation site are responsible for the impaired patency rate of the 90° bifurcated axillobifemoral bypass graft. Doppler ultrasound studies before and after axillobifemoral bypass grafting revealed a statistically significant mean increase in ankle-brachial pressure index of 30 % for all patients. However no significant difference in ankle-brachial pressure index changes could be identified between the two groups or between the ipsilateral and contralateral sides, a finding that confirms the laboratory studies (5,6). An explanation for the different performances might be that flow disturbances, like flow separation or turbulence, occur due to the bifurcation configuration. These flow disturbances may reflect hypercoagulable areas inducing thrombus formation and eventually occlusion.

5.7 Conclusion

Our newly designed axillobifemoral bypass graft with a symmetrical bifurcation and a flowsplitter showed a highly significant ($P<0,0001$) better patency rate of 84% after two years compared to the patency rate of the 90° angled axillobifemoral prosthesis of 38 %, confirming the clinical relevance of bifurcation geometry.
We therefore recommend the use of an axillobifemoral bypass with symmetrical bifurcation and a flowsplitter, when axillobifemoral grafting is indicated.

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CHAPTER 6

SUMMARY AND CONCLUSIONS

6.1 Summary and conclusions

The axillofemoral bypass operation is an example of an extra-anatomic vascular reconstruction of bloodflow to the lower extremities. The operation was first introduced by Blaisdell in 1963 as an alternative route for an aortofemoral bypass in a patient with an unacceptably high operative (cardiac) risk. Since that first operation the technique has become widely accepted as an alternative for aortofemoral grafting in poor risk patients and also in patients with an infected abdominal aortic graft. The indications, patency rate, and the factors influencing patency rate are reviewed and discussed together with the mortality rate and complications in **chapter 1**.

In 1987 the authors' clinical experience with this type of graft in 17 patients was evaluated and published. The configuration of the axillobifemoral graft used in all these patients consisted of a straight tube running from the axillary artery to the ipsilateral femoral artery, with a cross-over branch to the contralateral femoral artery connected to the main stem at an angle of 90°. Noninvasive continuous wave Doppler investigations and duplex studies found an asymmetric blood flow distribution over the two distal branches in favour of the ipsilateral side. This finding was in contrast with other reports in literature published up till then. In addition to this observation, duplex studies showed turbulence at the bifurcation site of the graft, a phenomenon which might theoretically influence the patency rate of such grafts. From these observations it was concluded that the configuration of the bifurcation could be responsible for the asymmetrical flow distribution over the two distal branches, in favour of the ipsilateral branch. These findings are discussed in **chapter 2**.

The clinical observation of an asymmetric bloodflow in conventionally used graft configurations lead to the concept of a new design for an axillobifemoral prosthetic graft with a symmetrical bifurcation and a flowsplitter in order to achieve a symmetrical blood flow distribution over the two distal branches without causing turbulence. This new graft configuration was tested in an in-vitro study in the laboratory, comparing this graft with three currently used configurations of axillobifemoral prostheses with contralateral branches at angles of 30°,90° and 150°. Based on the linear relationship between flow and pressure, a model was created in which flow distribution was analysed by measurement of pressure distributions in four different axillobifemoral bypass configurations under pulsatile flow conditions using a Newtonian fluid. At the bifurcation site of currently used axillobifemoral prostheses a pressure drop across the bifurcation was measured, and found to be generally higher in the contralateral distal branch. The pressure drop increased significantly with increasing flow rate and also with increasing angle between the distal branches. Within the physiological range of flow rates a pressure drop as high as 30 mmHg was observed. No pressure drop was measured in the experimental axillobifemoral prosthesis with a symmetrical bifurcation and flowsplitter, neither with changing flow rates nor with varying angles between the distal branches. From this experiment it was concluded that a symmetrical bifurcation, obtained with the use of a flowsplitter, had a haemodynamically more favourable configuration compared to other bifurcation configurations. These in-vitro experiments are described in **chapter 3.**

To evaluate the favourable in-vitro haemodynamical properties of the new axillobifemoral prosthesis under more physiological conditions an in-vivo study using pigs was conducted. Whereas the in-vitro study was performed with a sinusoidal flow of a Newtonian fluid, the in-vivo study was performed under physiological pulsatile flow conditions, using a non-Newtonian fluid, namely blood. These changed conditions have a different impact on flow profiles and flow disturbances. Two different configurations of axillobifemoral bypass grafts were analysed. These two grafts differed only in configuration of the bifurcation: one with a contralateral branch at an angle of 90° and one with a symmetrical bifurcation and flowsplitter. All pressure drops, measured across the bifurcation ipsilaterally and contralaterally of the 90° angled bifurcation were significantly greater as compared to the pressure drops found in the flowsplitter prostheses which were so small that they were considered to be negligible. The pressure drops in the 90° angled grafts increased significantly with increasing flow rate. The in-vivo results were completely in line with and confirmed the in-vitro results. The results of this in-vivo study are described in **chapter 4.**

After obtaining experimental proof that the newly designed axillobifemoral prosthesis with a flowsplitter had highly significant better haemodynamical properties as a result of the geometry of the bifurcation, a clinical trial was conducted in order to evaluate the clinical relevance of these findings. An international multicenter clinical trial was performed in a prospective randomized fashion. The patency rates were analysed of two different axillo-bifemoral bypass grafts, differing only in configuration of the bifurcation: one with a contralateral branch at an angle of 90° and one with a symmetrical bifurcation and a flowsplitter. In 19 centers 117 patients were randomized, 59 receiving a prosthesis with a flowsplitter and 58 a prosthesis with a 90° bifurcation. Indications for operation and risk factors were equally distributed in both groups. Statistical analysis after 3 years with a mean follow up of 12 months (range 3-36 months) showed that the prosthesis with a symmetrical bifurcation and a flowsplitter had a significantly better patency rate of 84 % after 2 years compared to a patency rate of 38 % of the prosthesis with a 90° angled bifurcation (P < 0,0001; Log-Rank test). The data were not influenced by indication for operation, associated risk factors (e.g. diabetes mellitus, hypertension or myocardial infarction), outflow tract or mode of anticoagulant therapy. Other endpoints like death and graft infection did not differ significantly between the two groups. This study is described in **chapter 5.**

It is concluded that the new axillobifemoral bypass graft with a flowsplitter showed an impressively better patency rate after two years when compared to the 90° angled axillobifemoral prosthesis. This study confirms that the geometry of the bifurcation of an axillobifemoral bypass graft is of clinical importance and consequently this finding has important clinical implications: The use of a symmetrically bifurcated axillobifemoral prosthesis with a flowsplitter is recommended for patients who need an extra-anatomical reconstruction of blood flow to the lower extremities.

6.2 Samenvatting en conclusies

De axillofemorale bypass operatie is een voorbeeld van een extra-anatomische reconstructie van de bloedstroom naar de benen. De operatie werd geintroduceerd in 1963 door Blaisdell als een alternatieve route voor een aortofemorale bypass bij een patient met een onacceptabel hoog (cardiaal) risico. Sindsdien is deze operatie techniek algemeen geaccepteerd als een alternatief voor een aortofemorale bypass bij patienten met een hoog operatie risico en ook bij patienten met een geinfecteerde abdominale aorta prothese. De indicaties, patency rates en de factoren die de patency beinvloeden worden besproken samen met de mortaliteit en de complicaties in **hoofdstuk 1**.

In 1987 werd door de auteur van dit proefschrift de klinische ervaring met dit type prothese bij 17 patienten geevalueerd en gepubliceerd. De axillobifemorale prothese die gebruikt werd in al deze patienten bestond uit een rechte pijp lopende vanaf de arteria axillaris naar de ipsilaterale arteria femoralis, met een cross-over poot naar de contralaterale arteria femoralis. De afgang van de cross-over poot maakte een hoek van 90° met de aanvoerende tak van de prothese. Non-invasieve continuous wave Doppler en duplex onderzoeken toonden een asymmetrische verdeling van bloedstroom over de twee distale poten van de prothese ten nadele van de contralaterale poot. Deze bevinding was in tegenstelling tot reeds gepubliceerde data. Bovendien werd middels duplex onderzoek turbulentie aangetoond ter hoogte van de bifurcatie van de prothese, een fenomeen dat op theoretische gronden de patency van dit soort prothesen negatief kan beinvloeden. Uit deze observaties werd geconcludeerd dat de vorm van de bifurcatie waarschijnlijk verantwoordlijk was voor de asymmetrische flow distributie over de twee distale poten, ten nadele van de contralaterale poot. Deze bevindingen worden besproken in **hoofdstuk 2**.

De klinische observatie, dat er sprake was van een asymmetrische bloedstroom, bij de conventionele prothese configuratie heeft ertoe geleid dat een nieuwe axillobifemorale prothese met een symmetrische bifurcatie en een flowsplitter werd ontwikkeld ten einde een symmetrische flow verdeling naar beide distale poten te bewerkstelligen zonder turbulentie te veroorzaken. Deze nieuwe prothese werd vervolgens in-vitro in het laboratorium getest samen met drie andere typen axillobifemorale prothesen met asymmetrische bifurcatie configuraties met distale contralaterale poten afgaande onder hoeken van 30°, 90° en 150° ten opzichte van de ipsilaterale poot. Ervan uitgaande dat er een lineair verband is tussen flow en druk werd er een model gecreëerd waarin de flowdistributie werd geanalyseerd middels drukmetingen op verschillende plaatsen in deze vier verschillende axillobifemorale prothesen, onder pulsatiele flow condities met een vloeistof die de wetten van Newton volgt. Over de bifurcatie van de conventionele axillobifemorale prothesen werd een drukverval gemeten. Dit drukverval was over het algemeen hoger aan de contralaterale zijde. Het drukverval liep significant op bij toename van de flow en ook als de hoek tussen de distale takken toenam. Binnen de grenzen van fysiologische flow werd maximaal een drukverval van 30 mmHg gemeten. De experimentele axillobifemorale prothese met een symmetrische bifurcatie en flowsplitter veroorzaakte geen drukdaling, noch bij een wisselende hoek tussen de distale poten noch bij een wisselende flow. Uit deze studie werd geconcludeerd dat een symmetrische bifurcatie, verkregen door het gebruik van een flowsplitter, een betere heamodynamische configuratie heeft dan de andere bifurcaties. Deze in-vitro experimenten staan beschreven in **hoofdstuk 3**.

Ten einde deze superieure in-vitro haemodynamische eigenschappen van de experimentele prothese onder meer fysiologische omstandigheden te onderzoeken werd een in-vivo onderzoek op varkens gestart. In tegenstelling tot de in-vitro studie, die gebruik maakte van een sinusoidale flow en een zg. Newtonse vloeistof, werd in de in-vivo studie gebruik gemaakt van een fysiologische pulsatiele flow met een vloeistof die niet aan de wetten van Newton voldoet, namelijk bloed. Beide aspecten hebben een andere invloed op flow profielen en stoornissen daarin. Twee verschillende axillobifemorale prothesen werden geanalyseerd. Alleen de vorm van de bifurcatie was bij deze prothesen verschillend: één had een contralaterale distale poot afgaande onder een hoek van 90°, terwijl de andere prothese een symmetrische bifurcatie had met een flowsplitter. Alle drukdalingen over de bifurcatie van de 90°-bifurcatie prothese waren significant groter dan de drukvervallen over de flowsplitter-bifurcatie prothese. Deze laatsten waren zo klein dat zij als verwaarloosbaar beschouwd kunnen worden. De drukvervallen over de 90° prothesen namen significant toe bij een toegenomen flow. Deze in-vivo resultaten waren volledig in overeenstemming met en bevestigden de in-vitro resultaten. De resultaten van deze in-vivo studie worden beschreven in **hoofdstuk 4**.

Na op deze wijze in twee experimentele studies bewezen te hebben dat de nieuw ontwikkelde axillobifemorale prothese met een symmetrische bifurcatie en een flowsplitter veel betere haemodynamische eigenschappen heeft ten gevolge van de geometrie van de bifurcatie, werd een klinische trial gestart ten einde de klinische relevantie van deze bevindingen te onderzoeken. Een internationale prospectief gerandomizeerde multicenter studie werd verricht. De patency rates van twee axillobifemorale prothesen met een verschillende bifurcatie configuratie, namelijk één met een contralaterale distale poot onder een hoek van 90° en één met een symmetrische bifurcatie en een flowsplitter, werden in deze trial met elkaar vergeleken. In 19 centra werden 117 patienten gerandomizeerd, waardoor 59 patienten een prothese met een flowsplitter kregen en 58 patienten een prothese met een 90° hoek. De indicaties voor de operatie en de risicofactoren waren gelijk verdeeld over beide groepen. De statistische analyse na 3 jaar, met een gemiddelde follow up van 12 maanden (3-36 maanden), liet een significant beter doorgankelijkheids percentage na 2 jaar zien van 84 % voor de prothese met een flowsplitter in vergelijking met een doorgankelijkheids percentage van 38 % na 2 jaar voor de prothese met een 90° bifurcatie ($P < 0{,}0001$; Log-Rank test). Deze uitslag werd niet beinvloed door de indicatie voor de operatie, risico factoren (b.v. diabetes mellitus, hypertensie of myocard infarct), outflow traject of het anticoagulantia regime. Een aantal andere studie eindpunten zoals overlijden en prothese infectie was niet significant verschillend tussen de twee groepen. Deze studie wordt beschreven in **hoofdstuk 5**.

Tenslotte kan geconcludeerd worden dat de nieuwe axillobifemorale prothese met een flowsplitter een imposant hogere patency rate heeft na twee jaar in vergelijking met de axillobifemorale prothese met een contralaterale distale poot onder een hoek van 90°. Deze studie bevestigt het klinische belang van de bifurcatie geometrie in een axillobifemorale prothese. Dit heeft dan ook een belangrijke klinische consequentie, namelijk dat bij patienten waarbij een extra-anatomische revascularisatie naar de benen geindiceerd is het gebruik van een axillobifemorale prothese met een symmetrische bifurcatie en een flowsplitter sterk aanbevolen wordt.

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