PRE AND PER-OPERATIVE ASSESSMENT OF FEMORO-DISTAL NON-REVERSED VEIN GRAFTS.

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A thesis submitted to the University of Leicester for the degree of Doctor of Medicine

VASCULAR STUDIES UNIT

BRISTOL ROYAL INFIRMARY

AUGUST 1990

PREFACE

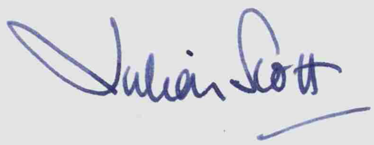
Dedicated to my parents for their continued support during my surgical career.

I would like to thank all the staff of the Vascular Studies Unit and especially my supervisor, Mr Michael Horrocks and his wife Liz Horrocks for their enthusiastic support and guidance. My thanks to Dr Robert Skidmore of the Medical Physics Department for his invaluable technical advice and support. I am also indebted to Mr Gary James of the Medical Illustration Department for his outstanding illustrations.

The work described in this thesis was performed in the Vascular Studies Unit at the Bristol Royal Infirmary whilst I was Tutor in Surgery and Honorary Surgical Registrar. The work was entirely my own except for the parts described below which were conducted with the assistance of the following:

Long saphenous vein histology
(Prof JWB Bradfield, Dr C Milroy and Mr PF Heap)

Statistical Analysis
(Mr JI Gowers)



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ABBREVIATIONS

ABI	Ankle/Brachial Index
ADP	Adenosine diphosphate
AKA	Above Knee Amputation
APTT	Activated partial thromboplastin time
ARCH	Pedal arch
Art	Arteriogram score
AT	Anterior tibial artery
AVF	Arteriovenous fistula
BKA	Below Knee Amputation
BL	Basal lamina
CA	Conventional arteriography
CFA	Common femoral artery
CI	Confidence interval
CI UL	Confidence interval for upper limit of agreement
CI LL	Confidence interval for lower limit of agreement
cm	centimetres
CMF	Circular muscle fibrosis
CMH	Circular muscle hypertrophy
COL	Collagen
d	Cuff diameter
dAVF	Distal arteriovenous fistula
DIH	Diffuse intimal hyperplasia
DP	Distal Popliteal artery

ABBREVIATIONS (continued)

DP	Dorsalis pedis artery
DSA	Digital subtraction arteriography
EL	Elastin
EM	Electromagnetic flowmeter
END	Endothelium
F	Frequency or french gauge
FBC	Full blood count
FI	Fibres
FIH	Focal Intimal Hyperplasia
FM	Filamentous material
G	Gauge
GF_1	Graft flow at rest
GF_2	Graft flow after the administration of papaverine hydrochloride
GR_1	Graft peripheral resistance at rest
GR_2	Graft peripheral resistance after the administration of papaverine hydrochloride
HDL	High density lipoprotein
Hg	Mercury
Hz	Hertz

ABBREVIATIONS (continued)

ID	Internal diameter
IA DSA	Intra-arterial digital subtraction arteriography
IH	Intimal hyperplasia
ISCVS	International society for cardiovascular surgery
KHz	Kilohertz
LI	Lipid droplet
LMF	Longitudinal muscle hypertrophy
LMH	Longitudinal muscle fibrosis
LS	Luminal stenosis
LSV	Long saphenous vein
MHz	Megahertz
min	Minute
Min Diam	Minimum diameter
ml	Milliliter
MLR	Multiple linear regression
mm	Millimeter
MPR	Measured peripheral resistance
MRP	Manufactures recommended pressure
Mv	Microvilli
No	Number
Nu	Nucleus
P	Pressure

ABBREVIATIONS (continued)

P_1	Mean systemic arterial pressure
P_2	Mean common femoral artery pressure
PDGF	Platelet derived growth factor
PER	Peroneal artery
PGR	Pulse Generated Runoff
PGR/ARCH	Combined PGR and ARCH score
Pop	Popliteal
POA	Per-operative arteriogram
PPR	Predicted peripheral resistance
PR	Peripheral resistance
Prox Res	Proximal (Inflow) resistance
PRU	Peripheral resistance unit
PT	Posterior tibial artery
PT	Prothrombin time
PTFE	Polytetrafluoroethylene
PVD	Peripheral vascular disease
PVR	Pulse Volume Recorder
Q	Flow
Q_1	Total graft flow
Q_2	Distal graft flow
r	Pearson's correlation
rs	Spearman's rank correlation coefficient

ABBREVIATIONS (continued).

R0	Predicted resistance irrespective of the level
R1	Predicted resistance at a single calf vessel
R2	Predicted resistance at the tibioperoneal artery
R3	Predicted resistance at the distal popliteal artery
R_c	Catheter resistance
R_T	Total peripheral resistance
RF	Retrograde flow
RPRO	Predicted resistance in a prospective series of grafts using the established equations R1 and R3.
RSV	Reversed saphenous vein
sec	seconds
SCV	Single calf vessel
SD	Standard deviation
SEM	Scanning electron microscopy
sem	standard error of the mean
SFA	Superficial femoral artery
SF-P	Superficial femoral-popliteal veins
SLP	Segmental limb pressures
SMC	Smooth muscle cell
SSV	Short saphenous vein
SVS	Society for vascular surgery

ABBREVIATIONS (continued).

TcPO2	Transcutaneous oxygen tension
TEM	Transmission electron microscopy
TPT	Tibioperoneal trunk

PRE AND PER-OPERATIVE ASSESSMENT OF FEMORO-DISTAL VEIN NON-REVERSED VEIN GRAFTS.

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ABSTRACT

The expected increase in the elderly population over the next decade or so will result in an increase in the number of patients presenting with lower limb critical ischaemia. The use of non-reversed vein grafting and more distal bypasses has increased the scope for possible limb salvage and improved the quality of life, but case selection has become more difficult.

In order to improve patient selection calf vessel runoff and long saphenous vein suitability were assessed pre and per-operatively to try and prevent unnecessary reconstructions. In total 88 patients were studied. Conventional arteriography in combination with IA-DSA views of the distal runoff were performed in all cases. Three arteriographic scoring systems were used to grade the runoff. Pulse Generated Runoff (PGR) was used to assess calf vessel and pedal arch patency. Duplex ultrasound was used to assess the long saphenous vein before bypass.
At operation peripheral resistance and flow were measured before and after reconstruction. Samples of the LSV were taken before and after valve stripping for both light and electron microscopy.

Intra-arterial DSA improved the correlation between the scoring systems and the measured peripheral resistance in the distal popliteal artery, but not in single calf vessels. In contrast PGR correlated much better with peripheral resistance in single calf vessels (r_S = -0.82, $p<0.001$). Using multiple linear regression analysis, a non-invasive resistance value was determined which could accurately predict the measured peripheral resistance at the time of surgery. PGR assessment of the pedal arch confirmed that grafts to an absent pedal arch all failed and underwent amputation at six months. Duplex scanning of the long saphenous vein is an accurate method of determining the suitability for reconstruction and has helped to reduce the incidence of skin flap necrosis. The criteria for a successful graft were applied to a prospective series of 49 grafts with a sensitivity of 97%, specificity of 67% and a predictive value of the test of 90%. Both light and electron microscopy of the excised LSV revealed evidence of early neointimal hyperplasia before implantation and highlighted the damage caused by the passage of the Hall valvulotome. Long term follow up confirmed the value of PGR and graft resistance after papaverine (GR2) in predicting successful grafts. Grafts with a PGR score of > 2 had 1 and 2 year patency rates of 79% and 64% respectively which were significantly higher than grafts with a PGR score of < 2 of 14% (Lee-Desu $p<0.002$). Grafts with resistances (GR2) of < 1 and > 1 after the administration of papaverine had patency rates of 85% and 14% at one year.

PGR will identify patent calf vessel and confirm continuity with the pedal arch. Duplex assessment of the LSV will accurately identify suitable LSV for bypass. Per-operative haemodynamic monitoring will confirm the pre-operative assessment, define the level of the distal anastomosis and exclude the majority of technical errors. Morphological examination of the LSV has shown it to be a potential cause of graft failure and revealed evidence of early atherosclerosis previously thought to develop as a consequence of arterialization.
This approach will hopefully improve the selection of patients for femoro-distal bypass and ensure that patients are not rejected on the basis of the arteriogram.

CHAPTER 1

HISTORICAL REVIEW OF FEMORO-DISTAL BYPASS SURGERY.

Vascular surgery has its origins as far back as the third century when Antyllus, a Roman Surgeon described proximal and distal ligation of an aneurysmal artery using a double ligature of flax or gut, followed by incision and removal of the aneurysmal contents (Halstead 1921). Aetius in the sixth century described ligation of the brachial artery proximal to an aneurysm at the elbow followed by incision of the sac (Halstead 1921). This operation was later attributed to Guillemeau and Dominique Anel (1710) who performed a proximal ligation of a false aneurysm secondary to blood letting. By contrast, John Hunter in 1786 chose a more remote site for proximal ligation of an atherosclerotic popliteal aneurysm, which had the advantage of preserving the collateral supply (Home 1786). Ligation was to remain the principle mode of treatment in patients with arterial disease until Hallowell in 1759 reported the first successful repair of a brachial artery laceration. At the suggestion of Richard Lambert he placed a short steel pin through the edges of the wound and wrapped a suture around it, approximating the edges with apparent success. He later wrote to William Hunter in 1761 and suggested that if this was a successful treatment it "might be able to cure wounds of some arteries that would otherwise require amputation or be altogether incurable". Eight years later Asman (1773) repeated the same technique in a series of experiments without success. He concluded that such a procedure would not work and arterial repair did not reappear in the surgical literature for a hundred years.

A similar scenario of missed appreciation occurred following the work of John Abernethy in 1796, a pupil of John Hunter. He established the superiority of complete division of arteries over simple ligature in the treatment of aneurysm. Guthrie, Mott and Halstead all failed to grasp the significance of the work and persisted with the technique of ligature. It was not until 1942 when Emile Holman confirmed the superiority of complete division over ligature of a large artery.

Nikolai Eck, a Russian military surgeon, performed the first vascular anastomosis (porto-caval) in 1877 in a series of animal experiments to determine the value of fistulae in the treatment of ascites (Child 1953). Czerny in 1881 is credited with the first lateral suture repair of a large venous defect during an oesphagotomy for a foreign body, but the patient died from a secondary haemorrhage. Schede (1883) is cited with the first successful repair of a common femoral vein defect.

Jassinowsky (1891) in a series of animal experiments first reported the use of fine silk sutures avoiding the intima to repair an arterial injury. He concluded that complete division of either large or small vessels be dealt with by ligation and in the case of partial division, direct repair avoiding the intimal layer be attempted. Similar results were reported by Julius Dörfler in a series of 20 arterial repairs in 1899. He used two different methods of repair, (i) interrupted or running suture approximating the intimal surfaces and (ii) a continuous suture which included the adventitia and muscle but not the intima. Post-mortem examination of the full-thickness silk suture repair failed to reveal any evidence of inflammation or thrombosis. He concluded that both techniques were equally efficacious. The first successful end to end carotid arterial anastomosis using an everting U shaped suture was reported by Jaboulay and Briau in 1896.

Following the assassination of Sadi Carnot, the president of France, Carrel was highly critical of the management of the portal vein injury. He believed that blood vessels could be sutured as well as any other tissue. In 1902 Alexis Carrel published his article on " La Technique Opératoire des Anastomoses Vasculaires et la Transplantation des Viscères", which was a refinement of the previously described suture techniques. He highlighted the importance of gentle handling of the tissues, temporary haemostasis, peeling the adventitia off the site of the anastomosis, avoidance of dehydration, 3 stay sutures, fine suture materials and approximation of the intimal surfaces in an everting full thickness suture, the majority of which forms the basis of modern day vascular surgical techniques.

Goyannes in 1906 reported the first venous (popliteal vein) interposition bypass following excision of a popliteal anuerysm. During a visit to the Johns Hopkins Hospital, Carrel described his work on arteriovenous anastomosis to William Halstead. Later in 1907, Halstead faced with a patient with an absent popliteal artery and vein following an en bloc dissection for a popliteal space sarcoma, reversed the contralateral saphenous vein and performed a bypass from the common femoral artery to the popliteal vein, although the graft initially worked it soon thrombosed. This was followed by a series of reports confirming the value of venous interposition grafts in the treatment of aneurysms (Lexer 1907, Jeger 1913 and Pringle 1913). Inexplicably the technique of venous interposition was forgotten during the War years.

In 1913 Leriche reported the beneficial effects of a peri-arterial sympathectomy in the treatment of post traumatic neuralgias. Later, Leriche utilised the technique in patients with recently thrombosed arterial segments. In the majority of patients they developed warm feet and he concluded that the coldness of the limb was due to vasospasm rather than insufficient blood flow. Dissatisfied with the technique of peri-arterial sympathectomy, Diez performed the first lumbar sympathectomy in 1924, although it was to be later popularised by Leriche and Fontaine in 1933.

The technique of thrombectomy had been advocated as far back as 1880 by Severanu, but was universally unsuccessful because of rapid arterial re-thrombosis. Labey in 1911 performed the first successful embolectomy (Mosney and Dumont 1911), but it was not until the introduction of heparin and courmarin that thromboembolectomy gained clinical acceptance. In 1947 Jean Cid Dos Santos reported the first successful thrombectomy under heparin cover. As a result of sympathectomy and thrombectomy, European vascular surgery diverged away from the known concepts of grafting until the late 1940's.

Despite the reports of Lexer (1907) and Pringle (1913), interposition vein grafts were rarely used in acute vascular trauma in either World War. Arterial ligation formed the basis of treatment and invariably resulted in gangrene and loss of limb (Makins 1919). Arterial suture, although described well before the World War I, was rarely used because of the fears about sepsis and secondary haemorrhage. With the practice of extensive debridement and antibiotic therapy in World War II, end to end arterial anastomoses were occasionally undertaken. This is reflected in the report by DeBakey and Simeone in 1946 who recorded only 81 cases of arterial suture in a series of 2,471 cases of acute arterial trauma in World War II. Sutured vein grafts were not used in acute arterial occlusions but were successfully employed in the repair of traumatic aneurysms. In contrast non-sutured vein grafts were successfully used to restore arterial continuity in trauma cases.

Payr first described the technique of non-sutured anastomosis in 1900 and was later tested experimentally by Höpfner in 1903 and applied clinically by Lexer in 1907. Blakemore, Lord and Stefko in 1942 used vitallium tubes lined with autogenous vein to restore arterial continuity. The cut ends of the artery were tied over the ends of the connecting cannula. This technique was later modified by two tubes bridged by a vein graft. Further modifications included the use of glass tubes (Matheson and Murray 1941) and plastic tubes which had the advantage of being well tolerated by the tissues and could be altered in shape and size by placing in warm water.

Curiously the concept of venous bypass in femoro-popliteal occlusive disease was not to take place until 1947, by which time there had been notably advances in the understanding of anticoagulation (Howell and Holt 1918, Murray 1940), blood transfusion (Landsteiner 1901, Ottenburg 1911, Hustin 1914), and arteriography (Brooks 1924, Dos Santos, Lanas and Pereigi 1929, Farinas 1941, Seldinger 1953).

On the 3rd June 1947 Jean Kunlin performed the first femoro-popliteal venous bypass for critical ischaemia. Because of severe fibrosis following an endarterectomy, he was unable to perform the standard end to end anastomosis. In the same paper, he reported 10 further bypass grafts with two early failures. Despite these results, Kunlin concluded that in view of their state of knowledge, it would seem imprudent to perform a venous bypass in the first instance, and that a sympathectomy was the primary treatment option. Following Kunlin's paper, numerous reports appeared in the literature confirming the superiority of the autogenous saphenous vein graft to prosthetic grafts (Lord and Stone 1957, Dale, DeWeese and Scott 1959).

The onset of the Korean War in June 1950 led to a rapid increase in the knowledge of traumatic vascular injuries. Hughes (1958) reported 79 vascular injuries of which 47 were at or below the common femoral artery, but only 11 were repaired with autogenous vein grafts. Similar experiences were reported by Jahnke and Howard (1953) and Spencer and Grewe (1955). These techniques were later applied in the Vietnam War during which there had been a dramatic increase in the number of arterial repairs using reversed saphenous vein (Rich and Hughes 1969 & Whelan, Burkholder and Gomez 1968). Rich and Hughes reported that of 217 lower limb arterial injuries 73 were repaired with autogenous vein, some using prosthetic suture material rather than 5/0 braided silk.

In 1959 Professor Rob and Mr Kenyon performed the first in situ vein graft. The valves were rendered incompetent by passing the blunt end of an internal valve stripper in an antegrade fashion through the vein ("valve fracture") and the venous branches ligated. Unfortunately the graft failed, as did three further attempts, and Rob abandon the technique. Despite the early failure of the valve fracture technique, Connolly & Stemmer (1972) persisted with the valve fracture technique using a smooth-nosed internal valve stripper. In a series of 306 in-situ vein grafts they reported a 78% graft patency rate at two years. Histological examination of the vein post-stripping revealed that the valve cusps had fractured at the base and were directed distally against the vein wall (Connolly and Harris 1965). These changes were similar to those observed following valve incision (McCaughan, Walsh, Edgcomb et al 1984).

In 1962 Hall described a series of six cases where the valves were excised through transverse venotomies. This proved to be an effective method of valve disruption and enabled the vein to be left in situ. There were, however several disadvantages; (i) repeated trauma to the endothelial surface and vein wall, and (ii) technical problems associated with closure of the transverse venotomies.

The problem of multiple transverse venotomies was overcome by Skagseth and Hall (1973) who developed a new method of valve disruption similar to that reported by Samuels, Plested, Haberfelde et al (1968). This consisted of a series of graded valvulotomes (2-6mm) which were introduced into the distal end of the long saphenous vein after the saphenofemoral junction had been transected. The valvulotomes were designed to pass easily through the valves but on withdrawal the cutting edge would engage and destroy the competent valve leaflet. This procedure could be repeated with rotation of the valvulotome to ensure that all of the valves were destroyed. Although much simpler than valve excision, the valvulotome method still resulted in some endothelial trauma.

Barner et al (1969) in a non-randomised clinical study of 25 in situ and 25 reversed vein femoro-popliteal grafts concluded that the high late failure rate of 63% in the in situ group was unacceptable. A 3mm smooth olive head valve stripper was used to render the valves incompetent. Barner attributed the high failure rate to platelet deposition and neointimal hyperplasia at the site of the valves.

Despite this report Hall and Rostad (1978) persisted with the valve fracture technique in a consecutive series of 252 femoro-popliteal vein grafts between 1961 and 1968. They reported a graft patency rate in surviving patients of over 80% at 5 years.

Inspired by these results Leather, Powers and Karmody (1979) modified the in situ vein technique. Doppler ultrasound was used to map out the course of the long saphenous vein prior to surgery. At the time of surgery the proximal LSV was mobilised and disconnected with a cuff of femoral vein. The proximal valve was excised under direct vision. The remaining valves were identified by gentle distension of the LSV by a solution of Dextran 70 containing 2,500 units of heparin per 500 mls. In contrast to the previous techniques of valve fracture, specially designed microvascular scissors were introduced through small venous tributaries. With the valve leaflets in the functionally closed position the scissor would incise the valves along their major axis. This procedure was repeated until a satisfactory distal flow had been established. Arterio-venous fistula were clipped in continuity. Completion arteriography, intra-operative Doppler and pulse volume recordings completed the graft assessment. Eighty two consecutive in situ vein grafts were performed for critical ischaemia, the 1 and 2 year graft patency rates were 91% and 91% respectively. Of the 38 femoro-tibial grafts similar graft patency rates were obtained. Leather attributed these much improved results to the avoidance of endothelial trauma but failed to substantiate the claim with any real scientific evidence. Leather's comparison between the current in situ vein series and the two historic control series of reversed vein grafts (Naji et al 1975, Reichle & Tyson 1975) remains controversial.

Numerous advances had occurred within the previous decade that could have accounted for the improved patency rates. These included better suture material, improved instrumentation, illumination, magnifying loupes, completion arteriography and antiplatelet therapy.

Connolly and Kwaan (1982) in a non-randomised concurrent series of 300 reversed and 300 in situ vein grafts reported no difference in the 10 year graft patency rates of 43% and 41% respectively. Taylor et al (1987) in a series of 110 infra-popliteal reversed vein grafts reported 1 and 2 year graft patency rates of 90% and 85% respectively, which are comparable to recently reported in situ vein series. In addition they highlighted the use of arm veins, short saphenous vein and vein segment splicing techniques, all of which have resulted in an improved vein utilisation rate of 94%. In particular they emphasised the value of the reversed vein technique over the in situ vein in the 23% of patients with an absent ipsilateral LSV. Harris et al (1987) in the only randomised study of in situ versus reversed vein grafts failed to demonstrate any significant difference in graft patency between the two groups. There was no difference in the incidence of late fibrous stricture formation, but the in situ vein grafts appeared more compliant than the reversed vein grafts.

Several theoretical advantages have been proposed to explain the improved results with the in situ vein technique including preservation of endothelial cells and the vaso vasorum and improved haemodynamics. Beard and Fairgreave 1986 were unable to demonstrate any significant difference in compliance between fully mobilised and undisturbed in situ vein grafts. Histological examination of the vein grafts failed to support the concept that preservation of the vaso vasorum resulted in less neointimal hyperplasia. These findings were substantiated by Cambria, Megerman, Brewster et al (1987) who used a phase locked ultrasound device to measure vessel wall compliance. In the same paper Cambria reported no significant difference in the absolute intimal thickness nor in the percentage of the total wall thickness occupied by the intima in a animal series of reversed and in situ vein grafts. Boyd et al in 1987 using an animal model reported no significant difference in the light microscopy or ultrastructure of in situ versus reversed veins. Fibrinolytic activity as measured by fibrin plate and slide assays were not significantly different between the two groups of grafts. Beard et al 1986 were unable to show any significant difference in either resting or hyperaemic flow between reversed and in situ vein grafts. Gannon et al 1986 reported no significant improvement in the flow pattern of in situ vein grafts.

The results of both experimental and clinical studies on reversed versus in-situ vein grafts have failed to substantiate the original claims by Karmody, Leathers and Powers. However, with the development of the in-situ technique, there has been an increased willingness on the part of vascular surgeons to perform more distal vein grafts in an attempt to salvage more limbs. In those cases where the long saphenous vein is absent or inadequate, the reversed vein technique using vein from the contralateral leg or arm offers a suitable alternative method of reconstruction and is better than a prosthetic graft, particularly in the below knee position.

Femoro-distal grafts.

Morris et al (1959) were the first to describe the anteromedial approach to the infrageniculate popliteal artery. A year later Palma reported 4 autogenous vein grafts to the posterior tibial artery and in 1961 McCaughan reported a series of grafts to the anterior tibial and peroneal arteries. Since then numerous reports have confirmed the value of femoro-distal grafting in limb salvage (Table 1.1). More recently Ascer et al (1988a) have performed bypass grafts to plantar and lateral tarsal arteries in the foot. Although the numbers and length of follow up are small the initial results are encouraging with 1 and 2 year patency rates of 74% and 67% respectively, (Table 1).

Table 1.

Cumulative Femoro-distal graft patency.

Author	Year	No	Type	Follow up	Graft patency
Bernhard	1972	41	LSV	1 year	63%
Nicholas	1973	44	LSV	1 year	70%
				5 years	61%
Imparato	1974	81	LSV	1 year	56%
				5 years	52%
Dardik	1975	32	LSV	1 year	57%
Edwards	1976	97	LSV	1 year	74%
Reichle	1979	164	LSV	1 year	57%
				5 years	54%
Kacoyanis	1981	105	LSV	1 year	56%
				5 years	46%
Veith	1981	204	LSV/ PTFE	1 year	64%
				5 years	47%
Corson	1984	83	LSV	1 year	85.2%
Sidaway	1986	78	LSV	1 year	71%
Shah	1988	294	LSV	1 year	89.7%
				5 years	76.4%

Short vein grafts

Traditionally the common femoral artery has been used as the origin of the proximal anastomosis. With the recent trend towards more distal grafts, Veith et al (1981) have utilised the superficial femoral and popliteal arteries as inflow sites for distal bypass grafts. This has several advantages including the avoidance of previously scarred and infected groins, shorter vein grafts and reduced operating time.

During a six year period Veith and his colleagues (1981) found no difference in the cumulative graft patency rates for those grafts originating from either the superficial femoral or popliteal arteries compared to a similar group originating from the common femoral artery (Table 2).

Table 2.

Cumulative short vein graft patency rates.

Type of bypass	No	Graft Patency rates
CFA-to-Pop	61	75%
SFA-to-Pop-to-Pop	27	75%
CFA-to-Distal	25	71%
SFA-to-Distal	34	60%
Pop-to-Distal	139	65%

Short vein grafts (SVG) (< 40cms) appeared to perform better than long vein grafts (LVG) (> 40cms), with 3 year graft patency rates of 45% and 63% respectively. In the absence of a pedal arch, SVG performed significantly better than LVG, with graft patency rates of 22% and 53% respectively (Ascer, Veith, Gupta et al 1988).

The obvious disadvantage of this technique is progression of proximal disease as a cause of graft thrombosis. In the Ascer series, conventional biplanar arteriography was used to exclude significant upstream disease. Stenoses of 20-40% were considered not haemodynamically significant and grafts were placed distal to these stenoses. However Flanigan, in response to Ascer's paper, reported that in their experience a stenosis of > 20% was a significant risk factor in graft thrombosis. Despite this, only 6% of the 71 failures in Ascer's series were attributed to proximal disease, a finding supported by Schuler, Flanigan, Williams et al in 1983.

Alternative sources of autogenous vein

Alternative sources of autogenous vein are often required in re-do femoro-popliteal grafts or where the long saphenous vein is absent or inadequate. Kakkar (1969) first described the use of arm veins as an arterial conduit. He reported that the cephalic vein averaged 54 cms in length and was usually 20% longer than the distance from groin to mid calf, sufficiently long for a femoro-popliteal bypass. Size appeared not to be a problem, the cephalic vein being capable of distension to approximately the size of the LSV. Subsequent reports (Clayson, Edwards, Allen et al 1976 and Whittemore, Clowes, Couch et al 1981) have confirmed the value of arm veins as an acceptable arterial conduit especially when the saphenous vein is inadequate or absent. Some workers, however, have expressed dissatisfaction. Rosenfeld et al (1981) reported an increased incidence of dilatation, aneurysmal change and inadequate length as the major drawbacks of the technique. Similar findings were reported by Schulman and Badrey in 1982, six of the seven patients who had late post-operative arteriograms were noted to have some degree of elongation or aneurysmal dilatation. Although the initial graft patency results were poor (Table 3), Harris et al (1984) in a series of 70 cephalic vein bypass grafts, (not all for critical ischaemia), reported 1 and 5 year graft patency rates of 85% and 68% respectively. The use of distal inflow sites, composite and sequential grafts may have helped account for these excellent results.

In order to preserve these veins, every effort should be made to re-educate medical and nursing staff as to the potential value of arm veins in limb salvage procedures. Previous venesection or intravenous cannulation may result in thrombosis of the forearm veins. Grigg and Wolfe (1988) have recently described a non-reversed (cephalic) proximal and reversed (basilic) vein graft which precludes the need for a veno-venous anastomosis.

Table 3.

Femoro-distal grafts using arms veins.

Author	Year	No of Pts	Graft Patency	Follow Up	Level of Anastomosis
Kakkar	1969	7	100%	4-12 mths	Fem-pop
Stipa	1972	10	90%	1 month	Fem-pop
			68%	6 months	Fem-tib
Bernhard	1972	10	84%	1 month	
			57%	3-57 mths	Fem-tib
Clayson	1976	18	63%	1 year	
Campbell	1979	33	88%	1 year	Fem-distal
Schulman	1982	41	90%	1 month	Fem-pop
			62%	1 year	
		16	81%	1 month	Fem-tib
			43%	1 year	
Harris	1984	31	85%	1 year	Fem-pop
			80%	4 years	
		39	85%	1 year	Infra-pop
			63%	3 years	

Other alternatives include the short saphenous vein which, because of its position, lack of visual clues to its size and patency, surgeons have been reluctant to use. Weaver et al in 1987 harvested both short saphenous veins to obtain adequate length for femoro-distal reconstructions. Of the fifty femoro-distal reconstructions 29 were entirely with the short saphenous vein. The 1 year patency rate being 72%.

Superficial femoral-popliteal veins (SF-P).

Schulman et al in 1981 reported the use of the deep veins of the leg as an alternative to either the long saphenous vein or prosthetic material in femoropopliteal reconstructions. Encouraged by the early results, Schulman randomised patients to either SF-P or reversed saphenous veins (RSV) for femoro-popliteal reconstruction, the majority of which were performed for critical ischaemia. The 3 year cumulative graft patency rate for SF-P and RSV grafts were 68% and 63% respectively. The 3 year cumulative limb salvage rates for SF-P and RSV grafts were 80% and 76% respectively. Although venous hypertension and ankle swelling are not reported to be a major problem, there has been little confirmatory data in the literature. As a result the technique has yet to gain acceptance amongst vascular surgeons.

Sequential Grafts

The concept of sequential grafting, as with that of arteriovenous fistulae, has been to maintain flow in grafts with compromised distal outflow tracts. The technique was first established by cardiac surgeons during coronary artery bypass grafting and was later reported by Edwards, Gerety, Larkin et al in 1976 in the peripheral circulation.

The addition of a second distal anastomosis often resulted in a 20-75 % increase in flow. Third distal anastomoses were rarely beneficial and were later abandoned. Similar increases in flow through sequential grafts have been reported by Bliss and Fonseka (1976) and Jarrett, Berkoff, Crummy et al (1978). Hadcock et al (1983) in a series of animal experiments highlighted the possibility of a steal phenomenon when performing sequential grafts. Whether this occurs in all sequential grafts remains controversial and may in part be dependant upon the outflow peripheral resistance at the site of the anastomoses. It is therefore not surprising that several authors have reported continued graft patency in the presence of occlusion of either the proximal or distal part of the graft. The results to date do not support the claim that sequential grafts are a superior option to the standard femoro-tibial vein bypass graft (Table 4).

Table 4.

Cumulative graft patency rates for sequential grafts

Author	Year	No pts	GPR	Follow Up
Flinn	1980	40	76%	18 months
Rosenfeld	1981	33	76%	1 month
			58%	1 year
		22	86%	1 month
			59%	1 year
Jarrett	1981	23	74%	1 year
			68%	2 years
			62%	4 years

Sequential grafts can be used when there is an absent or inadequate long saphenous vein. Prosthetic material, eg PTFE, can be used in the above knee position with autogenous vein used to cross the knee joint, so avoiding the problems of kinking. The disadvantages of sequential grafts using prosthetic material include the late development of neointimal hyperplasia at the site of the anastomosis between vein and prosthetic material and the problems of the endarterectomised popliteal segment.

Distal arterio-venous fistula (dAVF).

The first experimental arterio-venous fistula was performed by Francois-Franck in 1881. The technique was later used in a patient with severe ischaemia by San Martin Y Sastrustegui in 1902. By 1912 over 58 arterio-venous fistulae had been performed for gangrene, the majority with little clinical improvement (Halstead and Vaughan 1912). Its use as a adjunct to femoro-distal bypass grafting in poor outflow tracts was first suggested by Blaisdell, Lin, Hall et al in 1966. Since then there have been a few clinical reports on the use of dAVF in femoro-distal bypass.

Several theoretical objections have been raised including (i) the development of cardiac failure secondary to an increase in blood volume, (ii) venous hypertension and oedema and (iii) a steal phenomenon. All of these appear to be relatively minor compared to the potential gains of the procedure.

Ibrahim et al in 1980 reported a series of 13 femoro-peroneal grafts using human umbilical vein and a dAVF with a mean follow up of 3 months. There were 2 early failures, both of which resulted in above knee amputations. In the remaining case a below knee amputation was performed for persistent gangrene despite a patent graft.

Harris and Campbell (1983) evaluated the role of the dAVF in the presence or absence of the pedal arch. In those patients with an occluded pedal arch on the per-operative arteriogram, the flow increased from 83.6 ± 9.9 mls/min (mean ± sem) to 236 ± 20.5 mls/min with the dAVF open. The cumulative graft patency rates for grafts to an occluded pedal arch with a dAVF and to a patent pedal arch were 46.5% and 40.5% respectively. To date there remains little evidence to support the use of dAVF in proximal calf reconstructions. Further work is required to evaluate the role of dAVF in distal calf reconstructions particularly when using prosthetic material in high resistance outflow vessels.

Magnification.

The increasing number of femoro-distal reconstructions has highlighted the need for better visualisation of the distal vessels during the construction of the distal anastomosis. The majority of vascular surgeons now employ some form of magnification (x 2.5-4.0), be it loupes with or without extended field of vision or the operating microscope. This approach has also resulted in an increase in the use of microvascular instruments.

CHAPTER 2

CAUSES OF GRAFT FAILURE

Virchow (1862) described three factors which could influence the development of thrombosis in blood vessels ie blood flow, the vessel wall, and the constituents of blood. Originally described in veins, Virchow's triad can be applied in the arterial system and to the potential cause of grafts failure.

Blood Flow

The importance of turbulent flow in the development of arterial thrombosis was recognised by Eberth and Schimmelbush in 1888. Goldsmith and Karino (1982) observed that, in the region of high grade stenoses, flow separation and vortex formations resulted in platelet migration towards the vessel wall with subsequent aggregation and layering. The accumulation of clotting factors and mediators of platelet aggregation within the vortices may result in arterial thrombosis.

Vessel Wall

Endothelial cell damage occurs in hypertensives, smokers (Asmussen and Kjeldsen 1975) and patients with hypercholesterolaemia (Faggiotto and Ross 1984). Not surprisingly endothelial cells are lost during vein harvesting (Adcock, Adcock, Wheeler et al 1984) and after the use of the Hall valvulotome (Scott, Milroy, Beard et al 1988a). The resultant exposure of the underlying collagen increases platelet aggregation and adhesiveness and initiates the platelet release reaction. A platelet monolayer is formed which is relatively nonthrombogenic (Groves, Kinlough-Rathbone, Richardson et al 1982), the cause of which remains uncertain but is almost certainly due to a change in the platelet surface proteins. Thrombosis will ensue if there is a reduction in vessel wall products eg plasminogen activator, prostacyclin (PGI_2), thrombomodulin, Protein C and proteogylcans, and a low or turbulent state.

Blood Constituents.

Blood acts as a non-Newtonian fluid. As flow decreases the viscosity increases, partly due to red cell aggregation or "rouleaux" formation, and partly due to an increase in plasma protein eg fibrinogen. Raised haematocrits (Bonhoutsos, Morris, Chauatz et al 1974) and fibrinogen levels (Harris, Harvey and Bliss 1978) have been implicated in rethrombosis following vascular reconstruction. The use of haemodilution (Yates, Berent, Andrews et al 1979) and lowering of fibrinogen (Dormandy, Goyle and Reid 1977) may improve the circulation in the ischaemic limb and prevent early thrombosis, but as yet there is little evidence to support this in patients undergoing femoro-distal reconstruction.

Immediate / Early Graft Failure (< 30 days)

During the first 30 days, 5-19% of grafts will fail (Levine, Bandyk, Bonier et al 1985, Brewster, LaSalle, Robinson et al 1983, Harris, How and Jones 1987). Poor case selection and operative technical errors account for the vast majority of these failures. The cause are listed in Table 5.

Table 5.

Causes of Graft Failure.

Technical Problems	Selection
Endothelial Damage	Poor vein quality
Poor Anastomoses	Distal Disease and Emboli
Twisting and Kinking	Proximal Disease
Persistent Valves or Tributaries	Coagulation
Sepsis	

Technical problems.

Endothelial Damage

Numerous workers have investigated the effect of (i) surgical technique, (ii) the type and temperature of various irrigation solutions, (iii) distension pressures and (iv) the use of additional pharmacological agents on preserving endothelial cells. The importance of minimising surgical trauma during vein harvesting was observed by Abbott, Welland and Austen (1974). Crystalloid solutions are known to cause extensive endothelial damage (Ramos, Berger, Mansfield et al 1976 , Sottiurai, Stanley and Fry 1983 and Gundry, Jones, Ishihara et al 1980). Tissue culture media and colloid solutions have been used but heparinised autologous blood offers the best protection to endothelial cells (Ramos, Berger, Mansfield et al 1976, Sottiurai, Stanley and Fry 1983, Gundry, Jones, Ishihara et al 1980). The use of cold solutions (< 4° C) avoids prolonged warm ischaemia and improves endothelial cell survival.

Distension pressures in excess of 700 mmHg have been recorded using a hand held syringe (Bonchek 1980). Malone et al 1978 reported that pressures in excess of 700 mmHg would produce complete endothelial cell loss. Storm et al (1975) observed that veins distended to 200 mmHg did not differ from non-distended veins three months following implantation. As a result various devices have been made to limit the pressure exerted during vein preparation (Bonchek 1980, Dimitri and Williams 1986). Sottiurai et al (1985) reported that papaverine hydrochloride helped to improve the preservation of endothelial and smooth muscle cells and prevented leukocyte infiltration during vein graft preparation. Polymorphonuclear leukocytes are known to damage endothelial cells (Harlan, Killen, Harker et al 1981) and stimulate smooth muscle cell proliferation (Ross, Glomset, Kariya et al 1974), the latter being implicated in the response to injury phenomenon and the development of intimal hyperplasia.

Poor Anastomoses

The introduction of the in situ vein technique has enabled vascular surgeons to undertake more distal grafts. The use of magnification, fine monofilament suture material and the avoidance of arterial wall damage are important factors in ensuring a satisfactory anastomosis. Klein et al (1982) reported that continuous sutures significantly reduced arterial wall compliance compared to interrupted sutures and that the resultant compliance mismatch may result in turbulence and subsequent graft failure. Comparable graft-artery diameters are also important to avoid impedance mismatch, which has been implicated in the development of intimal hyperplasia. The optimum cross-sectional area ratio between artery and graft being 1:1.1 (Schultz 1967). Energy losses were also thought to occur as a result of the angle of the anastomosis. Crawshaw et al (1980) reported boundary-layer separation with adverse pressure gradients when the distal anastomosis was constructed with a high inlet angle. In contrast, Klimach et al (1984) concluded that the anastomotic angle did not significantly alter pulsatile energy or flow through the graft.

Twisting or Kinking

When transected, the distal portion of the saphenous vein has a tendency to rotate through 360 ° degrees. This can be avoided by (i) careful attention to detail (Corson, Leather, Shah et al 1986), (ii) leaving a proximal and distal tributary attached (Beard, Wyatt, Scott et al 1989) and (iii) marking the anterior surface of the vein with methylene blue (Levine, Bandyk, Bonier et al 1985).

Prosthetic grafts have been reported to kink on knee flexion (Taylor, MacFarland and Cox 1987), the resultant turbulent flow producing localised areas of neointimal hyperplasia. The introduction of externally supported grafts may well prevent this problem.

Residual Valves and tributaries

Inadequate mobilisation of the long saphenous vein may result in an arteriovenous fistula (AVF). Two types have been recognised (i) superficial AVF's which produce a painful cutaneous flare and (ii) deep AVF's which steal blood away from the graft and into the deep venous system (Figure 1).

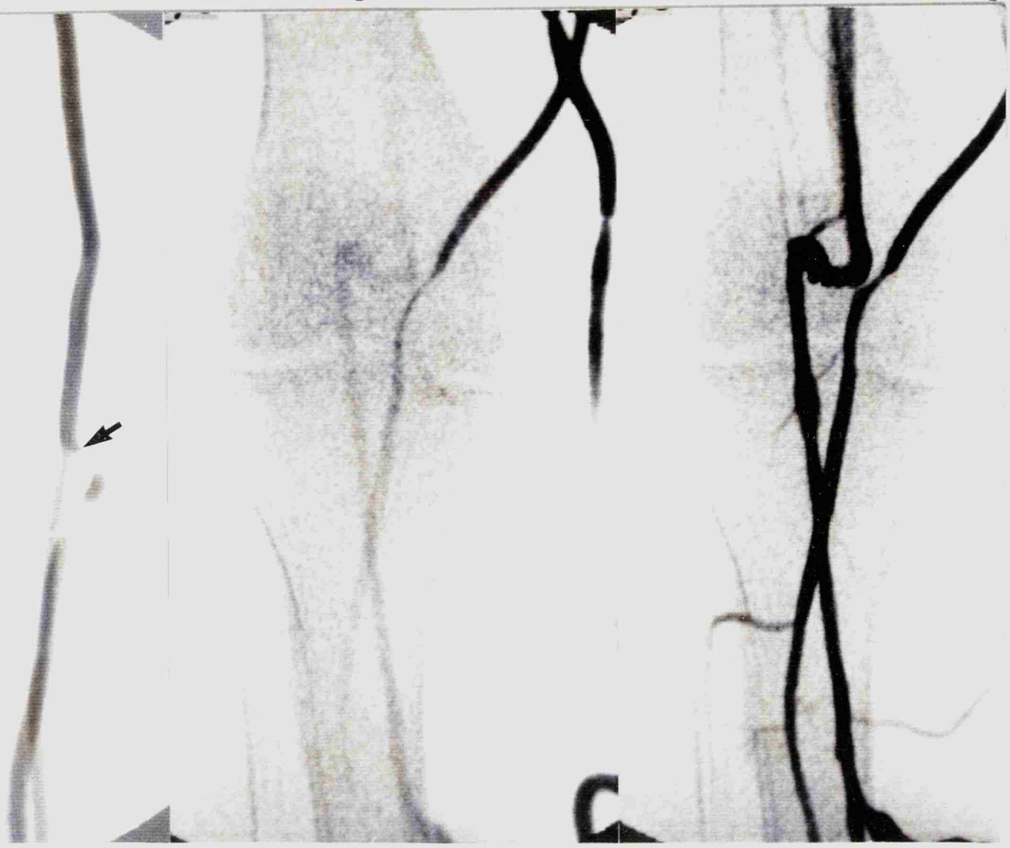


Figure 1. Arteriovenous fistula (black arrow) in a failing graft. Early filling of the popliteal vein can be seen in the middle and right hand plates.

The latter has been implicated as a cause of early graft failure, Gannon, Goldman, Simms et al (1986a) reported a 16.5% incidence of AVF's of which 37% went on to graft occlusion.

Diversified methods of abolishing AVF's have been described in the literature. These include full mobilisation of the vein (Denton, Hill and Fairgreave 1983), orthograde and retrograde saline irrigation (Dundas 1970, Skagseth and Hall 1973), completion arteriography (Leather, Powers and Karmody 1979), flow measurements (Cave-Bigley, Ackroyd, Campbell et al 1984 and Gannon, Goldman, Simms et al 1986b), continuous wave Doppler wave insonation (Spencer, Goldman, Hyslop et al 1984) and a squirt test (Shearman, Gannon, Gwyn et al 1986a). Residual valve cusps may predispose to graft thrombosis as a result of turbulent or obstructed flow. Bush et al 1983 reported a 10% incidence of residual valves despite completion arteriography. Intraoperative continuous wave Doppler has been claimed to identify residual valve cusps (Spencer, Goldman, Hyslop et al 1984).

With the rapid advances in fibreoptic technology the availability of the video angioscope provides the vascular surgeon with yet another technique of graft assessment. Technical errors such as (i) intact valve leaflets, (ii) misplaced anastomotic sutures, (ii) emboli and thrombosis (Figure 2) and (iv) unsuspected partial occlusions of either the graft or distal runoff vessels can now be identified and corrected (Grundfest, Lituack, Hickey et al 1987).

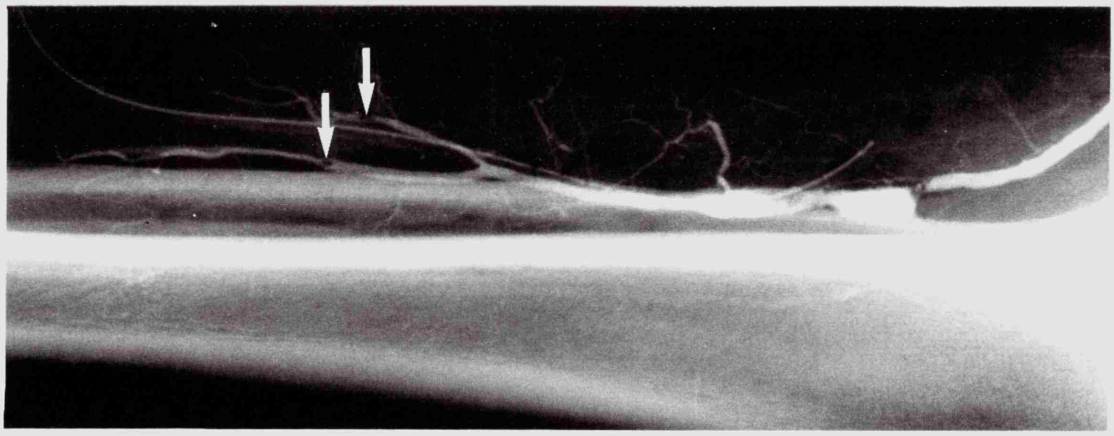


Figure 2. On table arteriogram showing distal emboli (white arrows) in the runoff vessel.

Sepsis

Wound and graft infections carry a significant morbidity and mortality in vascular surgery (Casali, Tucker, Thompson et al 1980). Several risk factors have been identified including age, diabetes, obesity, malnutrition, prolonged operations and post-operative stay (Cruse and Foord 1973, Davidson, Clark and Smith 1971). In addition, the presence of active infection in the lower extremity, a remote source of infection and the degree of contamination are all associated with a significant increase in wound infections (Liekweg and Greenfield 1977). In femoro-distal reconstructions, Hasselgren et al (1984) reported an increase in wound infections with long thigh incisions. The resultant undermining of the skin edge with exposure of the underlying subcutaneous tissues and lymphatic damage have all been implicated in the development of infections. As with any other branch of surgery, prophylactic antibiotics have reduced the incidence of post-operative sepsis (Kaiser, Clayson and Mulherin 1978, Hasselgren, Ivarsson, Risberg et al 1984). Interestingly no additional benefit was noted with a 3 day course of antibiotic as apposed to single dose therapy.

Selection

Vein Quality

Vein quality encompasses size, wall thickness, the presence of varicosities, fibrotic valves, diffuse fibrosis of the vein, endothelial damage and previous thrombosis (Figure 3).

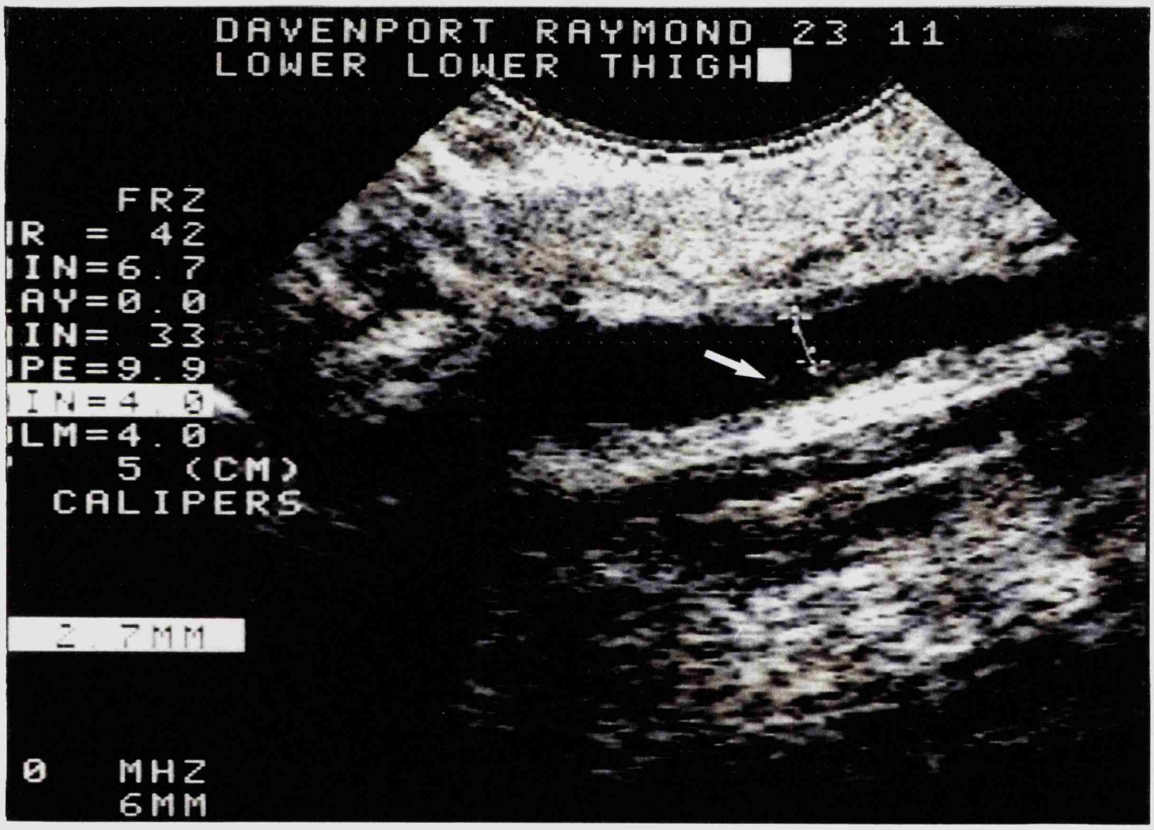


Figure 3. Pre-operative Duplex scan of the long saphenous vein showing a localised area of thickening.

LoGerfo et al in 1977 reported that poor quality fibrotic veins had significantly lower patency rates than good quality veins. These findings have been confirmed by Szilagyi, Hageman, Smith et al (1979). To date there is little consensus in the literature as to what constitutes a minimum vein size (Table 6). Prior to the introduction of the in situ technique most surgeons would accept 4 mm as the smallest sized vein. However with the smaller Hall valvulotomes (2mm) and the Mills valvulotome veins as small as 2mm have been used with some success.

Table 6.

Minimum vein size for femoro-popliteal / femoro-distal bypass.

Author	Year	Size(mm)
Baddeley	1970	>5
Imparato	1973	>5
Reichle	1979	>4
Kacoyanis	1981	>4
Brewster	1981	<4
Leather	1981	<3.5
Connolly	1982	2
Ascer	1984	<4
Beard	1989	2

Buxton et al (1980) in a series of 186 reversed saphenous vein grafts reported that thin walled veins greater than 5mm diameter had significantly higher patency rates than thick walled 3mm veins. By contrast, Sonnenfeld et al (1980) found that vein size (3mm) did not affect the graft patency rates at 1 and 5 years. However, significantly lower volume flows were recorded in the smaller veins (<3mm), but this may have been compensated by higher peak velocities. Corson et al (1984) reported no difference in patency rates between veins less than 3.5 mm in external diameter and those greater than 3.5 mm external diameter.

<u>*Distal disease*</u>

The presence of an adequate runoff has long been recognised as an important factor in successful femorodistal bypass (Linton and Darling 1962, DeWeese and Rob 1971). Conventional preoperative arteriography may fail to demonstrate patent calf vessels usually as a result of severe multisegment disease, contrast sedimentation and poor cardiac function. The technique of single sided femoral injections using intra-arterial digital subtraction arteriography (IA DSA) with reactive hyperaemia has been reported to improve the visualization of the distal calf and pedal vessels (Turnipseed, Detmer, Berkoff et al 1982), (Figure 4).

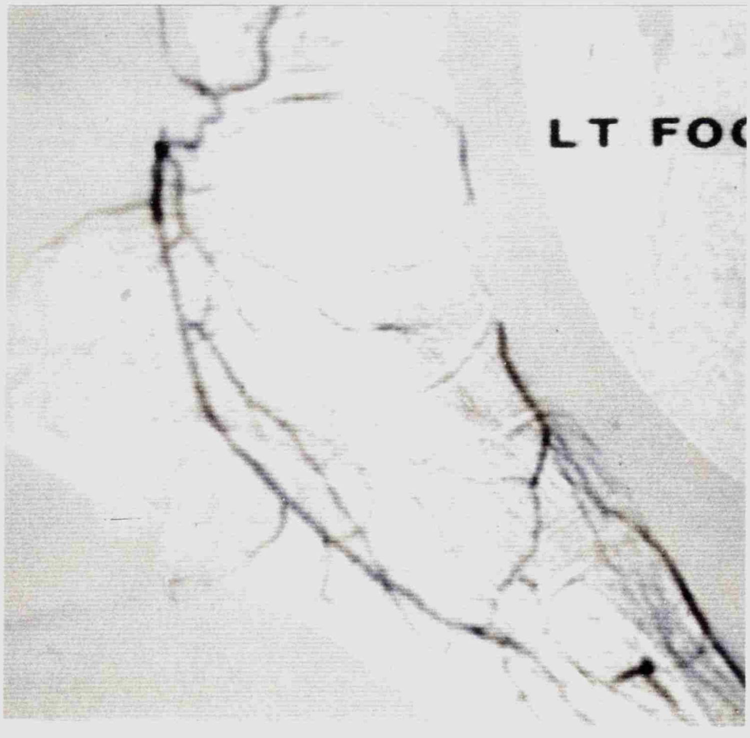


Figure 4. IA DSA view of the pedal arch.

Intraoperative arteriography has been reported to improve calf vessel visualization in 90% of cases (Flanigan, Williams, Keifer et al 1982).

Despite these improvements, per-operative arteriography fails to provide any real functional assessment of runoff. Until recently the physiological assessment of runoff was limited to Doppler pressure indices and vessel scoring systems. Shearman et al in 1986 used a scoring system based upon clinical and Doppler data to successfully predict the level of the distal anastomosis. The adoption of this technique led to a significant reduction in the number of preoperative arteriograms but has not shown a significant correlation with patency.

Doppler waveform analysis has been used but appears of limited value in the presence of multisegment disease, particularly where the distal waveform is severely damped. The concept of generating a new pulse wave called Pulse Generated Runoff (PGR) was reported by Beard, Scott, Evans et al in 1988 and was subsequently reported to correlate with peripheral resistance and outcome following femorodistal bypass (Scott, Beard, Farmilo et al 1988b).

Proximal Disease

The presence of significant aorto-iliac disease has been implicated in early femoro-popliteal bypass failure (Charlesworth, Harris, Cave et al 1975), presumably as a result of poor graft perfusion. Correctly identified, these lesions can either be dilated preoperatively or bypassed at the time of surgery.

The quality of the femoral pulse provides a useful guide to the severity of aorto-iliac disease (Campbell 1984). More sophisticated methods of assessment have been used, including computer analysis of femoral artery Doppler waveforms, pulsatility index (Gosling, Dunbar, King et al 1971), Laplace transform analysis (Campbell 1984), and principal component analysis

(Macpherson, Evans and Bell 1984).

Conventional single planar arteriography has up until recently, remained the "gold standard" by which all other tests have been judged. Udoff et al (1979) reported that haemodynamically significant stenoses may be missed, particularly if oblique views were not performed.

Macpherson et al (1984) concluded that the measurement of pressure at rest and after the administration of papaverine was the most reliable test of aorto-iliac disease. It can be used as a diagnostic test at the time of arteriography and to confirm a successful balloon dilatation.

Poor Graft Perfusion

An adequate graft perfusion pressure is necessary to maintain graft patency. Poor cardiac function and uncorrected hypovolaemia are the commonest causes of peri-operative hypotension. The use of central venous and right atrial wedge pressures in high risk cases should enable an adequate perfusion pressure to be maintained in the early peri-operative period. The manipulation of peripheral vascular resistance by sodium nitroprusside and glyceryl trinitrate may improve graft perfusion (Collier, Lorge and Robinson 1978), but have not been proved to increase patency.

The resultant sympathetic nerve block following epidural anaesthesia is known to reduce peripheral vascular resistance, increase graft blood flow, and increase skin temperature (Cousins and Wright 1971). The same authors reported that post-operative analgesia avoided the marked vasoconstrictive effect of pain.

Intermediate Graft Failure (30 days to 1 year)

Intermediate graft failure has been attributed to the development of (i) intimal hyperplasia, (ii) valve cusp fibrosis and (iii) aneurysmal dilatation. Szilagyi et al (1979) were the first to report the relationship between these structural vein grafts abnormalities and subsequent graft failure.

Neointimal hyperplasia.

The pathogenesis of neointimal hyperplasia remains unclear, but it appears to be part of a "response to injury" phenomenon (Fuchs, Mitchener and Hagan 1978). Gunstensen et al (1982) postulated that the degree of intimal hyperplasia was proportional to the severity of trauma during the harvesting of the vein.

During the first week following implantation, vein grafts show focal endothelial disruption with fibrin deposition, medial oedema, and an acute inflammatory infiltrate (Ramos, Berger, Mansfield et al 1976). Platelets rapidly adhere to the underlying collagen and release thromboxane A_2, ADP and platelet derived growth factor (PDGF) which stimulates smooth muscle cells and may be responsible for the marked degrees of intimal hyperplasia following grafting.

By two weeks the luminal surface is covered by regenerated endothelial cells which are morphological normal, but doubt remains about their functional capabilities. Smooth muscle cells continue to be lost from the media with evidence of focal subendothelial SMC deposits which become diffuse by twelve weeks. Mural ischaemia has been postulated as a cause of graft failure. Wyatt et al (1964) reported partial regeneration of the vaso vasorum by 72 hours and a return to normality by 2 weeks. The absence of the vaso vasorum may not be as critical as once thought, since the vein wall is accustomed to a hypoxic environment. Endothelial cells are known to survive following cessation of flow in the vaso vasorum, presumably as a result of a direct nutrient supply from the blood.

Late failure

After the first post-operative year, grafts fail at the rate of 2.5% per annum (DeWeese and Rob 1977, Harris, deCossart, Moody et al 1988). These are attributed to progression of proximal and distal disease (Figure 5).

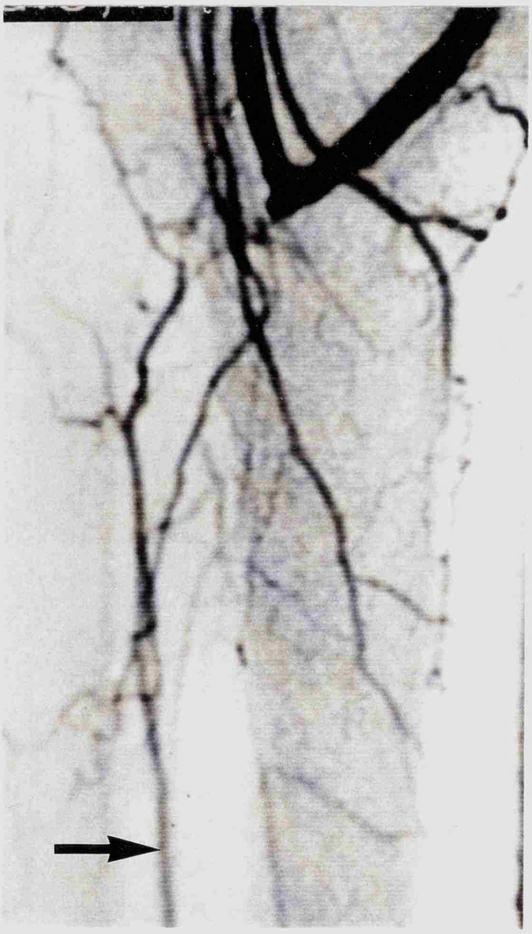


Figure 5. Post-operative arteriogram showing a patent graft but with an occluded outflow tract. The proximal anterior tibial artery (Black arrow) is filled by large collateral vessels around the site of the distal anastomosis. The distal popliteal artery is thought to have occluded because of progression of disease.

DeWeese et al (1977) reported that 48% of patients had died at 5 years following femoro-popliteal bypass, myocardial infarction and cerebrovascular disease accounting for 71% of all deaths. Only 30% were alive at 5 years with a patent graft. Risk factors associated with cardiovascular deaths included smoking, hyperlipidaemia and a hypercoaguable state.

Smoking

Myers et al (1978) conducted a postal survey which reported a 90% graft patency rate in non-smokers compared to 60% in the current smoking group. Although open to criticism, these results were confirmed by Greenhalgh, Laing, Cole et al (1981) who used carboxyhaemoglobin (COHb) levels as a marker of current smoking activity.

The pathogenic effects of smoking include reduced high density lipoproteins (HDL) (Brooks, Blenkenhorn, Chin et al 1980, Miller, Hammett, Saltissi et al 1981), increased platelet aggregation (Pittilo, Mackie, Rowles et al 1983), a toxic effect to endothelial cells (Prerovsky and Hladovec 1979), and decreased fibrinolytic activity and increased fibrinogen levels (Epstein, Rosing, Brakman et al 1970).

Cholesterol

Hyperlipidaemia has been implicated in the development of atherosclerosis and subsequent late graft failure. In particular, raised plasma trigylcerides are associated with peripheral vascular disease (PVD) (Greenhalgh, Rosengarten, Mevart et al 1971) and raised cholesterol with coronary heart disease (Keys 1970). Fish oil supplements have been used with some success in reducing plasma triglycerides levels (Phillipson, Rothrock, Connor et al 1985), but only a few studies have demonstrated angiographic evidence of atherosclerosis regression following a reduction in the dietary intake of lipids.

Hypercoaguable state.

The role of antiplatelet therapy in femoro-distal bypass has yet to be established. There are good theoretical reasons for the pharmacological manipulation of the clotting system. In patients with peripheral vascular disease both the resting fibrinolytic activity and fibrinolytic potential have been shown to be reduced (Naimi, Goldstein and Proger 1963), (Browse, Gray, Jarrett et al 1977). Earnshaw et al (1988a) reported a significantly lower fibrinolytic activity in patients with more advanced peripheral vascular disease (gangrene and rest pain). This may account for the high failure rate of grafts in these patients. Current studies are underway to investigate the alteration of clotting in patients undergoing bypass surgery for limb salvage.

CHAPTER 3

REVIEW OF ARTERIOGRAPHY.

Arteriography.

The discovery of X-rays by Röentgen in 1895 was to change the face of medicine. Numerous cadaveric studies appeared in the scientific literature highlighting the ability of X-rays to delineate fine vascular structures. In 1910 Franck and Alwens performed the first successful intravenous contrast (bismuth in oil) study in animals. Nine years later Heuser successfully injected potassium iodide into a child's hand vein. By 1924 Brooks had performed the first femoral arteriogram using a 10ccs solution of sodium iodide. Brooks exposed the femoral artery in the proximal part of Hunter's canal and after the application of a thigh tourniquet and a Crile clamp, a medium sized needle was inserted into the lumen of the vessel. Films were then taken of the distal runoff. Two further reports by Sicard and Forestier (1923) using iodized poppeyseed oil (Lipiodol) and Berberich and Hirsch (1923) with strontium bromide failed to establish the potential value of arteriography. Stimulated by the work of Moniz, Dos Santos and his colleagues (1929) carried out the first aortogram using an automatic injection system. This injected sodium iodide at a rate of 3-4 cc/sec. Despite excellent visualization of the abdominal vasculature the technique met with certain reservations, in particular, those related to contrast toxicity.

Contrast Agents

These fears were later resolved with the introduction of newer contrast agents. In particular the binding of iodine to either a benzene or pyridine ring significantly reduced the incidence of side effects. Water solubility was achieved by the addition of either a carboxyl or acetic acid ring and radio-opacity was further improved by the addition of two iodine molecules.

Arterial catheterization

Arterial catheterization was reported as far back as 1831 by Dieffenbach. He attempted to revive a collapsed patient, by inserting a catheter through the brachial artery and into the left ventricle (Stützbecher 1971). Not surprisingly, he was unsuccessful in his attempts. Its use in vascular imaging was reported one hundred years later by Forssman who introduced a catheter through his own basilic vein and into the right ventricle. In 1941 Farinas reported a similar arteriographic technique in which the femoral artery was first exposed and a trocar inserted. A urethral catheter was passed through the trocar and into the aorta. Vertebral and later thoracic arteriography were described by Radner in 1948 who catheterized the exposed and ligated radial artery.

Percutaneous catheterization.

The development of percutaneous catheterization avoided the major disadvantage of the previous techniques, that of exposure of the vessel. In 1949 Jönsson punctured the common carotid artery using a blunt cannula with a removeable needle. The technique was later abandoned because of fears about damage to the lumen. However, with the development of thin walled polyethylene tubes, Pierce (1951) and Donald, Kesmodel, Rollins et al (1951) confirmed the value of the percutaneous method. Despite this, haemorrhage remained a significant problem, particularly on removal of the needle. This was overcome by Seldinger (1953) who perfected the technique by passing a catheter over a guide wire after the withdrawal of the needle. The development of automated injections of contrast, film and cassette changers and fluoroscopy all improved the quality of arteriograms and the visualization of the peripheral vasculature.

Conventional Arteriography.

Conventional pre-operative arteriography became the investigation of choice in the assessment for vascular reconstruction of patients with critical ischaemia. Arteriography helps identify patients who may benefit from an improved inflow, either by a proximal reconstruction or by balloon dilatation, and it provides the surgeon with information to help select the appropriate vessel and level of the distal anastomosis (Imparato, Kim, Madayang et al 1973). However, the visualization of the distal runoff may be hampered by a combination of factors including severe multisegment disease, poor myocardial function and ectatic vessels, all of which lead to rapid layering and sedimentation of contrast media. As a result, the arteriogram may be misleading and may fail to identify patent distal vessels in the lower calf (Campbell, Fletcher and Hands 1986). Numerous techniques were developed to improve distal vessel imaging including tourniquet occlusion (Kahn, Boyer, Moran et al 1968), limb exercise, multiple injections of contrast (Boijsen and Dahn 1965), vasodilators (Jacobs and Hanafee 1967), the use of Doppler ultrasound to improve the timing of film exposure (James and Galloway 1971) and epidural anaesthesia (Fuchs, Fagaeus and Lumb 1982).

In an attempt to improve the predictive value of arteriography, various scoring systems have been devised ranging from the simple to the complex (Menzoian, LaMorte, Cantelmo et al 1985, LaMorte, Menzoian, Sidawy et al 1985, Rutherford, Flanigan, Gupta et al 1986, Shearman, Gwyn, Curran et al 1986b). Despite the advantages in technique many patients were considered inoperable and underwent amputation. Dible (1966) in a pathological study of 140 amputated legs for critical ischaemia reported that the majority of the legs had occlusion at or just below the knee, but those vessels towards the periphery were often patent (Dorsalis pedis 65%, lateral plantar 70%, medial plantar 82.5% and digital 92%).

These results confirmed the impression that patients with critical ischaemia often have a patent isolated calf vessel suitable for distal reconstruction. The inability of conventional arteriography to demonstrate these vessels has stimulated interest in alternative methods of assessing calf vessel runoff by including intra-arterial digital subtraction arteriography (IA DSA) and non-invasive Doppler studies.

Intra-arterial digital subtraction arteriography (IA-DSA).

The development of computerized digital subtraction techniques resulted in improved visualization of the distal vasculature (Pond, Osbourne Capp et al 1982). In contrast to conventional arteriography, IA DSA requires only 2-3 % intravascular concentration of contrast medium compared to 40-50% for conventional studies. As a result, the risks of renal toxicity is reduced and patients experienced less pain, principally due to the use of non-ionic contrast media. Turnipseed, Detmer, Berkoff et al (1982) in a study of 20 patients undergoing conventional arteriography prior to femoro-distal reconstruction failed to demonstrate the tibial vessels and pedal arches in all of the cases, despite the use of 7 minutes of reactive hyperaemia. Using IA DSA in the same patients, a patent popliteal with a single calf vessel was seen in 70 % of cases. These result were later confirmed by intra-operative arteriography which also identified 3 more cases suitable for reconstruction. The addition of IA DSA has become an accepted radiological technique in the pre-operative assessment of patients with critical ischaemia.

Per-operative arteriography.

Dissatisfied with the results of conventional arteriography and stimulated by the apparent success of reconstruction in patients with no evidence of runoff on the pre-operative films, Doscher, Bole, Babu et al (1979) reported the use of on-table arteriography in selecting of patients for femoro-distal reconstruction. Contrast injections at or below a clamped femoral artery can be used before committing the patient to either a distal reconstructive procedure or primary amputation. Flanigan et al (1982) in a study of 32 patients reported a 90% improvement in the visualisation of the distal runoff. On the basis of the pre-operative films, 14 (44%) of the cases would have undergone amputation had it not been for the per-operative arteriogram. Similar findings were reported by Ricco, Pearce, Yao, et al (1983) in a series of 113 pre-operative arteriograms. In twenty three cases there were no distal vessels visualised on pre-operative arteriography, yet at operation 83% were found to have a suitable distal vessel and underwent successful reconstruction. Of those with adequate visualisation, seven patients had the operative approach modified as a result of the per-operative arteriogram, a similar finding to that reported by Scarpato, Oembarowicz, Farbers et al (1981).

Per-operative arteriography does, however, have several disadvantages. Firstly it is a uniplanar investigation and may underestimate disease. Secondly it gives no physiological information about runoff, and thirdly may not give full information about continuity with the pedal arch. Finally it does not allow surgery to be planned ahead with possible inefficient utilization of resources.

CHAPTER 4.

REVIEW OF NON-RADIOLOGICAL TECHNIQUES.

Pre-operative

Introduction.

In critical ischaemia, two important factors have to be addressed before surgery; (i) is there an adequate inflow and (ii) is there sufficient distal runoff to support a femoro-popliteal / distal bypass graft.

Inflow disease.

Clinical examination.

The presence of a good femoral pulse by an experienced vascular surgeon is often considered sufficient to exclude significant aorto-iliac disease. However, palpation of the femoral pulse may be difficult, particularly in the obese patient or where the vessels are heavily calcified.

Doppler waveform analysis.

Quantification of common femoral velocity signals by waveform analysis including pulsatility index (Gosling, Dunbar, King et al 1971), Laplace transform (Skidmore and Woodcock 1980) and Principal component analysis (Macpherson, Evans and Bell 1984), has been used in the assessment of the aorto-iliac segment. All the techniques have their supporters, but the last method appears to be the most sensitive method of detecting stenoses in the aorto-iliac segment.

Ultrasound imaging.

Ultrasound B-mode imaging in combination with a pulsed Doppler velocimeter have also been used in the assessment of the aorto-iliac segment, but are operator dependant, time consuming and prone to the errors of estimating blood flow (Gill 1985).

Direct pressure measurements.

Direct pressure measurements in combination with a papaverine test can be performed as an outpatient, at the time of arteriography, or intra-operatively. At rest, two cutoff values have been reported to identify significant aorto-iliac disease. Firstly a pressure difference between brachial and femoral artery of > 10 mmHg at rest (Macpherson, Evans and Bell 1984) and secondly a femoral pressure 20% less than the brachial (Weismann and Upson 1963). Following the administration of papaverine, a 20-25 mmHg pressure difference between brachial and femoral (Macpherson, Evans and Bell 1984) or a 15% fall in common femoral artery pressure (Brewster, Waltman, O'Hara et al 1979), are reported to identify significant inflow disease.

Distal Disease.

Doppler ankle systolic pressures.

Doppler ankle systolic pressures and ankle / brachial indices are useful in assessing the severity of disease (Bell, Charlesworth, DePalma et al 1982), but are unable to predict the outcome of femoro-distal bypass (Corson, Johson, LoGerfo et al 1978, Samson, Gupta, Veith et al 1985). Careful Doppler examination of the ischaemic foot in the dependant position may help identify patent vessels not seen on arteriography (Campbell, Fletcher and Hands 1986, Simms 1988).

Doppler vessel scoring system.

Shearman et al (1986b) have reported the value of a simple clinical / radiological scoring system in determining the level of reconstruction, but did not address the problem of selecting patients for femoro-distal reconstruction.

Segmental limb pressures (SLP).

Segmental limb pressures are a simple non-invasive assessment of peripheral vascular disease and are compared with either a brachial pressure or pressure from the same level in the contralateral leg. Froneck et al (1973) suggested that a vertical gradient of > 40 mmHg or a horizontal difference of > 20 mmHg can be used as a indicator of significant disease. By contrast, Flanigan, Williams, Keifer et al (1982) have shown that SLP's are of limited value in the assessment of combined aorto-iliac and femoro-popliteal disease. In patients with calcified incompressible distal vessels, the measurement of segmental limb pressures becomes invalid.

Stress Testing.

Simple treadmill exercise tests have been use to grade the severity of disease. Laing and Greenhalgh (1983) reported that of 100 limbs assessed, 78% had a normal resting pressure. After a 1 minute exercise test at 4 km/h at 10° incline, 41% of the "normal limbs" had an abnormal pressure. This test is unfortunately not applicable to the majority of patients with critical ischaemia who are unable to complete the test (Wyatt, Muir, Tennant et al 1990). Alternative methods have been evaluated including occlusive calf hyperaemia (Baker 1978) and ankle flexion (Wyatt, Muir, Tennant et al 1990).

Doppler waveform analysis.

Doppler waveform analysis of distal calf vessels are not applicable in the assessment of severe distal disease as the waveforms are often severely damped and not suitable for analysis.

Pulse volume recorder (PVR).

This is a semi-quantitative segmental air plethysmograph which gives a non-invasive pressure wave trace. Air filled cuffs can be applied to the thigh, calf, ankle and toe. Amplitude and upstroke times can be calculated from a series of five waveforms. The PVR has been used in (i) the assessment of the severity of peripheral vascular disease (Darling, Raines, Brener et al 1972), (ii) intra-operative monitoring (Baird, Davies and Bird 1979) and (iii) in the selection of patients for femoro-popliteal bypass (Kram, Appel and Shoemaker 1988). Kram et al (1988) found that pre-operative ankle PVR's (amplitude) were unable to predict successful femoro-popliteal bypass.

Transcutaneous oxygen (TcPO2).

Transcutaneous oxygen has been evaluated in the assessment of the peripheral vascular disease (Clyne, Ryan, Webster et al 1982), in the prediction of wound and stump healing (Ratcliff, Clyne, Chant et al 1984) and as a form of intra-operative monitoring (Gannon, Goldman, Simms et al 1986c). More recently, Kram et al (1988) have reported the value of post-occlusive foot transcutaneous oxygen recovery time in predicting outcome following femoro-popliteal bypass.

Pulse Generated Runoff (PGR).

Pulse Generated Runoff (PGR) (Beard, Scott, Evans, et al 1988) overcomes the problem of damped distal Doppler signals in severe peripheral vascular disease. A new pulse wave is generated by rapid inflation of a sphygmomanometer cuff wrapped tightly around the upper calf. The augmented flow at the ankle can then be detected if the calf vessel is patent. Recent studies have reported a good correlation between the PGR score and peripheral resistance and the subsequent outcome following femoro-distal bypass (Scott, Beard, Farmilo, et al 1988b).

Per-operative.

Direct Method of Graft Assessment

A variety of techniques have been used in the per-operative assessment of femoro-distal grafts. These include arteriography, ultrasound, vascular endoscopy, and peripheral resistance and flow measurements.

Arteriography.

Intra-operative arteriography has been used to (i) identify patent distal calf vessels missed on the pre-operative arteriogram, (ii) select the level of the distal anastomosis and (iii) check the completed graft. It does not, however, provide any real physiological information about the runoff and is unable to help in pre-operative planning and has all the drawbacks of uniplanar arteriography.

Ultrasound

Intra-operative Doppler and duplex ultrasound have both been used for intra-operative assessment. Spencer et al (1984) studied 25 femoro-popliteal grafts using a 5 MHz Doppler probe. Increased peak systolic and diastolic frequencies were associated with retained valve leaflets or persistent arterio-venous fistulas. Duplex scanning is difficult to use in theatre because of sterility and access problems, and is limited in that little function information about runoff can be obtained.

Vascular Endoscopy

Although an exciting tool it has yet to find a defined role in per-operative graft assessment. Several authors have advocated the use of the vascular endoscope in; (i) checking the distal anastomosis, (ii) locating venous side branches and (iii) excluding retained valve leaflets. The disadvantages include; (i) overdistension of the vein with an irrigating solution which may be harmful to endothelial cells, and (ii) the limitation of size and steerability and (iii) damage to the vein.

Flowmeters

The development of electromagnetic flowmeters enabled clinicians to measure completion graft flow and resistance, but the machines were expensive and difficult to use in theatre (Wyatt 1984). The problems associated with EM flowmeters were overcome by the development of a Doppler flowmeter with the facility to measure PR before and after reconstruction (Beard, Scott, Skidmore et al 1989).

Review of haemodynamic measurements during femoro-distal bypass.

Resting flow.

Basal flow rates of less than 100 mls per minute have been associated with a higher incidence of graft failure (Cappelen and Hall 1967, Terry, Allan and Taylor 1972). Flow is not absolute and there are reports of patent grafts with flow rates of less than 30 mls per minute (Mannick and Jackson 1966a, Barner, Kaminski, Codd et al 1974). Mannick et al (1966b) reported no direct relationship between resting blood flow and muscle blood flow in the early post-operative period. The dichotomy between flow rates and graft patency may be due to other causes of graft failure including vein quality, size, proximal and distal disease, cardiac output, type of anaesthesia, technical errors and haematological abnormalities.

Resting flow and arteriographic run-off

Hall and Fjeld (1973) reported no significant difference in resting flow between grafts with good and poor runoff. Similar results were reported by Mundth, Darling, Moran et al (1969) and Cappelen and Hall (1964). By contrast, Kaminiski et al (1972) and Sonnenfeld and Cronestrand (1980) both reported a clear relationship between flow and arteriographic runoff. The explanation for this difference remains uncertain, but may represent inadequate arteriographic assessment. Stiremann and Triller (1986) reported a significant difference between the flow rates at the proximal popliteal level and a single calf vessel.

Hyperaemic Flow.

Vasodilators.

The lack of correlation between resting flow and graft patency led workers to investigate the relationship between hyperaemic graft flow and graft outcome. Golding and Cannon (1966) reported a two fold increase in graft flow after the administration of 30 mg papaverine hydrochloride, from 85 to 190 mls per minute. Hall and Fjeld (1973) in 1973 reported a correlation between the maximum intra-operative graft flow after the administration of a 2 ml solution of 2% papaverine and flow in the popliteal artery after 2 minutes of active ankle flexion on the first post-operative day. At 2 years there were no graft failures in those patients with a 200% increase in flow after the administration of papaverine hydrochloride. Albrechsten (1976) in a series of 48 reversed vein grafts reported an increase in the mean "basal" flow from 132 mls/min to 285 mls/min following the intra-arterial injection of 40 mg of papaverine hydrochloride. At 3 months there were no graft failures in those patients with a 100% increase in the basal flow following the administration of papaverine hydrochloride. Sonnenfeld et al (1979) in a study of femoro-popliteal vein grafts for claudication reported a dramatic increase in graft flow from an average of 81 to 287 mls/ min and a concomitant fall in the PR from 0.167 to 0.003 PRU's with papaverine hydrochloride.

Sympathectomy

Similar increases in flow have been reported with sympathectomy. Terry et al 1970 reported a 77% increase in graft flow following lumbar sympathectomy.

Peripheral resistance

The measurement of peripheral resistance (PR) during femoro-popliteal bypass is a relatively new technique which has yet to gain wide acceptance amongst vascular surgeons. Several authors have advocated the use of PR in the selection of patients for primary amputation or bypass. Where reconstruction is contemplated PR may be used to determine the appropriate level of reconstruction.

Peripheral resistance can be measured using either a constant infusion (Serise, Le Héron, Janvier et al 1982, Ascer, Veith, Morin et al 1984, Parvin 1987) or pressure (Beard 1987) system. The latter has the advantage of being cheaper and simpler to use. Peripheral resistance was first measured in vivo by Vetto and Dunphy (1964), who reported a correlation between PR and outcome. Six patients were studied and the PR calculated by infusing cold bank blood into the popliteal artery at a known flow rate and measuring the pressure generated by a separate cannula.

Bliss (1971) measured PR in the distal popliteal artery prior to reconstruction using a roller pump system. He reported no correlation between PR and the outcome, but observed a series of complex relationships between PR and infusion rates. Later Bliss (1973) stressed the importance of reducing vasomotor tone. He observed a significant fall in PR after the administration of 40 mg of papaverine hydrochloride and a good correlation between PR and arteriographic vessel irregularity.

Changes in the intravascular volume have a marked effect on the PR of the leg (Cronestrand and Ekeström 1970, Sonnenfeld, Cronestrand and Nowak 1979). Sonnenfeld et al (1979) in a series of 11 femoro-popliteal grafts studied basal and maximal flow rates before and after blood transfusion and the administration of 40 mg papaverine hydrochloride. Graft flow increased by 165% from 81 ± 46 to 215 ± 67 mls / min after blood transfusion. They concluded that vasodilatation and an increased intravascular volume had a marked effect on the vascular resistance of the leg. Ascer et al (1984) measured the total, proximal and distal outflow resistance after the completion of the distal anastomosis in 101 bypasses (46 FP, 55 FD). He reported a significant relationship between the total outflow resistance and early graft patency. By contrast there was no correlation between the total outflow resistance after papaverine hydrochloride and early graft patency. The presence of diabetes, arterial wall calcification and the site of the distal anastomosis had no effect on the percentage decrease in total outflow resistance. In an expanded series of 134 grafts, Ascer, White-Flores, Veith et al (1987) reported patency rates of 95% and 67% for femoro-popliteal grafts to outflow tracts with a PR of < 0.17 PRU's and > 0.4 PRU's respectively. By contrast femoro-distal grafts with a PR of 0.25 - 0.4 PRU's and > 0.4 PRU's had patency rates of 48% and 0% respectively.

Parvin (1987) using a constant infusion system was unable to demonstrate any relation between PR and graft patency in a series of femoro-tibial grafts. By contrast there was a clear relationship between PR before and after papaverine hydrochloride and outcome up to 9 months in a series of femoro-popliteal grafts. A PR level of 1200 mPRU's was defined as the best cutoff level for a successful graft, much higher than that of Ascer, White-Flores, Veith et al 1987 .

Beard et al 1989 in a retrospective multidiscriminant analysis of 49 femoro-distal non-reversed vein grafts for critical ischaemia reported that the combination of a PR value of less than 1 PRU's after the administration of papaverine hydrochloride and a retrograde flow of less 33% was able to predict success with a sensitivity of 97% and a specificity of 83%.

Flow velocity

Peak systolic flow velocities have been reported to correlate with graft outcome. Bandyk et al (1985) reported 100% graft patency at three months in grafts with end diastolic flow velocity > 0. Two of the three graft failures had peak systolic flow velocities of < 40 cms/sec and absent diastolic forward flow. Wilson et al (1988) in a combined series of vein and prosthetic grafts reported no difference in flow rates between successful and failed grafts, but there was a significant difference in the basal velocities at one month.

Input impedance

Limb impedance is the relationship between oscillatory flow and oscillatory pressure. In the absence of any significant inflow disease, limb impedance reflects down stream disease. A theoretical objection to the measurement of peripheral resistance in the arterial tree is that Poiseuille law does not apply in a pulsatile system. The arterial circulation has several features such as vessel wall compliance and blood inertia which alter the physical properties of blood flow, the electrical analogue being capacitance and inductance, both of which are frequency dependant. Input impedance therefore relates to the relationship between oscillatory flow and pressure. In theory this should be a better predictor than simple PR of graft outcome. Cave et al (1976) measured impedance at the popliteal level, but did not find this predictive of outcome. Law et al (1983) was unable to demonstrate any difference in pre and post-reconstruction impedance both at rest and after a vasodilator. Beard (1987) used Fourier transform analysis to derive an impedance value from a series of stored flow and pressure waves. He was unable to demonstrate a significant difference in the resting impedance value between successful and failed grafts but noted a marked difference in the impedance value after the administration of 15 mg of papaverine hydrochloride.

The ability to measure peripheral resistance at the time of calf vessel exploration is a more attractive proposition to the surgeon than measuring peripheral resistance on completion of the graft. This approach will help the surgeon to identify the most suitable vessel and level for the distal anastomosis. Although impedance is theoretically superior to peripheral resistance, there is as yet no on-line facilities to compute impedance.

Indirect methods of Graft assessment

Several indirect methods have been used to assess per-operative graft function including; (i) Doppler ankle pressures (Wood, Bishara and Darke 1985), (ii) air plethysmography (Clifford and Baird 1981) and (iii) TcPo2 (Gannon, Goldman, Simms et al 1986c). The disadvantage of all these techniques is the potential delay between a positive result and a successful graft.

CHAPTER 5.

PATIENTS.

Introduction.

Between October 1986 and August 1988, a total of eighty eight patients with critical ischaemia were studied in the Vascular Studies Unit at the Bristol Royal Infirmary. Of these, forty nine patients were studied prospectively, the remaining thirty nine patients were being followed up in the vascular laboratory as part of the previous research fellows work. All the patients were under the care of either Mr M Horrocks or Mr R N Baird, consultant vascular surgeons. During the prospective study, seventy three patients underwent femoro-distal reconstruction, the 24 missed cases were due to a combination of factors, including simultaneous femoro-distal reconstructions on different lists, inadequate time for assessment and absence from the department. During the same period there were 64 above knee and 71 below knee amputations, of which 3 required revision. The remaining work load of the department included 153 grafts to abdominal aortic aneurysms, (105 elective : 48 ruptured), 71 carotid endarterectomies and 119 operations for aorto-iliac occlusive disease.

Femoro-distal reconstructions.

The vast majority were admitted as an emergency either via the general practitioner or from the vascular outpatients. The patient was clerked and blood sent for (i) full blood count (FBC), (ii) plasma viscosity, (iii) cross matching, (iv) urea and electrolytes, (v) fasting blood glucose, (vi) fasting lipids and (vii) clotting studies (APPT, PT). An arteriogram was requested as a matter of urgency and the patient scheduled for urgent surgery.

Pre-operative assessment.

The pre-operative assessment usually took place the night before the operation and lasted approximately two hours. This included Doppler ankle pressures / indices at rest, calf and thigh PVR's, Pulse Generated Runoff (PGR) assessment of the calf vessels and pedal arch (see Chapter 6b) and a long saphenous vein scan (see Chapter 6d). All of these investigations were performed by myself.

Operative technique.

Femoro-distal non-reversed vein technique.

The femoro-distal non-reversed vein technique used in Bristol has been previously described in the literature (Beard, Wyatt, Scott et al 1989). In summary the important points are as follows.

Pre-operative skin preparation.

Prior to surgery all patients underwent a standard skin preparation regime. Culture swabs were taken from the feet and in particular any necrotic or frankly gangrenous areas. The affected limb was shaved and the patient had 2 betadine baths. Povidone iodine spray was applied 2 hours prior to surgery from the groin to the foot. The foot was then wrapped in a paper drape. On induction 1.5 grams of cefuroxime and 500 milligrams of metronidazole were give intravenously and continued for a further two doses in the post operative period. In the long femoro-distal reconstruction (> 4 hours) an additional dose of antibiotics was given prior to skin closure.

In the post-operative period the presence of skin erythema with a positive culture was considered a significant wound infection and was treated by antibiotics. This was then recorded on the vascular audit computer programme.

Anaesthesia.

Epidural anaesthesia using 0.25% bupivicaine was used to supplement a light general anaesthetic. This has several advantages including better haemodynamic stability, higher leg blood flow and good post operative pain control (Haljamäe, Frid, Holm et al 1988).

Exposure of the distal calf vessels.

On the basis of the PGR study, the vessel chosen for the distal anastomosis was exposed. A peripheral resistance measurement (Chapter 6f) was performed to confirm the PGR findings of a low resistance outflow tract.

The anterior tibial artery was exposed antero-laterally in the distal third of the calf. The posterior tibial artery was exposed in the distal third of the calf through a medial approach. The peroneal artery was exposed laterally by excising a short segment of the fibula. This approach was later abandoned in favour of the medial approach because of the potential dangers of damaging the peroneal artery and nerve.

Vascular control.

Proximal and distal control of the vessel was obtained by silastic slings. The small arterial branches were controlled either by a vicryl tie or a soft neurosurgical clip.

Exposure of the long saphenous vein.

During the early part of this study, the entire long saphenous vein was exposed and fully mobilised to avoid arterio-venous fistulas. Two large venous tributaries were left attached, one in the groin and the other at the level of the knee joint to help avoid the problem of twisting. The LSV was transected beyond the site of the proposed distal anastomosis, its suitability determined by the free passage of a 2mm Hall valvulotome. Following heparinization, the long saphenous vein was divided with a cuff of femoral vein after application of a curved arterial clamp. The defect in the femoral vein was then oversewn with continuous 6/0 polypropylene. The proximal LSV was incised along its posterior aspect and the end spatulated. The upper valves were then excised using microvascular scissors under direct vision.

Proximal anastomosis.

The proximal anastomosis was usually performed end to side to the common femoral artery with 6/0 polyproplene and patency confirmed with a soft Portex catheter before releasing the clamps.

Valve stripping.

The Hall valvulotome was then passed up through the vein from the distal end until it passed into the femoral artery. The valvulotome was then carefully withdrawn, at the same time rotating through 90° so as to engage and destroy all the valves. An adequate down flow was noted by allowing the blood to spurt from the open distal end of the vein. Grafts to the anterior tibial and peroneal arteries were tunnelled through a cruciate defect in the interosseous membrane. Care was taken to ensure that the vein was not rotated, kinked or trapped. A short segment of long saphenous vein was taken before and after valve stripping for subsequent examination.

Distal anastomosis.

The long saphenous vein was cut to length and the distal end spatulated. Two 6F umbilical catheters are placed into (i) the distal end of the graft and (ii) the distal artery. This ensures accurate placement of the continuous polyproplyene sutures. All the anastomoses were performed using loupe magnification (x 2.5).

On completion of the graft, the remaining proximal venous tributary was cannulated using a 18G venflon catheter. This was connected to the pressure transducer to give a mean pressure trace for the calculation of peripheral resistance and avoided the problem of inserting a needle into the graft at the end of the operation.

Per-operative assessment.

I was present at all of the femoro-distal bypasses and undertook at least one of the anastomoses. A Doppler flowmeter (see Chapter 6f), previously developed in the department was used for all the per-operative haemodynamic monitoring. I helped record all the measurements of flow and peripheral resistance, both at rest and after the administration of papaverine hydrochloride.

The specimen of long saphenous vein was transported to the Department of Pathology where Dr Milroy, Registrar in Histopathology and I distended the vein segment with agar. Once this had been completed, the vein was fixed in 10% formalin. Sections of the vein were cut and stained by the technical staff in the department. Every month, the specimens were reviewed and graded by Dr Milroy and myself. The specimen for electron microscopy was transported to the Bristol Medical School, Department of Anatomy, where Mr Heap processed and evaluated the specimen.

Post-operative assessment.

During the period of this study, I established a graft follow up programme for the femoro-distal bypass grafts. Eighty one patients, which included the 49 prospective patients were recruited into the graft follow up programme. The patients were reviewed on the first and seventh post-operative day. The assessment included clinical review, a resting Doppler ankle pressure and index, and insonation of the graft in the mid-thigh position using a portable 10MHz

Doppler.

Following discharge, patients were sent appointments to attend the Vascular Studies Unit at one month following operation and at three monthly intervals for one year. Thereafter, the appointments were six monthly for up to 2 years. The assessment included (i) resting and post exercise Doppler ankle pressures and indices and (ii) Duplex derived volume flow at rest and after calf hyperaemia, using a Technicare duplex scanner.

Graft outcome.

A successful graft was defined as (i) patent on Duplex or IA DSA, (ii) a rise in the ABI of > 0.25 and (iii) an improvement in the patients clinical symptoms. All three factors had to be present for the graft to be deemed successful.

CHAPTER 6a.

METHODS OF ASSESSMENT.

ARTERIOGRAPHY

Introduction.

Prior to femoro-distal reconstruction, all patients underwent a conventional arteriogram with intra-arterial digital subtraction views of the calf vessel runoff. These were performed by one of two consultant radiologist (Dr W D Jeans, Dr GG Hartnell), a senior registrar attached to the vascular radiology suite or by a junior registrar under supervision. A weekly vascular radiology conference, enabled a close liaison to develop between the two consultant vascular surgeons and the radiology staff. In particular, the exclusion of significant inflow disease, the possibility of a pre-operative balloon angioplasty and good views of the distal runoff were regularly stressed at these meetings.

Equipment and arteriographic technique.

Equipment.

A L-U arm X-ray apparatus (IGE) with an undercouch tube and overcouch image intensifier was used in conjunction with either a 100 mm film or 14 Puck film changer, and the television monitor linked to an Idis add on digital subtraction unit recording 3 images per second. Selected images were permanently recorded with an Agfa film recorder using 2 images on a 25 cm x 20 cm film. Intra-arterial injections were performed at a rate of 12 mls/sec for standard aortograms using a Simtrack automatic injector.

Contrast Medium.

Omnopaque 300 mg I^2 per ml was used for all the aortograms. A total of 40-50 mls of contrast was used per run. Films were taken as follows;

1	at	1 / sec	for the abdominal aorta.
1	at	1 / sec	at the pelvis
1	at	1 / sec	for the hips and thighs.
2	at	1 / sec	for the knees.
3	at	1 / sec	for the lower calf and ankles.

Catheters.

From a femoral puncture aortic injections were performed with a 5 or 7F pig tail catheter introduced over a 0.35 guide wire with a 3 mm J tip. Standard views of the aorta, aorto-iliac segment, groin, thighs, knees and special views of the runoff were obtained.

Additional Views.

In the case of a suspected iliac stenosis, 20° oblique views were obtained (Figure 6) and direct arterial pressure measurements were made either side of the stenosis using the pull-through technique or with bilateral common femoral artery pressure lines. Pressure measurements were made at rest and after the administration of 30 mg of papaverine hydrochloride. A pressure difference of greater than 15 mmHg after papaverine hydrochloride was considered significant and the lesion dilated.

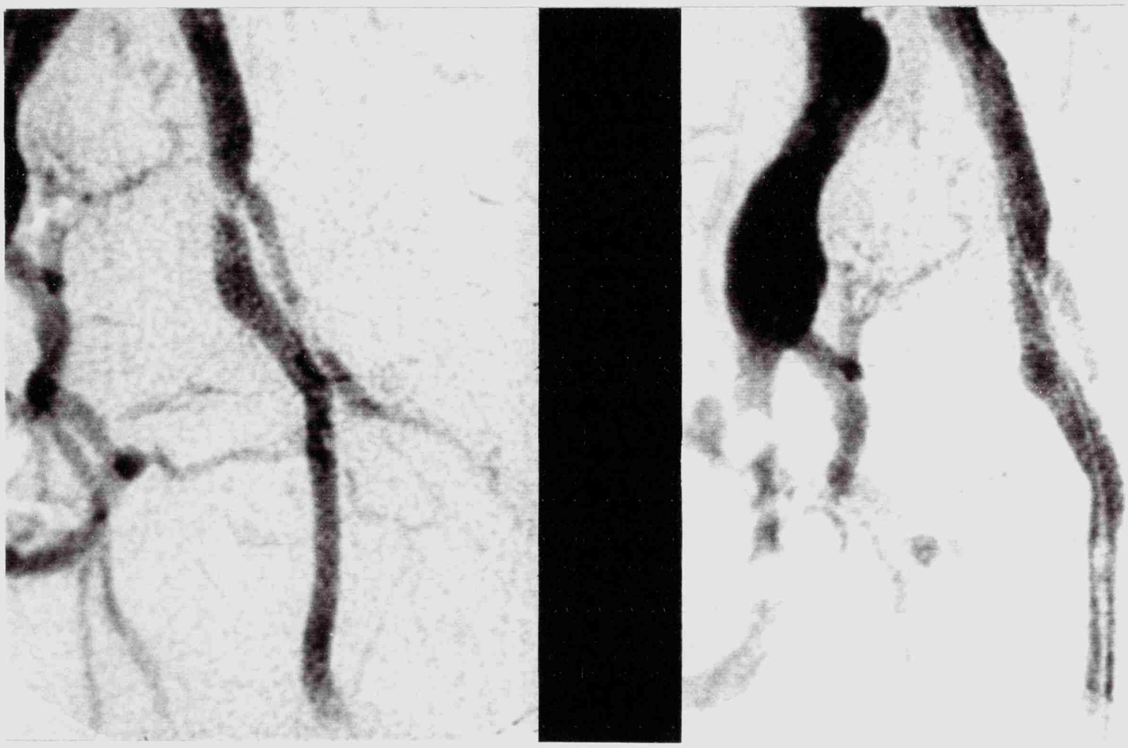


Figure 6. On the left is an oblique view of a left iliac system showing a previously unsuspected external iliac artery stenosis and on the right the post-angioplasty film.

<u>Balloon Angioplasty.</u>

Meditech balloon catheters (90 cms length) were introduced over a 0.35 guide wire. Iliac lesions were dilated with either a 6, 7 or 8 mm balloons and superficial femoral artery lesions with 4, 5 or 6 mm balloons. These were inflated to the manufactures recommended pressure (MRP) usually 5 - 16 atmospheres. On completion of the angioplasty, the pressures above and below the site of the stenosis were measured at rest and after the administration of papaverine hydrochloride.

Intra-arterial digital subtraction arteriography (IA DSA).

DSA views of the lower leg were obtained when there was inadequate visualization of the distal calf vessels. The leg was internally rotated to separate the fibula from the tibia, allowing all three calf vessels to be visualised (Figure 7).

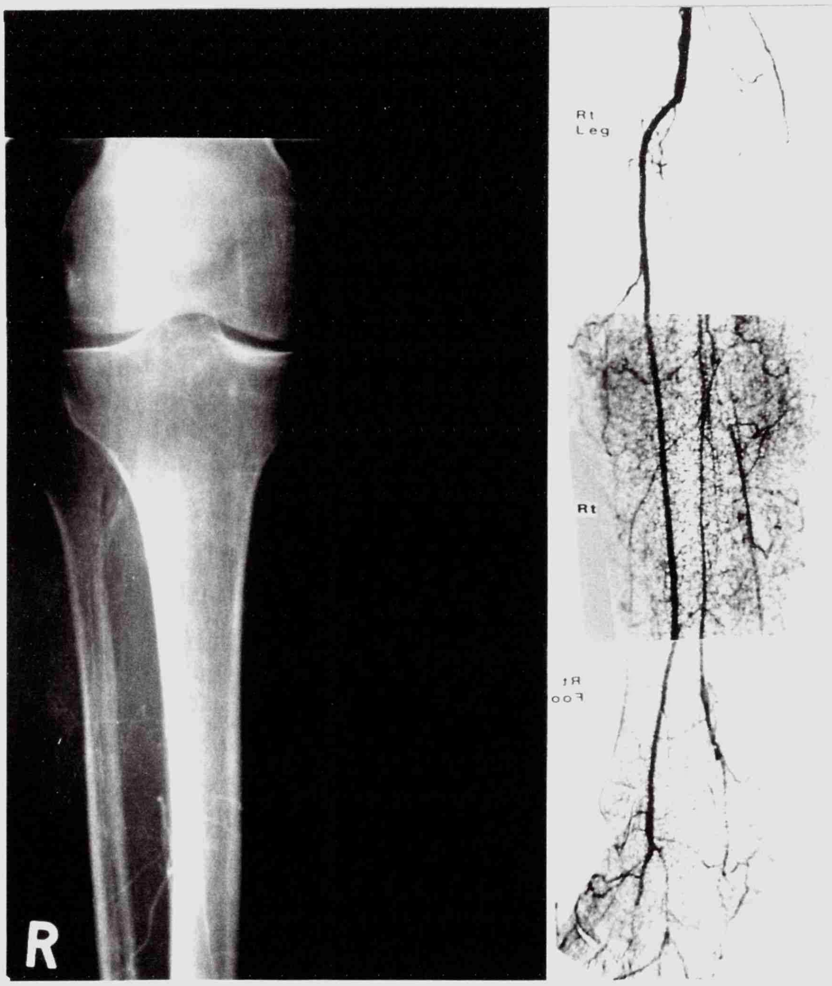


Figure 7. On the left is a conventional arteriogram, with little evidence of runoff. On the right is a IA DSA film of the same leg showing a patent anterior tibial artery in continuity with an incomplete pedal arch.

Dorsal and plantar pedal arches were visualised on a lateral oblique DSA view in the latter half of the series (Figure 8) .

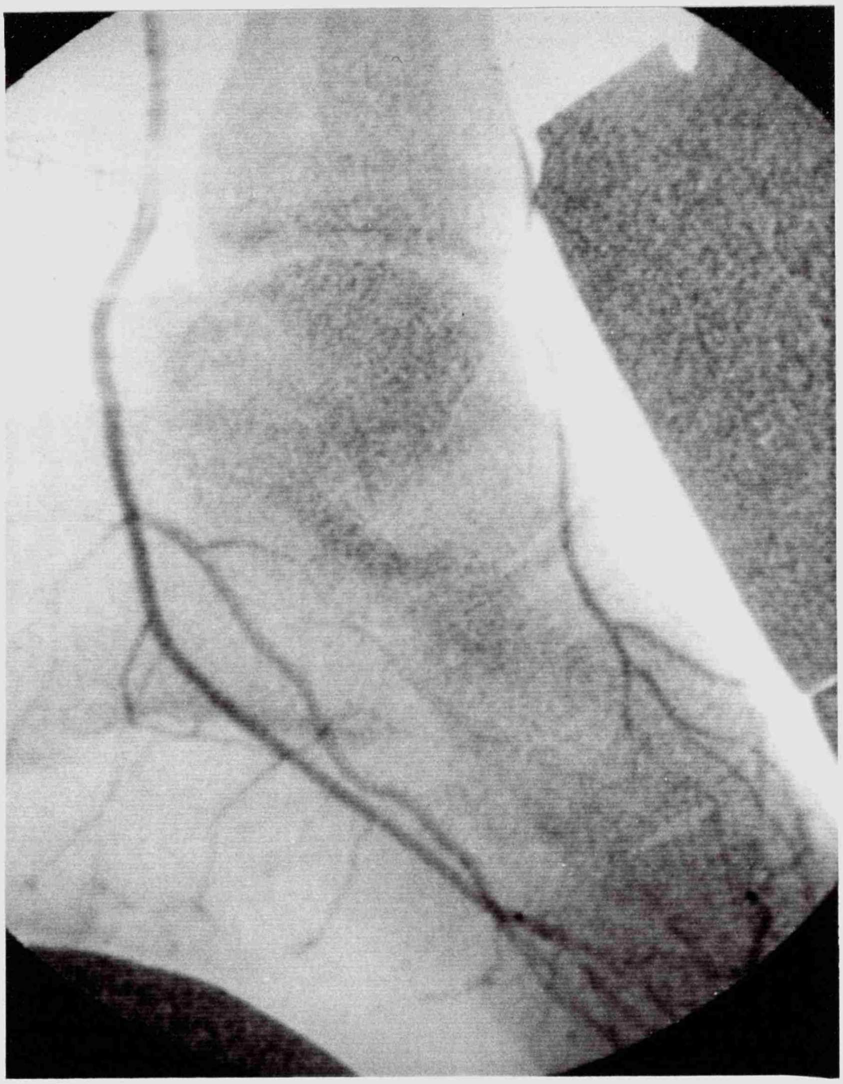


Figure 8. IA DSA film showing a patent distal posterior tibial artery dividing into the medial and lateral plantar arteries. On the dorsal aspect of the foot the dorsalis pedis artery is in continuity with the plantar arch via the deep plantar artery.

Per-operative arteriograms were only performed if the haemodynamic assessment highlighted a technical problem.

Post-operative IA DSA views.

A green needle (21G x 1½, Gillette) was inserted directly into the common femoral artery above the hood of the proximal anastomosis. This was connected to a 20 ml syringe. Eight ml bolus injections of Omnipaque 240 mgs I^2/ml were performed in conjunction with DSA imaging. A radiopaque ruler marker was placed alongside the leg to enable accurate measurement of vein size and to locate any arterio-venous fistulas. Particular attention was made of the proximal and distal anastomoses, the distal calf vessel runoff and the presence or absence of a dorsal/plantar arch (Figure 9).

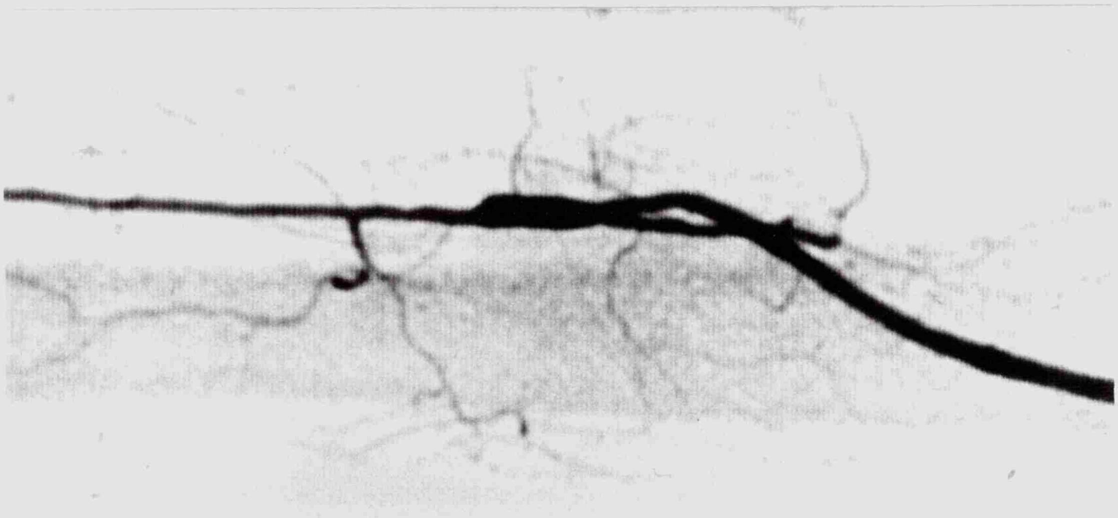


Figure 9. Post-operative IA-DSA showing a patent femoro-anterior tibial non-reversed vein graft with good runoff.

Arteriographic scoring systems.

Arteriographic visualization of distal calf vessel runoff may be hampered by the presence of multisegment disease and a poor cardiac output. In an attempt to improve the predictive value of arteriography, various arteriogram scoring systems have been devised, ranging from the simple to the complex. Three scoring systems A, B and C were evaluated in this study. Scoring system A had been widely used in the Vascular Studies Unit to semi-quantify calf vessel runoff. Scoring system B had been reported as part of combined clinical, Doppler and arteriographic assessment to determine the level of reconstruction (Shearman, Gwyn, Curran et al 1986). Finally scoring system C was the result of the ad hoc committee (Society of Vascular Surgeons, SVS and International Society for Cardiovascular Surgery, ISCVS) on reporting standards. They devised a new arteriographic scoring system to quantify runoff at the site of the proposed distal anastomosis. The scoring system could be used for any type of reconstruction below the level of the inguinal ligament.

Scoring system A

Two points were given to a widely patent vessel going down to the ankle, one point for a diseased but patent vessel to the ankle and no points for an occluded vessel, resulting in a range from 0 to 6, where 6 represents an excellent runoff (Figure 10).

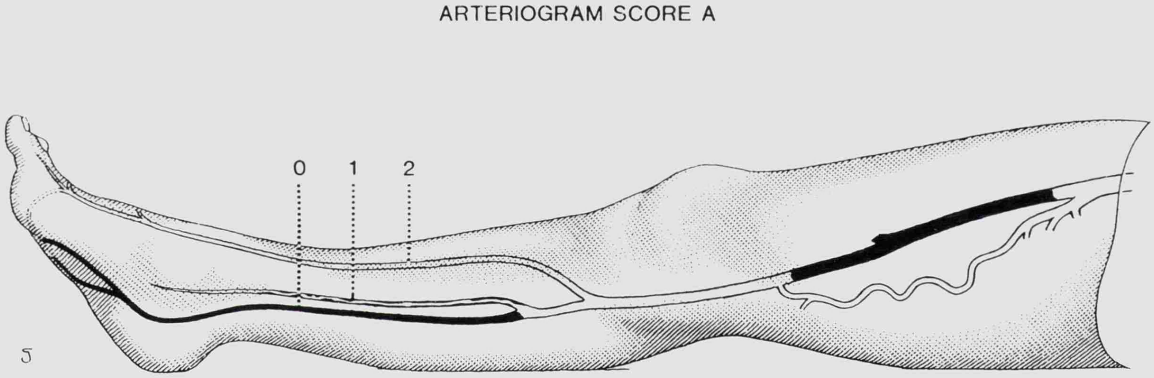


Figure 10. Arteriographic scoring system A.

Scoring system B

In this scoring system the calf vessels were assessed over the first 5 cms from their origins. Two points were given for a normal vessel, one point for a diseased vessel with a greater than 50% stenosis and no points for an occlusion resulting in a possible range of 0 to 6, where 6 represents an excellent runoff, (Figure 11), (Shearman, Gwyn, Curran, et al 1986).

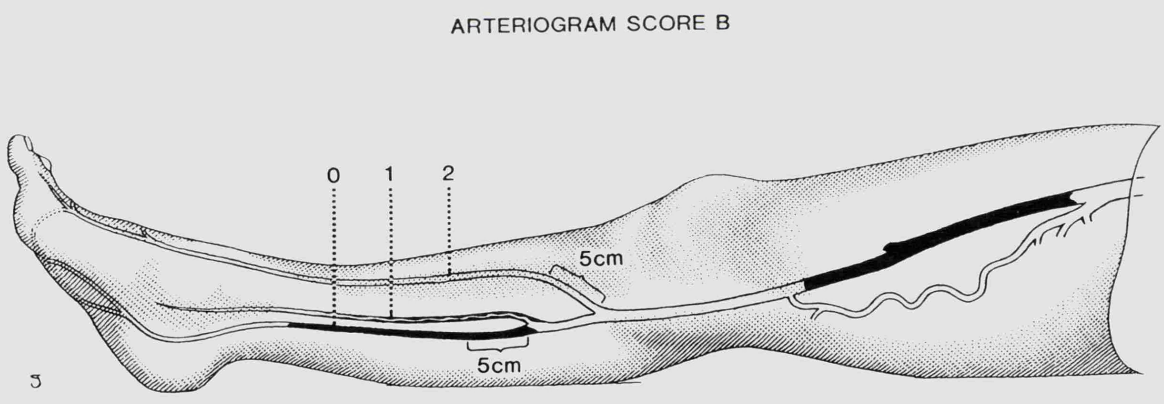


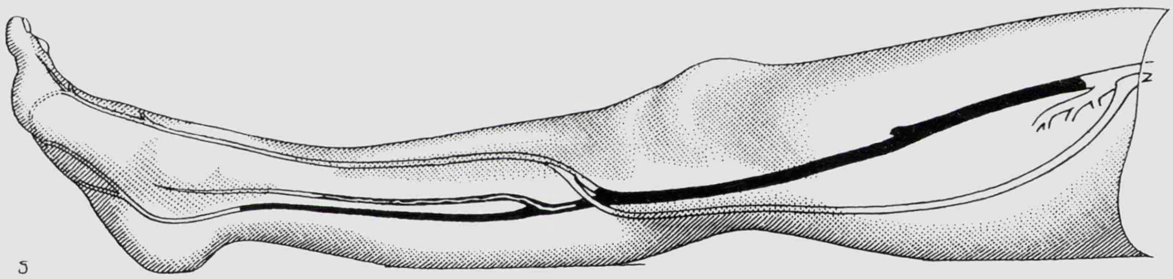
Figure 11. Arteriographic scoring system B.

Scoring system C

In an attempt to standardise the various arteriographic scoring systems the Committee on reporting standards of the Society for Vascular Surgery and the International Society for Cardiovascular Surgery (SVS/ISCVS) devised a new runoff grading system which could be applied to any level of the infra-inguinal arterial tree (Rutherford, Flanigan, Gupta et al 1986). The runoff was assessed at the proposed site of the distal anastomosis. This is a complex scoring system and is based upon the patency (degree of occlusion) of the recipient vessel and its relative contribution to the outflow tract (Table 7). Three points are assigned to the runoff vessels at the site of the proposed distal anastomosis (Table 7). This is multiplied by the degree of occlusion within the runoff vessels to give a maximum score of 9 (3x3). In the situation of a widely patent vessel to the ankle, there is a degree of resistance to the flow of blood ie a base resistance value, which is given a value of 1 point. In contrast to the previously described scoring systems a score of 1 corresponds to an excellent runoff and 10 to a blind segment (Figures 12 & 13).

In Figure 12, the graft is anastomosed to the proximal anterior tibial artery There are two runoff vessels, the distal tibial scores 2 points and the pedal arch 1 point, thus giving a total of 3. Each vessel score is then multiplied by the degree of occlusion present in that vessel. In this case zero. The arteriogram score for this graft is 2x0 (AT) + 1x0 (Pedal arch) + 1 (base resistance) = 1.

ARTERIOGRAM SCORE C

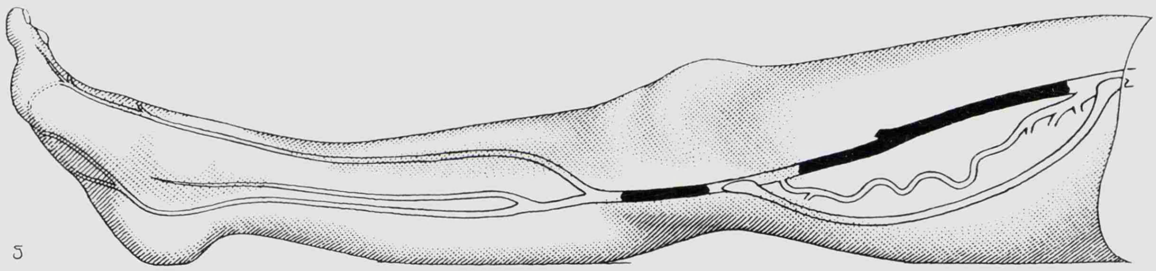


Anterior tibial = 2x0 : Arch 1x0 : Total 0+0+1=1

Figure 12. Arteriographic scoring system C. This shows a graft anastomosed to a patent anterior tibial artery and pedal arch.

In Figure 13, the graft is anastomosed to the above knee popliteal artery. The runoff vessel is the distal popliteal which scores 3 points (Table 7). This is multiplied by the degree of occlusion, in this case 3 for a total occlusion. The arteriogram score is therefore 3(DP) x 3 + 1 (base resistance) = 10.

ARTERIOGRAM SCORE C



Popliteal blind segment = 3x3+1=10

Figure 13. Arteriographic scoring system C. This shows a graft anastomosed to a popliteal blind segment with no runoff.

Table 7.Scoring system C;

Weighting of the individual vessels.

Site of	No of units assigned*		
Distal Anastomosis	3	2	1
Common iliac		Ext iliac	Hypogastric
External iliac	CFA	SFA	PFA
Common Femoral		SFA	PFA
Popliteal Above Knee		Distal Pop	AT PT PER
Anterior Tibial		Distal Tib	Pedal Arch
Posterior Tibial		Distal Tib	Pedal Arch
Peroneal		Pedal Arch	Collaterals to AT or PT arteries
Dorsalis Pedis		Pedal Arch +	

* Points assigned for degree of occlusion.

0 = Normal or minimal evidence of disease, < 20% narrowing.

1 = 20 - 49% stenosed.

2 = 50 - 99% stenosed.

2.5 = occluded for less than half its length with visible collaterals.

3.0 = occluded throughout most of its length.

\+ = Pedal Arch score, 0 = completely patent arch, 1.5 = partial occlusion, 3.0 = little or no arch visualised.

In this study a total of 88 patient arteriograms (forty nine prospective and thirty nine retrospective patients) were scored using the three scoring systems by myself and Dr Hunt, Registrar in the Department of Radiodiagnosis.

CHAPTER 6b

METHODS OF ASSESSMENT.

PULSE GENERATED RUNOFF (PGR).

Pulse Generated Runoff: Calf vessel assessment.

Arteriography is an expensive invasive procedure, not without complications. In patients with severe distal disease, arteriography may miss patent distal calf vessels as a result of contrast dilution and sedimentation. Simple Doppler examination of the dependant foot provides an alternative approach to the assessment of patients with critical ischaemia. However, the progressive damping effect of multisegment disease makes interpretation of the Doppler signals difficult. This problem has been overcome with the development of Pulse Generated Runoff (PGR), a simple, inexpensive non-invasive test of calf vessel patency.

Principles of the technique for assessing calf vessels.

In critical ischaemia, the distal calf vessel waveforms are often damped as a result of proximal disease. The interpretation of these signals is difficult, as the vessel may well be disease free and suitable for a femoro-distal bypass graft (Figure 14).

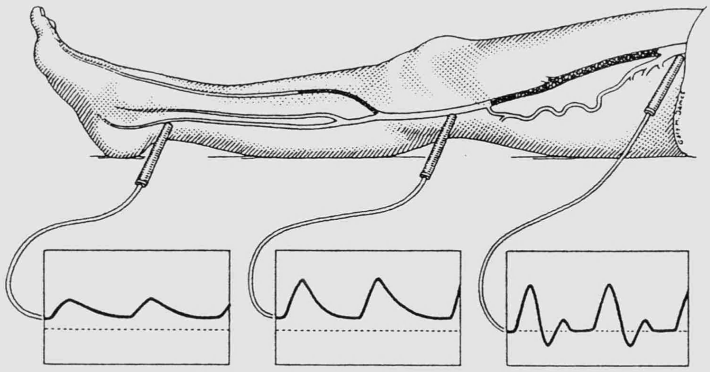


Figure 14. Progressive damping of the Doppler waveform down the arterial tree.

A new pressure wave was generated by a pulsatile cuff wrapped tightly around the upper calf. The augmented waveform could than be detected at the ankle if the calf vessel was patent (Figure 15).

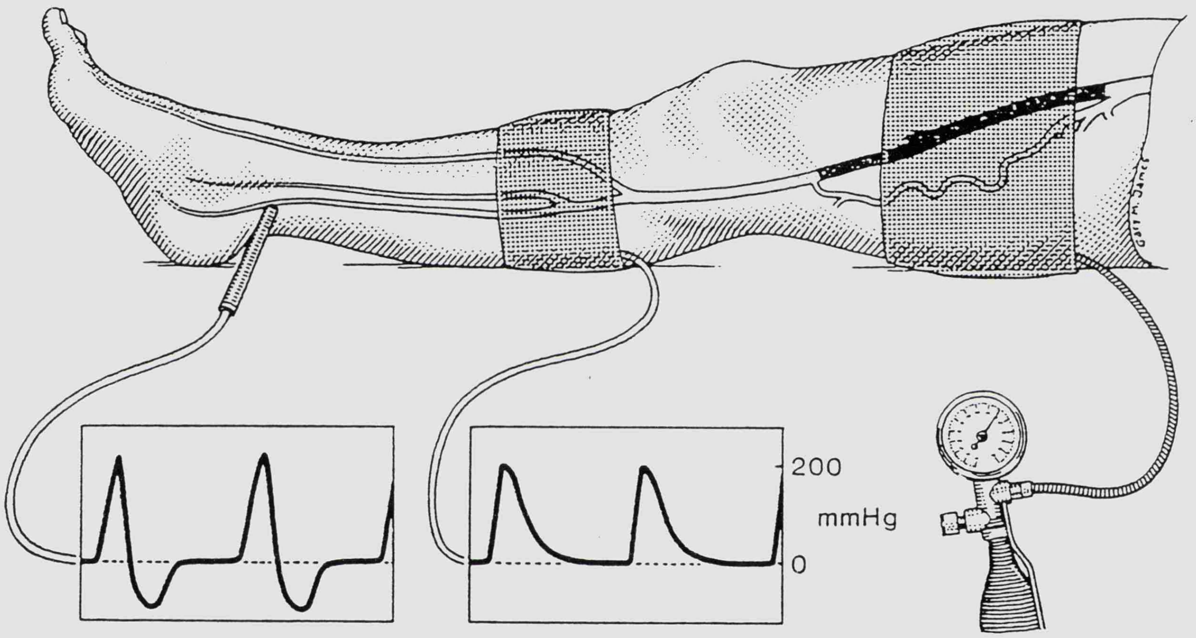


Figure 15. Pulsatile cuff at the upper calf with its corresponding pressure wave trace. The Doppler trace on the left shows the resultant augmented Doppler waveform at the ankle. The proximal thigh cuff is occasionally used in those patients with a patent superficial femoral artery, usually diabetics with distal disease.

The calf vessel required accurate insonation to avoid interference with the venae comitantes. In those patients with a patent superficial femoral artery a thigh occlusive cuff was often necessary to prevent retrograde flow. The presence of valves within the venous system prevented retrograde flow and misinterpretation of the Doppler signal. A simple non-invasive system, pulse generated runoff (PGR) has been developed to assess calf vessel patency. The system is based upon a standard 10MHz Doppler ultrasound velocimeter linked to a chart recorder (Figure 16).

Figure 16. 10MHz Doppler pencil probe linked to a chart recorder. Arrowed on the right is the compressed air pipe which drives the control unit on top of the Vasoflo.

The control unit for the cuff consists of 2 separate modules (pulsatile and occlusive). The occlusive thigh cuff was occasionally used for those patients, usually diabetic, with a patent superficial femoral artery. Inflation and deflation of the pulsatile cuff was controlled by a 2-way solenoid valve and an in-line solid state pressure transducer. This enabled the inflating pressure to be varied between 0-300 mmHg and the rate of inflation-deflation between 0-100 per minute. On the whole an inflation pressure of 300 mmHg and 50 cycles per minute were used in the assessment of these patients.

Before the PGR study all patients were rested for ten minutes with the legs in a dependant position. The nature of the test was explained to the patient, in particular, the sudden inflation of the cuff. This often avoided the problem of the patient suddenly moving the leg, during insonation of a distal calf vessel. The patient was placed in a supine position with the heels resting on a support. An inflatable cuff was wrapped tightly around the upper calf (Figure 17).

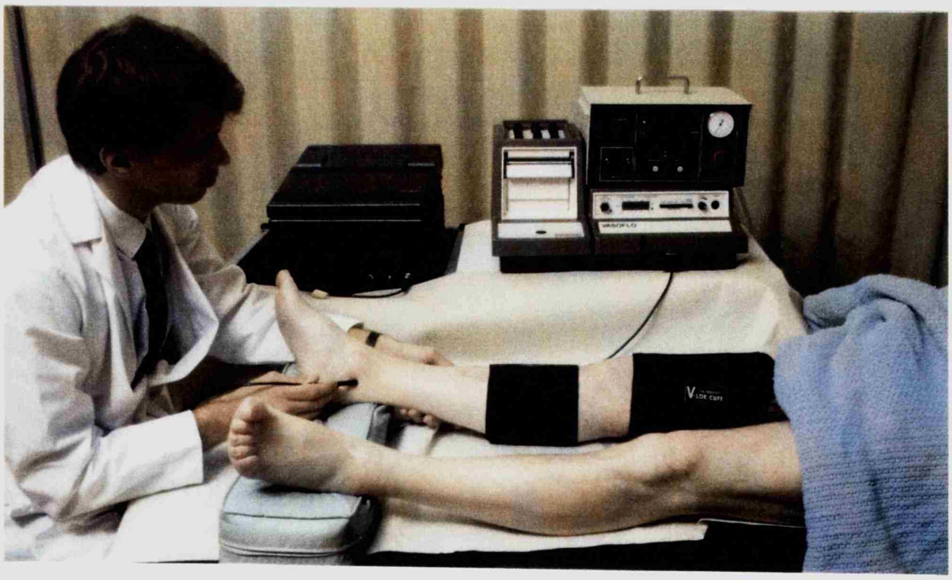


Figure 17. PGR system in clinical use.

This was rapidly inflated and deflated to a pressure of 300 mmHg at 50 cycles per minute. Pressure controlled release valves enabled the clinician to vary the pressure and rate of inflation The anterior tibial (AT), posterior tibial (PT) and peroneal (PER) arteries were assessed at the ankle using a 10 MHz Doppler hand held pencil probe (Figure 18). If no signal or a damped signal was obtained at the ankle, the proximal cuff was repositioned over the calf. In patients with severe ischaemia, there were often unable to tolerate prolonged examinations.

To ensure accurate identification of the calf vessel, the signals were traced into the proximal calf. This was particularly important in the case of the peroneal artery which often fed the dorsalis pedis artery via a collateral branch passing over the lateral malleolus.

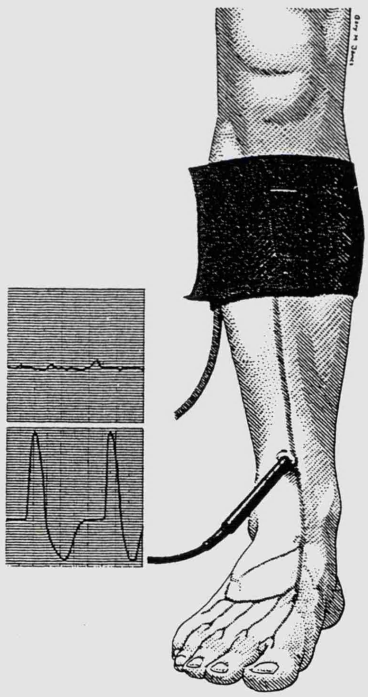


Figure 18. 10 MHz Doppler probe insonating the anterior tibial artery. The top trace on the left shows a non-pulsatile signal at rest and on the right a biphasic waveform with the PGR system.

Each vessel was scored out of 2 (0 = no signal, 1 = monophasic and 2 = biphasic waveforms), giving a maximum score of 6 for each leg (Figure 19).

Figure 19. PGR scoring system.

CHAPTER 6c
METHODS OF ASSESSMENT.
PULSE GENERATED RUNOFF (PGR) ASSESSMENT OF THE PEDAL ARCH.

Introduction

Calf vessel continuity with an intact primary pedal arch appears to be an important factor in successful femoro-distal bypass (Kahn, Lindenauer, Dent et al 1973, Dardik, Ibrahim, Koslow et al 1978, O'Mara, Flinn, Neiman, et al 1981, Simms 1988. Pre-operative arteriography may fail to demonstrate these vessels as a result of severe multisegment disease, poor myocardial function, both of which lead to contrast dilution, sedimentation and a failure to opacify the vessels. Pre-bypass operative arteriography (POA) avoids the problem of contrast dilution and has been reported to improve the visualization of both distal calf vessels and the pedal arches (Scarpato, Gembarowicz, Forber et al 1981, Flanigan, Williams, Keifer et al 1982). Using this technique Klimach and Charlesworth (1983) reported a significant correlation between the number of patent pedal vessels and graft patency at 12 months. Similar results were reported by O'Mara, Flinn, Neiman et al in 1981 who used completion arteriography to determine the state of the pedal arch. He reported a significant difference in the early graft patency between an intact primary pedal arch and an occluded arch.

Despite the improved visualisation with POA and completion arteriography, both techniques fail to provide any functional information about the most suitable vessel for the distal anastomosis. Both techniques are performed during the operation and do not allow for pre-operative selection, which is important not only in terms of graft outcome, but also in planning efficient theatre utilisation and resource allocation.

Dible in 1966 reported that in severe ischaemia the distal vessels were often patent; dorsalis pedis 65%, lateral plantar 70%, medial plantar 82.5% and digital 92%.

It is clear that there is a group of patients who have no evidence of runoff on arteriography but have patent distal calf vessels and in whom it is possible to reconstruct.

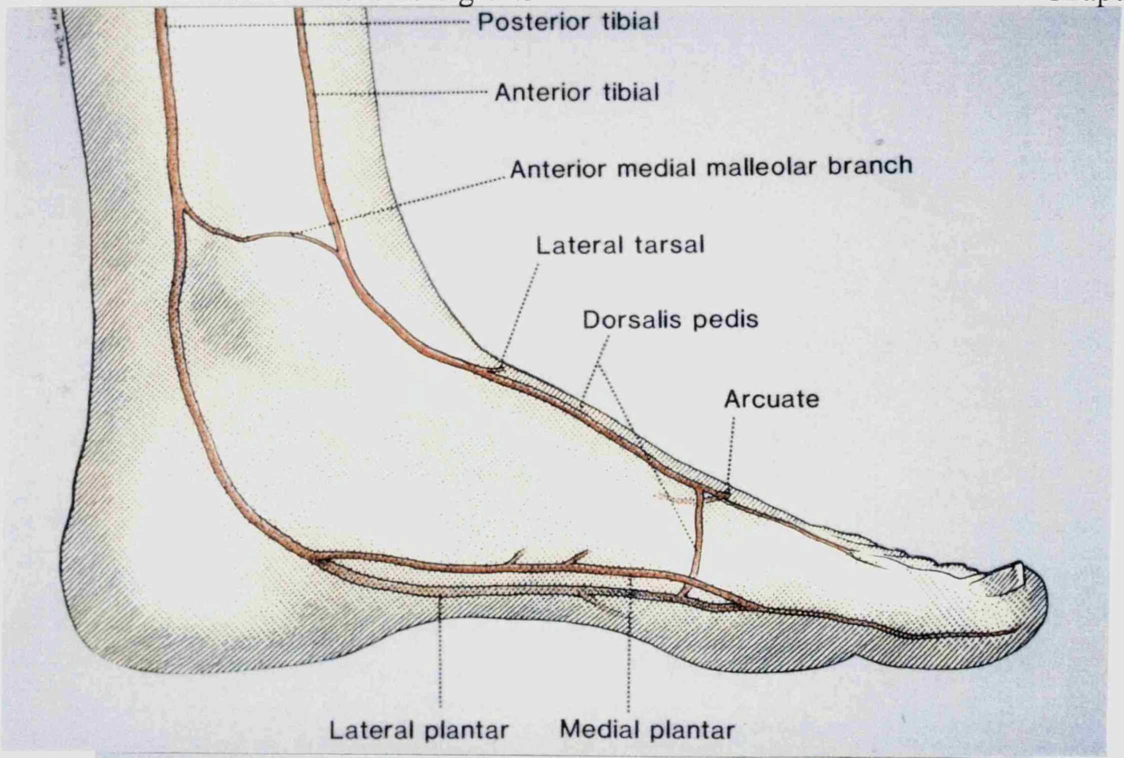
Doppler ultrasound assessment of the pedal arch was first described by Roedersheimer, Feins and Green in 1981. The pedal arch patency test identifies both the dominant and number of vessels feeding the pedal arch. More recently Simms (1988) has evaluated this technique in a series of patients undergoing femoro-distal bypass for critical ischaemia. He reported that an apparently occluded pedal arch could be shown to be patent following successful femoro-distal bypass. He concluded that selection for femoro-distal bypass be based upon a combination of Doppler and POA. This combined technique does not allow for pre-operative selection of the most appropriate distal calf vessel.

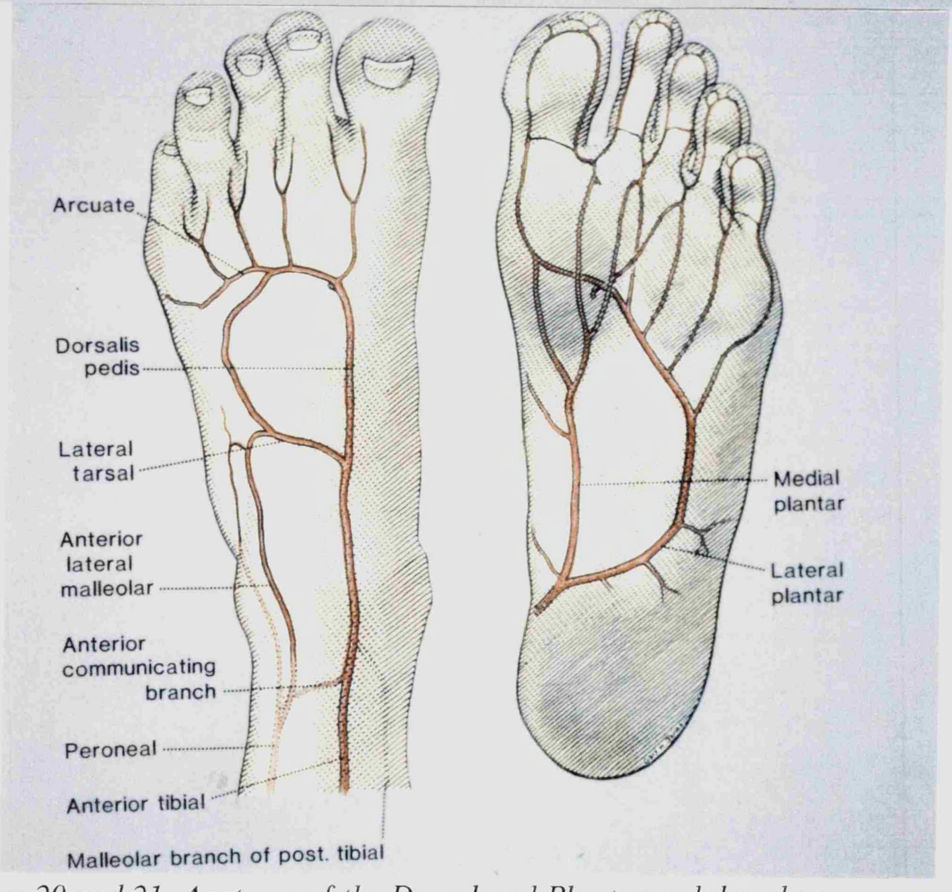
The measurement of peripheral resistance has recently been suggested as a better predictor of short term function in femoro-popliteal and femoro-distal graft (Ascer, Veith, White-Flores et al 1987, Parvin 1987). There have been few studies on the influence of the pedal arch on both graft flow and resistance (Dardik, Ibrahim, Koslow et al 1978, Harris and Campbell 1983). Dardik et al 1978 reported no difference in the resting flow between grafts with an intact and occluded pedal arch. Following the administration of papaverine higher flow rates were noted in grafts with an intact pedal arch. By contrast, Harris and Campbell (1983) reported a significantly higher flow rate in grafts to an intact pedal arch. In those patients with an occluded pedal arch, the construction of a dAVF resulted in similar graft flow rates between the intact and occluded pedal arch groups.

Anatomy of the pedal arches.

Anterior Tibial artery.

At the level of the ankle joint the anterior tibial artery continues into the foot as the dorsalis pedis artery (Figures 20 and 21). It passes along the medial aspect of the dorsum of the foot, lying lateral to the extensor hallucis longus tendon and medial to the first tendon of the extensor digitorum longus. At the level of the navicular the dorsalis pedis gives off medial and lateral tarsal arteries. The latter passes beneath the extensor digitorum brevis to anastomose with the arcuate, anterior lateral malleolar, lateral plantar arteries and with perforating branches from the peroneal. Opposite the medial cuneiform, the dorsalis pedis artery gives of the arcuate artery, which passes across the bases of the metatarsal bones deep to the extensor digitorum longus tendons. The dorsalis pedis artery terminates at the first web space, but before this it gives off the first dorsal metatarsal artery. At the first web space the artery passes through the two heads of the first dorsal interosseous muscle as the deep plantar artery to complete the plantar arch.





Figures 20 and 21. Anatomy of the Dorsal and Plantar pedal arches.

Posterior Tibial artery.

The posterior tibial artery divides under the abductor hallucis into the medial and lateral plantar arteries. The latter is the larger of the two and passes laterally to the base of the fifth metatarsal bone. It then courses medially to the space between the first and second metatarsal bones to join with the deep plantar artery from the anterior tibial artery to form the primary pedal arch. The medial plantar artery passes along the medial aspect of the foot to anastomose with a branch of the first metatarsal artery. It also supplies branches to the first, second and third plantar metatarsal arteries.

Peroneal artery.

The peroneal artery gives off anterior and posterior perforating branches 4 - 6 cms proximal to the ankle joint. The anterior branch joins with dorsalis pedis artery and the posterior with either the medial or lateral plantar arteries.

Primary and secondary pedal arches.

Primary pedal arch.

A primary pedal arch consists of a patent system between the dorsalis pedis artery via the deep plantar artery to the lateral plantar artery from the posterior tibial artery.

Secondary pedal arches.

The secondary pedal arches are formed by three major collateral networks; (i) medial plantar (PT) - medial tarsal group (DP), (ii) lateral tarsal (DP)- lateral plantar (PT) and the (iii) arcuate (DP) - lateral plantar (PT) group. All these systems provide filling of the dorsalis pedis (DP) and posterior tibial (PT) arteries.

Pedal Arch Patency Test of Roedersheimer.

A patent primary pedal arch can be defined anatomically as direct continuity between a patent dorsalis pedis artery, deep plantar artery, lateral plantar artery, and posterior tibial artery. This can be demonstrated on Doppler examination by an audible Doppler signal (pedal arch signal) in the first web space. Continuity between the tibial vessels and the pedal arch is determined by a modified Allen's test, previously described for the hand. The deep plantar artery is insonated in the first web space using a 10MHz Doppler probe. The individual calf vessels are then compressed in turn at the ankle joint. If only one vessel communicates with the pedal arch, the Doppler signal is obliterated. If more than one tibial vessel is in continuity with the pedal arch, compression will result in attenuation of the pedal arch signal. That which gives the greatest attenuation is defined as the major inflow vessel of the arch.

In severe ischaemia the pedal arch signal may be absent as a result of inadequate inflow. Simms in 1988 reported a 69% improvement in the pedal arch status, as defined by the pedal arch patency test of Roedersheimer, after successful femoro-distal bypass. To try and obviate this false negative result, PGR was used to improve the pedal arch signal and to physically map out the dorsal and plantar pedal arches (Figures 20 and 21).

The inflatable cuff was wrapped around the upper calf and ultrasonic jelly placed along the course of the dorsalis pedis, lateral tarsal and arcuate arteries. As before the cuff was inflated to a pressure of 300 mmHg at 50 cycles per minute. If no Doppler signal was obtained, the cuff was moved to the mid calf level. This was often poorly tolerated in patients with severe ischaemia and so only short periods of cuff pulsation could be used. The dorsal arch was easy to assess because of its superficial position. In contrast the plantar arch, in particular the medial plantar artery, was difficult to insonate due to its size and deep location in the sole of the foot.

Patency of the primary pedal arch, and by inference the lateral plantar artery, was determined by a persistent Doppler signal in the first web space with simultaneous compression of both of the anterior tibial and peroneal arteries. PGR was combined with the previously described pedal arch patency test of Roedershemier to determine the dominant inflow vessel and the total number of calf vessels feeding the arch (Figure 22).

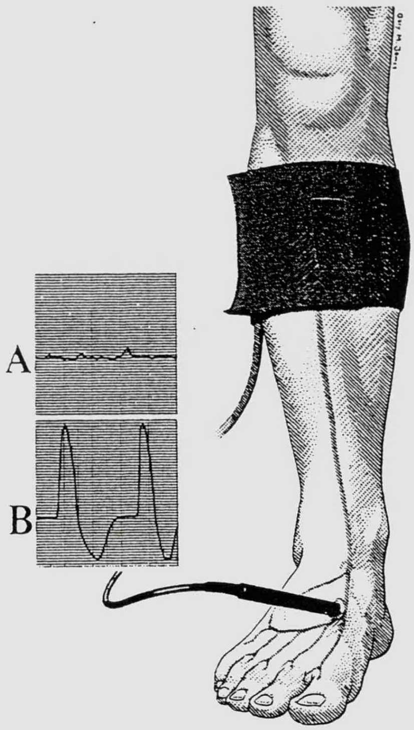


Figure 22. The deep plantar artery is isonated in the first web space. The top trace (A) shows a non-pulsatile signal but using the PGR system a biphasic waveform (B) was obtained suggesting a patent pedal arch.

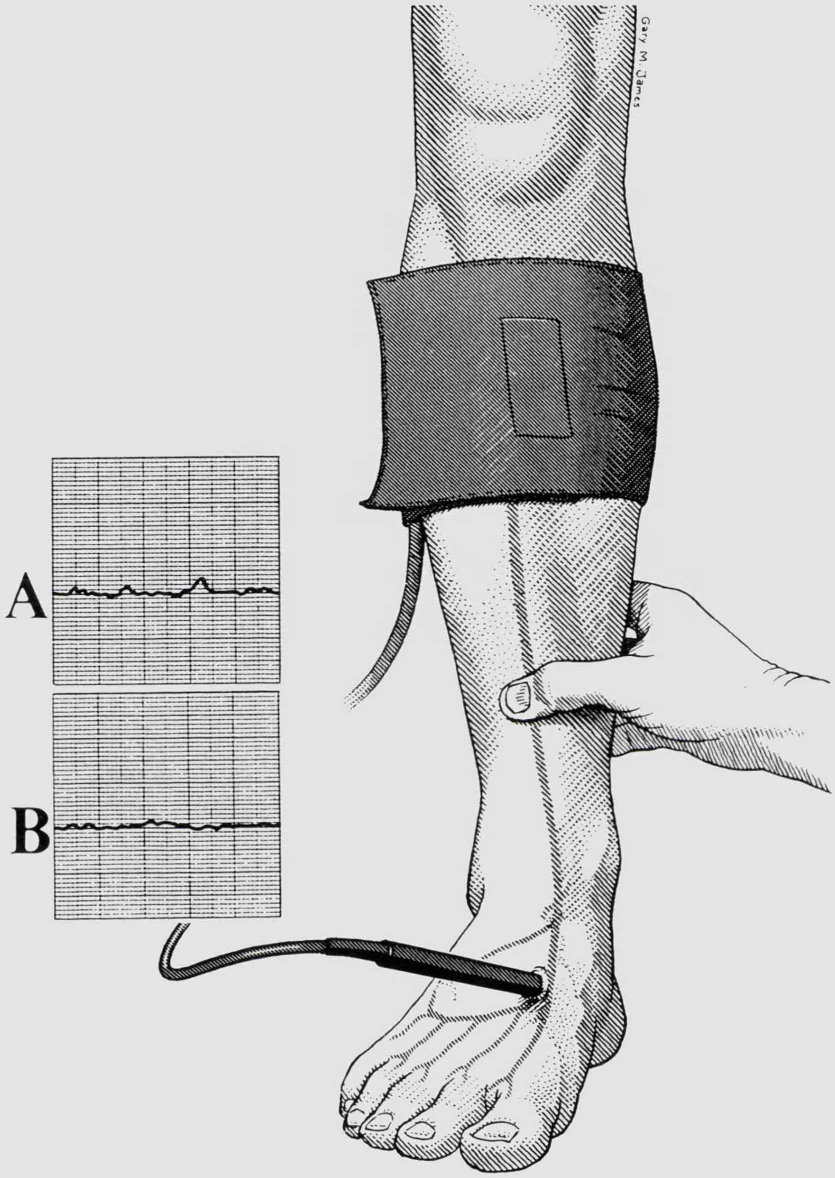


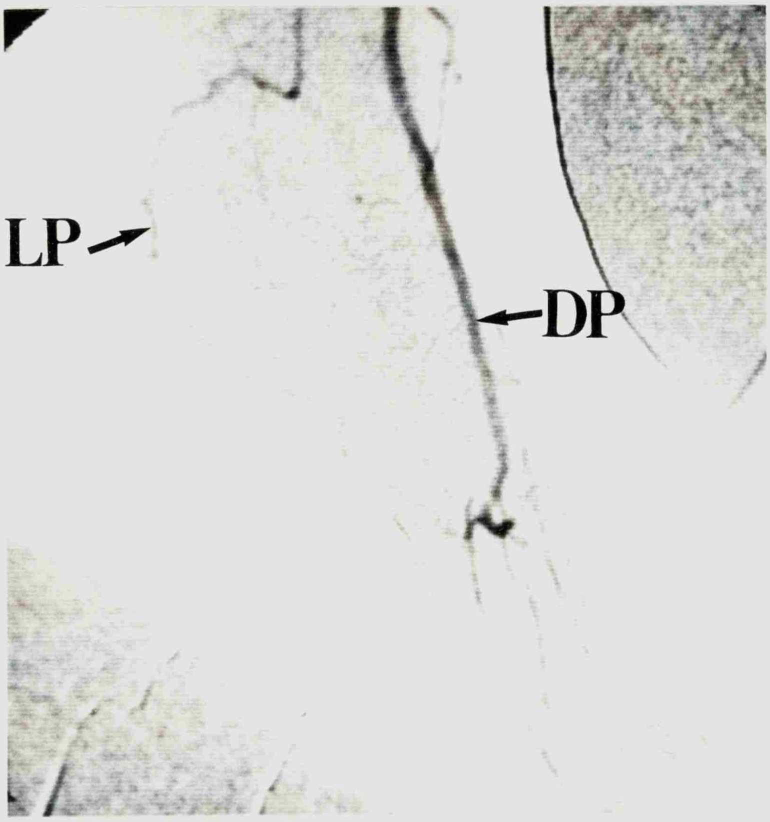
Figure 23. PGR combined pedal arch patency test of Roedersheimer. Compression of the anterior tibial artery has obliterated the biphasic pedal arch signal (B). Conclusion: Incomplete pedal arch.

Pedal arch scoring system.

A semi-quantitative grading system, previously described by Simms (1988) was used to define the pedal arch status. This was based upon the number of vessels feeding the arch; complete (2), incomplete (1) and occluded (0).

Radiological confirmation of pedal arch status.

Confirmation of the PGR status of the pedal arch was obtained in a series of one week post-operative IA DSA films of functioning grafts. Figure 24 shows an example of an incomplete pedal arch on the PGR mapping. The dorsalis pedis artery is patent to the first web space. Compression of the anterior tibial artery resulted in obliteration of the Doppler signal in the first space. The one week IA DSA oblique film of the pedal arches confirms a widely patent dorsalis pedis artery and a partially filled lateral plantar artery by an unnamed collateral vessel. Figure 25 shows an example of a complete pedal arch in a patient with a functioning distal anterior tibial graft. The pre-operative PGR map showed a patent primary pedal arch with the pedal arch Doppler signal remaining despite compression of the anterior tibial and peroneal arteries. This was confirmed on the one week IA DSA which shows contrast filling the lateral plantar artery and refluxing up the posterior tibial artery.



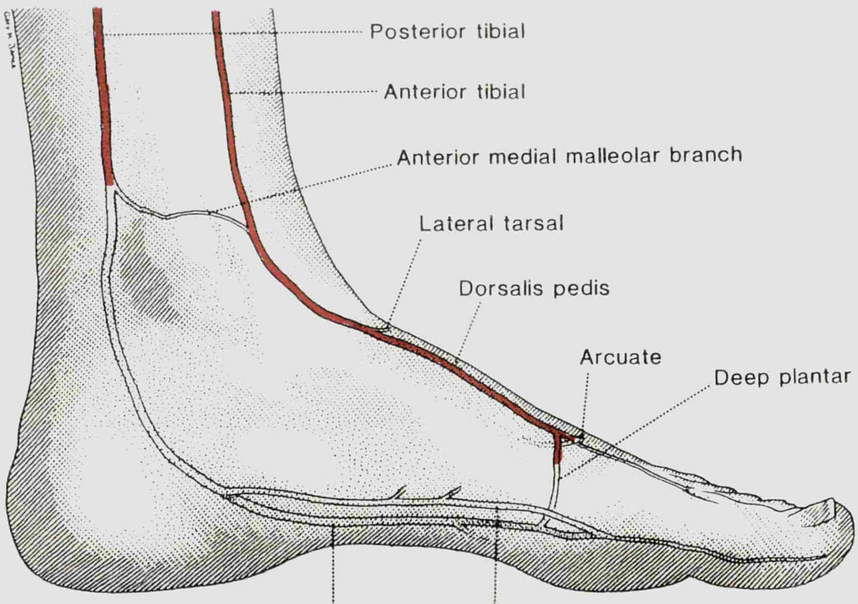


Figure 24. Incomplete pedal arch on PGR mapping and post-operative IA DSA.

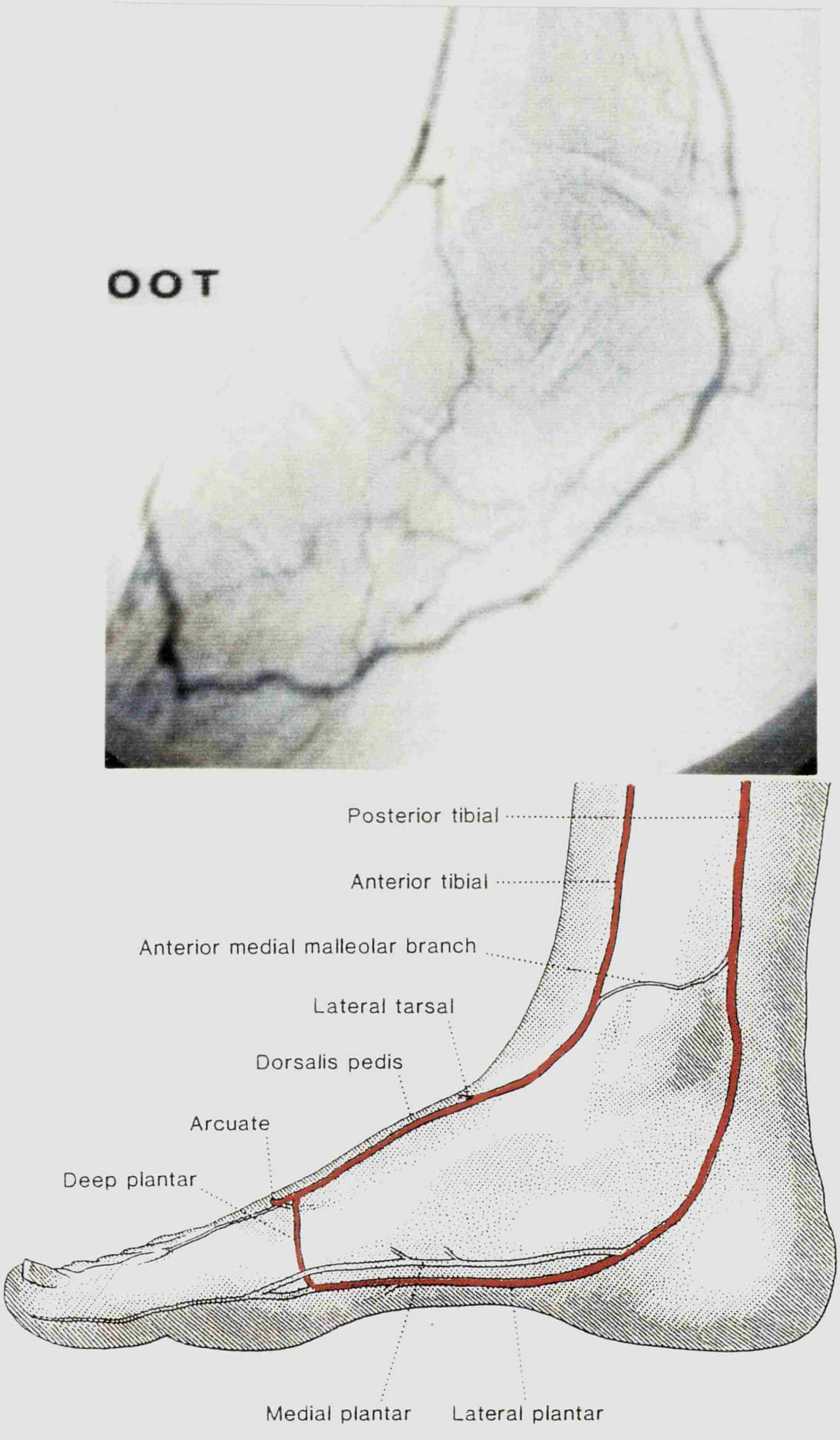


Figure 25. Complete primary pedal arch on PGR mapping and the one week IA DSA.

CHAPTER 6d
METHODS OF ASSESSMENT.
LONG SAPHENOUS VEIN DUPLEX SCANNING AND MAPPING.

Introduction.

The superiority of autogenous vein grafts in critical ischaemia has highlighted the need for improved pre-operative visualisation of the saphenous vein. Clinical examination is of limited value particularly in those patients with fat thighs.

Numerous studies have described the use of ascending contrast saphenous venography in the assessment of LSV patency, luminal diameter and the presence of varicosities within the superficial venous system. Various complications have been reported including thrombophlebitis, tissue necrosis, renal failure and anaphylactic shock (Abrams 1983). However with the introduction of low osmolality contrast media these complications are less likely to occur (Lea Thomas and Posniak 1983). Venography is unreliable in the pre-operative assessment of size, as this is dependant upon saphenous pressure which is affected by the speed of the injection, respiration and the position of the patient. Shah, Chang, Leopold et al (1986) reported that venography underestimated LSV size by 1.1 mm in 80% of cases. Venography is also of limited value in the evaluation of LSV continuity because the presence of a large perforating vein in either the thigh or the calf may result in preferential filling of the deep venous system and poor filling of the proximal LSV. The use of popliteal compression or a modified valsalva manoeuvre may reverse the flow in the perforating veins reducing this problem. Venography also has the disadvantage of being a two dimensional study which does not allow for accurate prediction of the depth and exact location of the venous systems.

Simple hand held Doppler examination in combination with clinical examination has been used to map out the LSV in thin legs with normal anatomy (Buchbinder and Flanigan 1985). Although Doppler may provide information about LSV patency, it is unreliable in assessing the site of tributaries and provides no information about venous valves, double systems and vein size (Buchbinder, Semrow, Ryan et al 1986).

B-mode ultrasound was first utilised in the deep venous imaging and compares favourably with venographic data (Talbot 1982, Sullivan, Peter and Cranley 1984). Several authors have reported the value of B mode imaging in the pre-operative assessment of the LSV (Sullivan, Peter and Cranley 1984, Leopold, Shandall, Corson et al 1986). It correlates accurately with the morphology, venous tributaries, double or triplex systems, varicosities, absent or occluded trunks and size at the time of operation. Pre-operative venous mapping helps to shorten operative time and reduces undermining of skin flaps, particularly important in elderly patients and those with fat legs.

Anatomy

Long saphenous vein (LSV)

The long saphenous vein is the longest vein in the body passing from the medial aspect of the foot to the femoral vein 3 cms below the inguinal ligament. However in only 38% of patients is the LSV a single continuous trunk in the thigh and calf (Shah, Chang, Leopold et al 1986). It is a continuation of the medial marginal vein of the foot and ascends in front of the medial malleolus lying between it and the tibialis anterior tendon. As it ascends into the calf it lies a fingers breadth medial to the tibial border within the superficial fascia. It then courses posteromedial to the medial tibial and femoral condyles and along the medial aspect of the thigh. At the groin it passes through the cribriform fascia at the level of the fossa ovalis, 2.5 to 3.0 cms below and lateral to the pubic tubercle to join the femoral vein. The medial and lateral femoral veins which drain the large areas of the thigh join the LSV a short distance below the saphenous opening. At this point the LSV receives up to four tributaries which often correspond to the four branches of the common femoral artery (superficial iliac, superficial epigastric, superficial external pudendal and the deep external pudendal), (Figure 26).

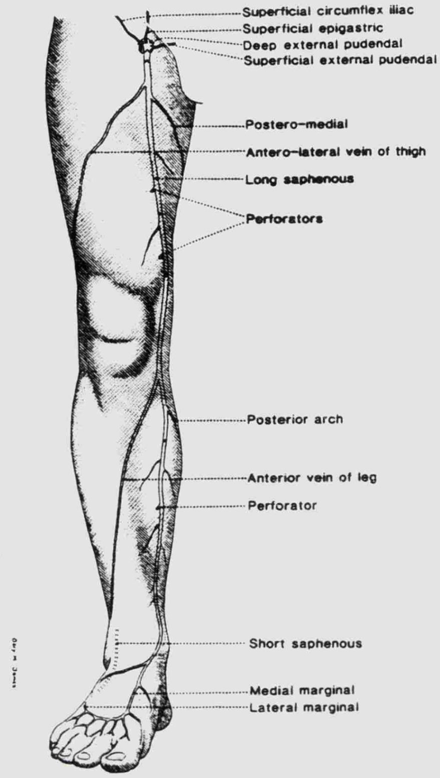


Figure 26, Anatomy of the long saphenous vein.

In the thigh the LSV is present as a single trunk in 65% of cases and is predominantly located in the medial aspect of the thigh. The remaining 35 % are duplex or triplex systems, most reconstitute within 10 cms of the knee joint. In only 11% of cases does it remain as a double system (Shah, Chang, Leopold et al 1986).

Valves.

There are numerous venous valves within the LSV. Shah et al (1986) reported an average of 6.3 ± 2.8 valves throughout its length. Several constant positions were noted; (1) saphenofemoral junction, (2) at the level where the LSV passes through the cribriform fascia, (3) mid thigh, (4) suprageniculate and (5) mid calf position.

Perforators.

There are two common sites for thigh perforators, (i) adductor hiatus and (ii) just above the knee joint/ mid thigh. On average there are 1.6 ± 0.8 surgically significant perforators in the thigh (Shah, Chang Leopold et al 1986). In the lower leg, perforators are usually located at the mid point between the foot and the knee joint, approximately 10 cms below the level of the knee joint.

Tributaries

In the leg the LSV receives several tributaries; (1) one from the ankle perforating veins, (2) one or two from the anterior aspect of the leg and (3) one from the short saphenous vein (SSV). At the level of the knee the LSV receives tributaries from (1) posterior aspect of the calf, (2) anterior vein of the leg and (3) posterior arch vein (Leonardo's vein). In the thigh the LSV is joined by the anterolateral and posteromedial veins. The former lies within the superficial fascia and drains the anterolateral aspect of the thigh. It curves diagonally upwards from the outer aspect of the thigh to join the LSV a few centimetres below the saphenofemoral junction. The posteromedial vein is formed by a small vein from the SSV just before its enters into the popliteal fossa and runs along the posterior aspect of the thigh in the deep fascia. It joins the LSV at a variable point and may enter the femoral vein independently of the LSV. In 15% of cases it represents the majority of venous drainage from the SSV system.

Short saphenous vein

The short saphenous is a continuation of the lateral marginal vein of the foot. It passes behind the lateral malleolus and ascends into the calf lateral to the tendoachilles. From then onwards it courses up the middle of the calf to eventually perforate the deep fascia between the two heads of gastrocnemius. On entry into the lower part of the popliteal fossa it joins with the popliteal vein between 3.5 and 7.0 cms above the level of the knee joint. Numerous anatomical variations have been described including; (1) where the SSV joins the LSV in the mid-thigh region, (2) a bifurcated SSV where one branch joins the popliteal vein and the other the LSV and (3) where the SSV ends below the knee joint and joins either the LSV or the deep veins of the calf. It possess between 7 and 13 valves.

Arm veins.

Cephalic

The cephalic vein passes across the anatomical snuffbox lying superficial to the branches of the radial nerve. It courses around the radial border of the forearm where it eventually reaches the antecubital fossa. At this point it gives off the median cubital vein which passes anterior to the bicipital aponeurosis to join with the basilic vein. The cephalic vein continues into the upper arm lying in a superficial position between brachioradialis and biceps. It crosses over the lateral border of biceps to lie between deltoid and pectoralis major. It enters the infraclavicular fossa behind the clavicular head of pectoralis major, and passes through the clavipectoral fascia to enter the axillary vein behind the clavicle. In a proportion of patients the cephalic vein may be absent or diminished in size. In this case the median cubital vein carries the majority of blood to the basilic vein.

Basilic

The basilic vein starts on the posterior ulnar aspect of the forearm. It inclines forward and across the ulnar to join with the median cubital vein at the elbow. At this point it ascends obliquely and superficially to lie between biceps and pronator teres. Just below the mid point of the arm it perforates the deep fascia to lie medial to the brachial artery. At the lower border of teres major it continues on as the axillary vein.

PRE-OPERATIVE VEIN SCANNING.

Position of the patient.

The patient is placed on an examination table in a controlled environment. The couch is positioned in 20 degrees of reverse Trendelenburg. The affected leg is externally rotated with 20 degrees of knee flexion (Figure 27). Where possible the below knee segment of the long saphenous vein is examined with the leg fully dependant, thus ensuring maximum filling of the LSV .

Figure 27. Pre-operative vein scanning, showing the 10 MHz duplex probe imaging the midthigh LSV and the PGR cuff in the below knee position.

Duplex scanning of the LSV was used in combination with the PGR system. In the assessment of the LSV, at the groin, the PGR cuff was placed above the knee. For the LSV at the level of the thigh, knee and upper calf the cuff was placed around the upper and lower calf respectively. Rapid inflation and deflation of the cuff resulted in a propagated wave which could be detected on the Doppler if the vein was patent. Because of the small volume of blood within the segment of LSV, it was not possible to repeat the pulsing over more than 2 to 3 seconds. This was often sufficient time to confirm the patency of the LSV. This combined approach of duplex scanning and PGR was often helpful in determining which part of the scan was the LSV.

Duplex scanning.

A Technicare Autosector Duplex scanner with B and M mode facility was used to assess the availability of a suitable autogenous saphenous vein for bypass grafting. The M mode was used to assess wall thickness and movement during PGR pulsation. B mode was used to assess patency, size and course of the LSV. A thick layer of ultrasonic transmission gel (Aquasonic 100) was placed along the anatomical course of the long saphenous vein (LSV). A 10MHz duplex probe was gently applied to the gel-skin interface as excessive pressure resulted in collapse of the vein. The saphenofemoral junction was initially identified at the groin (Figure 28).

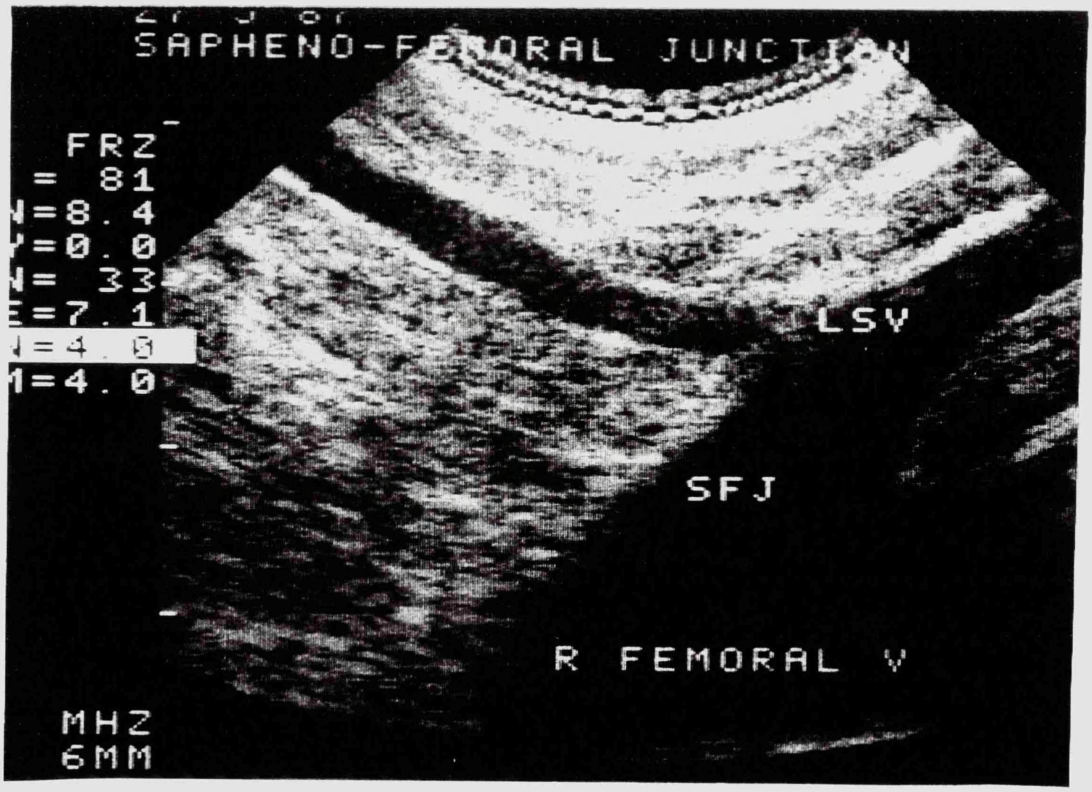


Figure 28. Saphenofemoral junction on Duplex scanning.

The LSV internal diameter was measured using two vernier calipers at the SFJ, midthigh, knee, midcalf and the medial malleolus at rest and after PGR assisted vein scanning. Intraluminal echoes were often seen in the proximal LSV and moved with respiration (Figure 29), the absence of such echoes often made visualisation of the vein impossible and was indicative of a thrombosed venous segment.

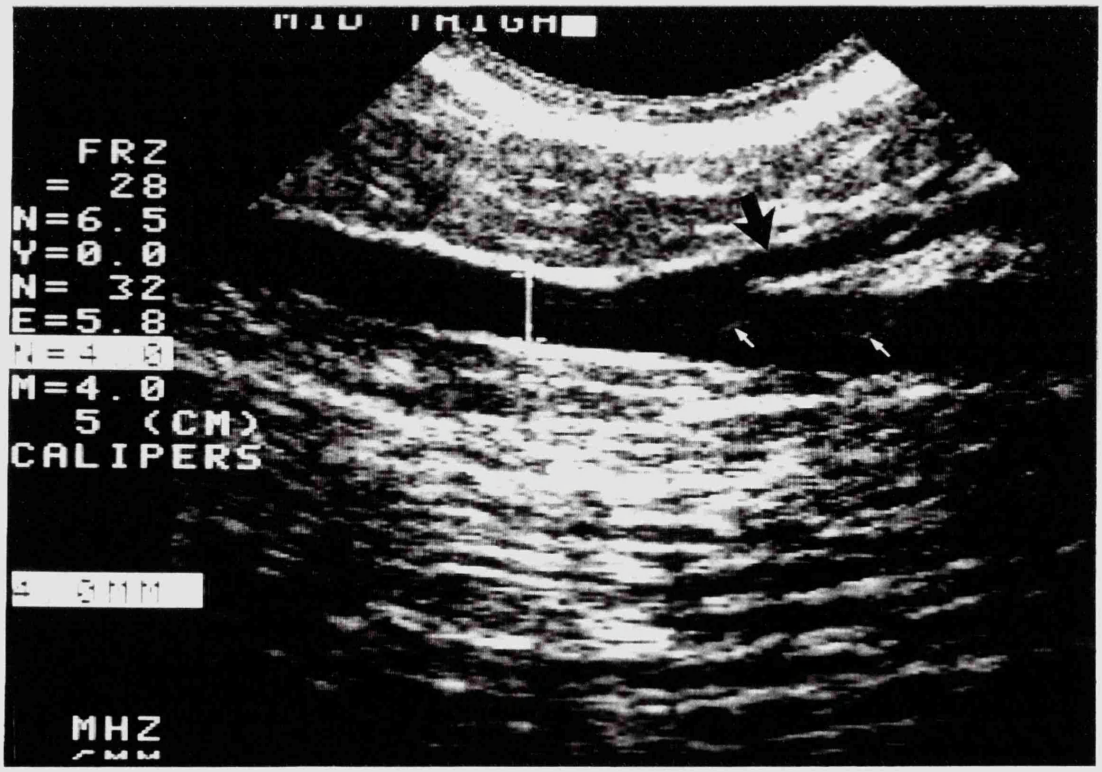
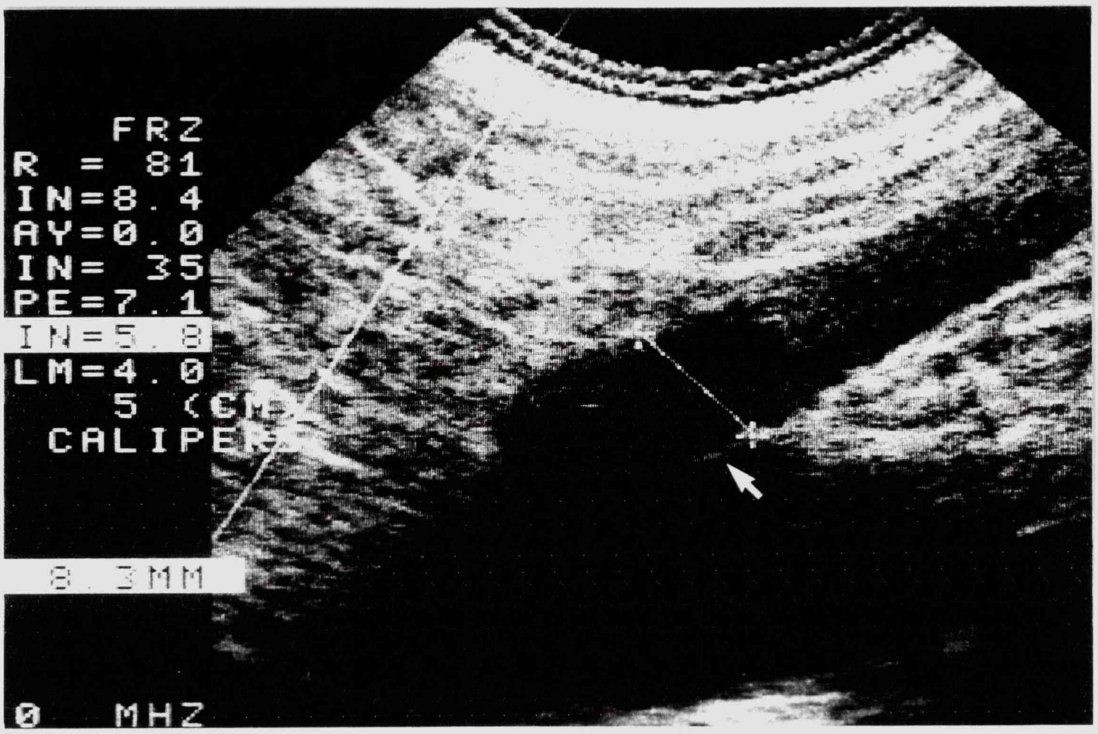
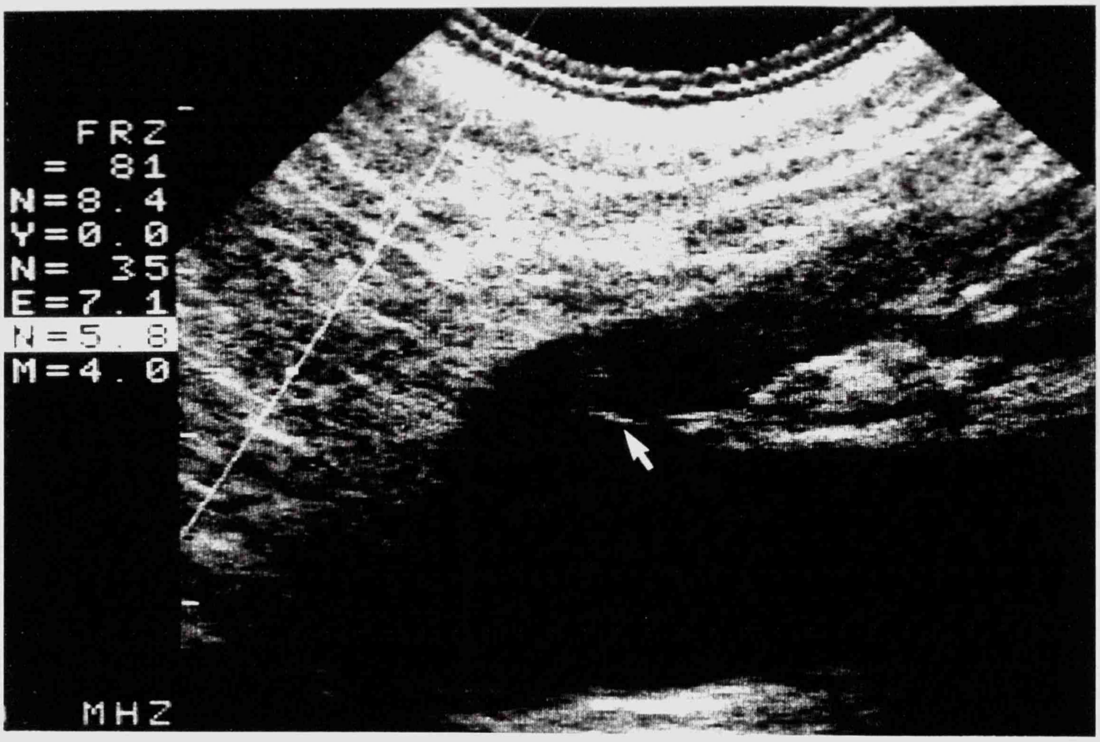


Figure 29. Large venous tributary, probably a duplex LSV system (Black arrow). The small white arrow denotes moving intraluminal echoes.

The LSV was scanned along the entire course from groin to the medial malleolus, noting the presence of bifid and triplex systems. During the learning period the significance of large venous tributaries, particularly in the thigh, was not realised and in retrospect these represented Duplex or triplex systems. This is shown in figure 29, where a large tributary is seen arising from the main trunk of the LSV in the mid-thigh and was found to be a bifid system at operation. The M mode was used to quantify the wall thickness into 0.5, 1.0 and 1.5 mm thickness. In all cases the fully mobilised vein technique was employed and so no attempt was made to identify or mark the site of venous valves or large tributaries although they were easily recognisable in the thigh. Proximal venous valves particularly at the saphenofemoral junction were often seen and observed to move with respiration. This is well demonstrated in figures 30 and 31 which show the valve arrowed in an open and closed position.





Figures 30 and 31. Valve at the SFJ. The top figure shows the valve (arrowed) in the open position and below in the closed position.

After noting the size, patency and distensibility of the LSV, the ultrasonic jelly was then wiped clear and an indelible skin marker (Ofrex) was used to mark out the course of the LSV. Cross hatches facilitated accurate closure of the incision (Figure 32).

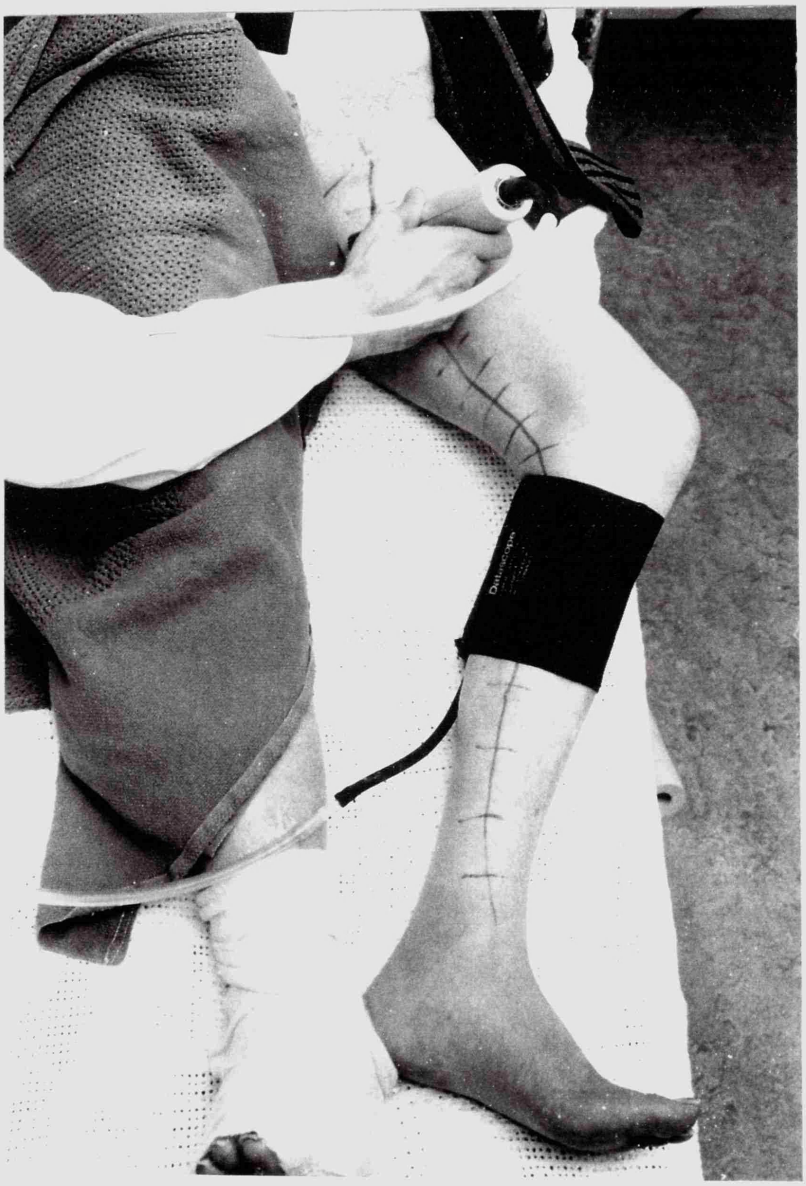


Figure 32. Pre-operative LSV mapping. The PGR cuff can be seen around the upper calf.

Great care was taken to avoid contact between the ultrasonic gel and the indelible skin marker as this often resulted in failure of the skin marker. On completion of the scan the gel was then removed from the patient using warm soapy water.

The entire process took between 60 and 90 minutes during the early part of the study. This was shortened to 45 minutes partly by experience and by the combined use of PGR and B mode imaging of the vein. A hyperaemic test similar to that described by Ruoff, Cranley, Hannan et al 1987 was incorporated into the venous assessment but later abandoned due to poor reproducibility and a failure to increase vein size compared to PGR assisted vein scanning.

On the basis of the Duplex findings the long saphenous vein was classified into one of four grades.

Grade 0	=	Normal, no evidence of disease.
Grade 1	=	Diseased but greater than 2mm internal diameter.
Grade 2	=	Grossly diseased, less than 2mm internal diameter.
Grade 3	=	Thrombosed.

Grades 0-1 were considered usable and 2-3 unusable.

CHAPTER 6e

METHODS OF ASSESSMENT.

HAEMODYNAMIC MONITORING.

Haemodynamic monitoring.

The ability to measure peripheral resistance at the time of calf vessel exploration, is a more attractive proposition to the surgeon, than measuring peripheral resistance on completion of the graft. This approach will allow the surgeon to identify the most suitable vessel and level for reconstruction. Although impedance is theoretically superior to peripheral resistance, there are as yet no on-line facilities to compute impedance.

In this study, a Doppler flowmeter with the facility to measure flow and peripheral resistance was used in the per-operative assessment of the femoro-distal grafts. This unit had been developed by the previous research fellow in conjunction with the Department of Medical Physics and was well proven in the clinical setting.

Methods of per-operative assessment.

A dedicated theatre unit was used to measure per-operative graft function. This consisted of a Doppler flowmeter, a Gould pressure monitor and a Apple 2E microcomputer (Figure 33).

Figure 33. Apple 2E microcomputer (A) linked to a Doppler Flowmeter (B) and a Gould pressure monitor (C).

The Doppler Flowmeter consisted of a 10 MHz Doppler pencil probe and a mean frequency estimator to measure flow. The output of the flowmeter was proportional to the first moment of the Doppler power spectrum and hence mean blood velocity. Vessel diameter and the angle of insonation were kept constant by a series of acrylic cuffs (Figure 34). Blood flow was calculated by using an experimentally determined calibration factor to compensate for uneven insonation of the blood vessel, the angle of insonation, and the vessel internal diameter.

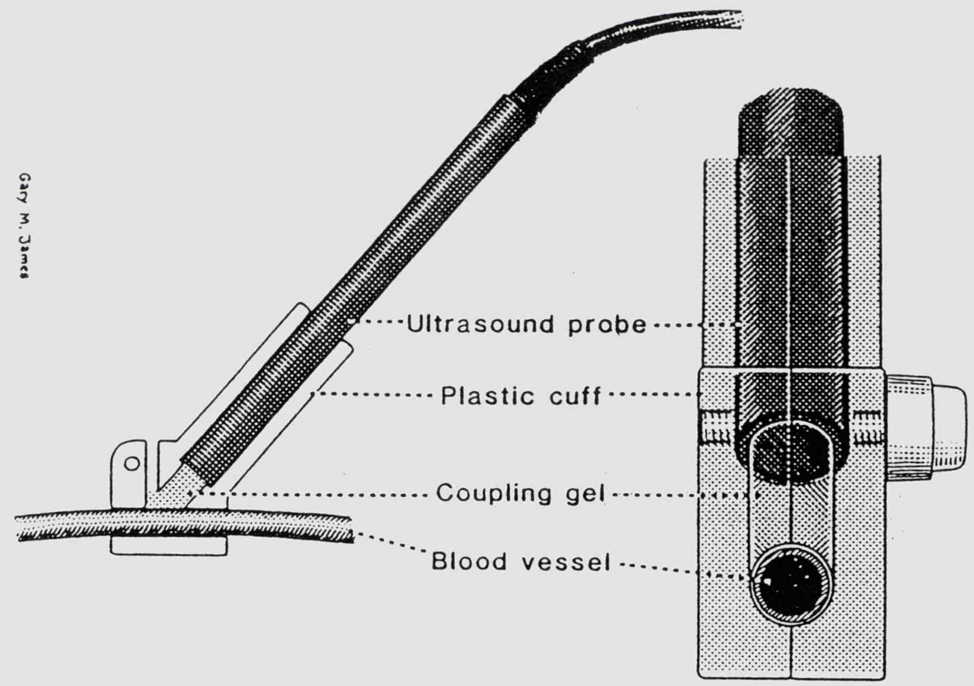


Figure 34. Doppler pencil probe in an acrylic cuff.

The system offers many advantages over conventional electromagnetic flowmeters including; (i) no electrical contact and hence no zeroing required, (ii) no variation in sensitivity with differing vessel wall or graft thickness and (iii) low variability of less than 10% (Beard 1987).

On the basis of the PGR calf vessel assessment, the vessel chosen for the site of the distal anastomosis was exposed. Proximal and distal control was achieved using rubber slings and the patients systemically heparinised. A vertical arteriotomy was made and extended using Pott's scissors. A newly developed end tapered 6/8 French resistance catheter (Portex Ltd, Hythe, Kent, England) was introduced into the artery and twenty ml. of heparinised saline injected (500 units of calcium heparin diluted in 1L of 0.9% sodium chloride). Twenty mls. of blood was aspirated back through the catheter for the peripheral resistance measurements. Blood rather than saline was used to avoid the need to correct for viscosity. In patients with severe ischaemia there was often insufficient blood from the distal vessel for the peripheral resistance measurements. Additional blood was obtained either from the common femoral artery or from the anaesthetic arterial line. A three way tap was attached to the end of the catheter, which was linked via a 10 cms length of Vygon "electrocath" manometer tubing to a pressure transducer,(Gould SP 1405, Gould Inc, Measurements system division, Oxnard, California). A size 3 (3mm external diameter) acrylic cuff was placed around the umbilical catheter and lignocaine gel used to couple the Doppler probe to the catheter (Figure 35). The gel came in a sterile container with a nozzle which allowed easy passage of gel into the cuff. The Doppler probe was inserted into the cuff ensuring; (i) a tight fit and (ii) adequate gel between the probe and umbilical catheter.

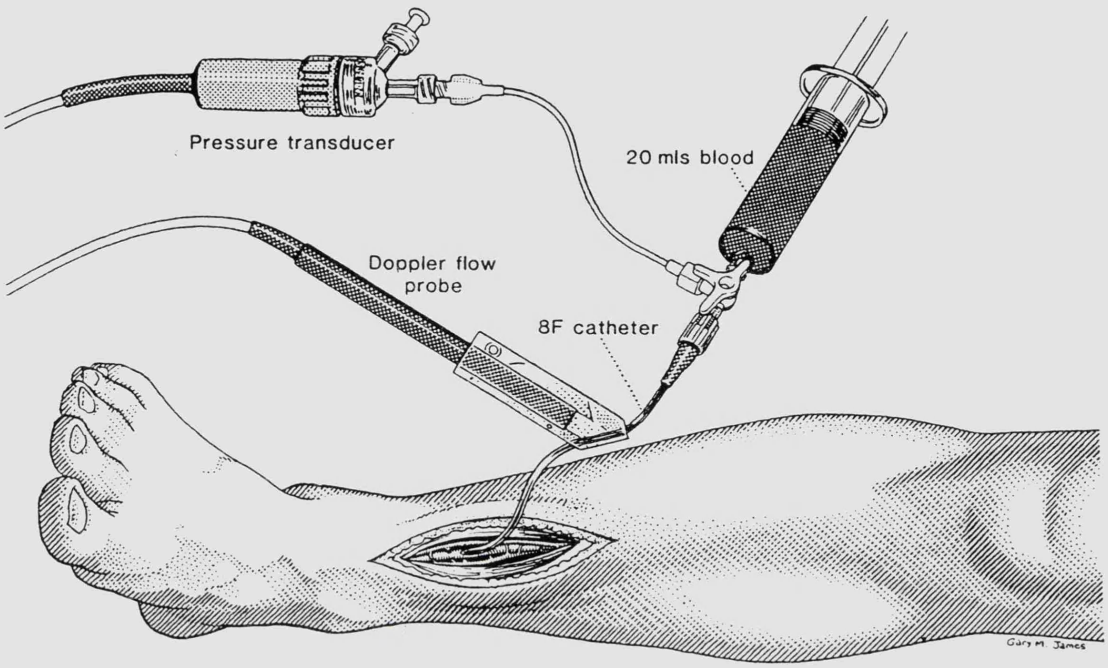


Figure 35. Peripheral resistance measurement.

An infusion of heparinised blood was made at a "physiological" pressure of approximately 100 mmHg. Simultaneous recordings of pressure (P) and flow (Q) were converted by the Apple 2E microcomputer into peripheral resistance units, where

1 PRU = 1 mmHg / 1 ml blood flow per minute.

The overall peripheral resistance;

$$PR = \frac{\text{Pressure (P) - Catheter Resistance } (R_c)}{\text{Flow (Q)}}$$

The resistance of the 6 and 8 French umbilical catheters had been previously determined at 1.75 PRU's and 0.55 PRU's respectively, but could easily be re-checked by allowing free flow from the end of the catheter.

Three peripheral resistance measurements were obtained from each artery and the mean calculated. If the peripheral resistance was greater than 2 PRU's, then an appropriate vessel was explored more distally in an attempt to obtain a low peripheral resistance outflow tract.

On completion of the graft a 18 G venflon catheter was inserted into the graft via a proximal venous tributary. A simple stainless steel gauge was used to determine the external and internal diameter of the vessel to within 0.25 mm. The external diameter corresponded to the size of the acrylic cuff to be used and the internal diameter was recorded on the computer to enable the flow and peripheral resistance to be calculated (Figure 36).

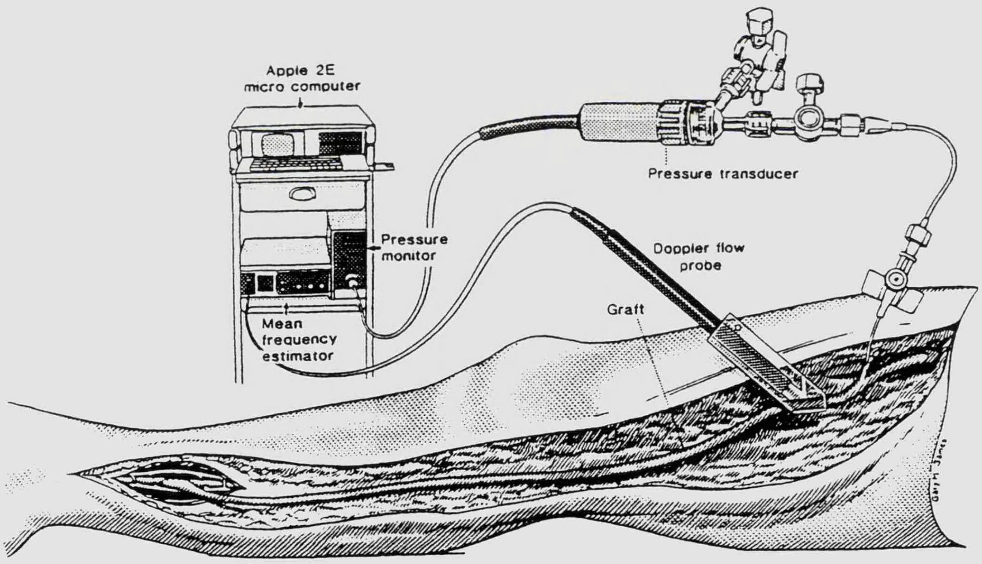


Figure 36. Measurement of peripheral resistance and flow on completion of the graft.

Retrograde flow (RF).

The cuff was placed around the proximal end of the graft and measurements of flow taken at rest with the proximal part of the distal vessel open and occluded (Figure 37). This allowed the proportion of retrograde flow (RF), ie steal to be calculated where;

$$(RF) = \frac{(Q_1) - (Q_2)}{Q_1}$$

RF = Retrograde flow (%)

Q_1 = Total Graft Flow (mls/min)

Q_2 = Distal Graft Flow (mls/min)

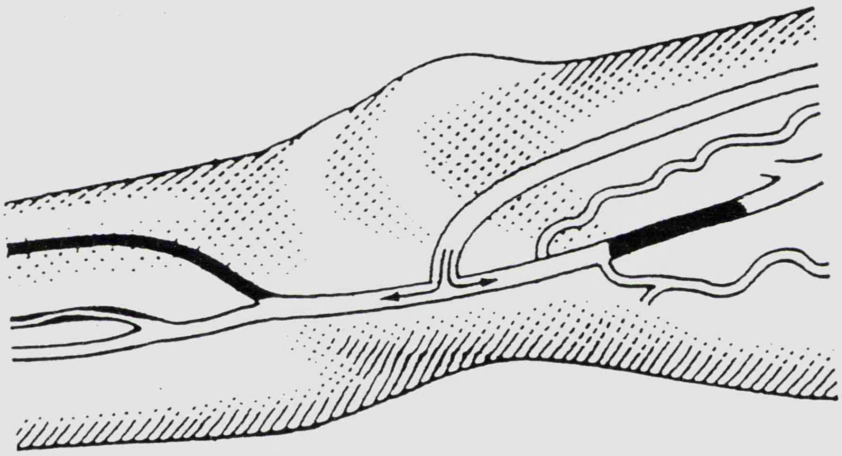


Figure 37. Measurement of retrograde flow (RF).

The proximal vessel was clamped and graft flow and peripheral resistance calculated at rest and after the administration of 30 mg of papaverine hydrochloride into the graft. If there was any discrepancy between the initial outflow peripheral resistance and the peripheral resistance after the administration of papaverine hydrochloride the hood of the distal anastomosis was opened and the valvulotome repassed. If there was no evidence of a technical error and the PR failed to fall below 1 PRU an on-table arteriogram was performed.

CHAPTER 6f

METHODS OF ASSESSMENT

LONG SAPHENOUS VEIN MORPHOLOGY.

Introduction

The development of safe and reliable methods of valve disruption has led to a wide acceptance of the in situ vein technique in femoro-distal reconstruction (Skagseth and Hall 1973), (Leather, Powers and Karmody 1979).

Early experience with the in situ vein technique suggested an improved graft patency and vein utilisation rate compared to historic reversed vein controls (Leather, Shah and Karmody 1981). Several theories were proposed including less endothelial damage (Buchbinder, Singh, Karmody, et al 1981), superior prostacyclin production (Bush, Graber, Jakubowski et al 1984), normal fibrinolytic activity (Furuyama, Kusaba, Moriyanma, et al 1980), improved flow characteristics, a natural tapering of the vessel with less compliance mismatch at the distal anastomosis (Binder 1955, Klimach, Chapman, Underwood et al 1984).

More recently doubt has been expressed about the superiority of the in situ vein technique (Harris, How and Jones 1987, Taylor, Edwards, Phinney et al 1987). Taylor reported a series of 110 reversed veins performed between 1980-86. The patency, vein utilisation and limb salvage rates were similar to reported in situ vein series.

Recent experimental studies have reported no significant difference between in situ and reversed vein grafts in (i) pulsatility index and a flow disturbance index (maximum frequency divided by the median frequency) (Gannon, Simms and Goldman 1986), (ii) resting and hyperaemic blood flow (Beard, Lee, Aldoori et al 1986) and (iii) compliance (Beard and Fairgreave 1986, Cambria, Mergerman, Brewster et al 1986).

During mobilisation of veins for bypass it was noted that some veins were thin walled and easily distended, whilst others seemed to be thick walled, fibrous and with a small internal lumen, particularly around the knee joint. We had noted that the thicker walled veins seemed to have a higher incidence of early failure. As a result of this observation it was decided to prospectively examine the LSV histologically before and after stripping and to try and correlate histological features with outcome.

<u>*Collection of samples.*</u>

Segments of undisturbed long saphenous vein, below knee, were taken in excess of that required for bypass, one before and one after the passage of a Hall valvulotome (Figures 38-40).

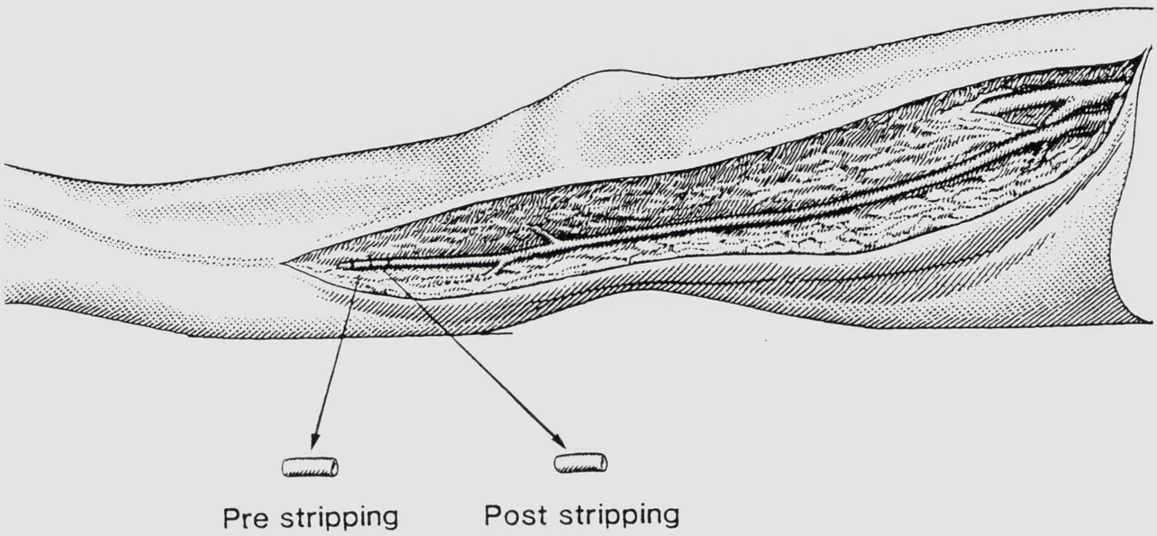


Figure 38. Segments of undisturbed long saphenous vein are taken in excess of that required for bypass, one before and one after stripping.

A small piece of the pre-strip specimen (0.5 cms) was immediately placed into 4% glutaraldehyde/formaldehyde at pH 7.2 and processed for electron microscopy. The remaining portion, approximately 3 cms, was placed in heparinised blood containing 15 mgs of papaverine hydrochloride at 4° C and transported immediately to the pathology department.

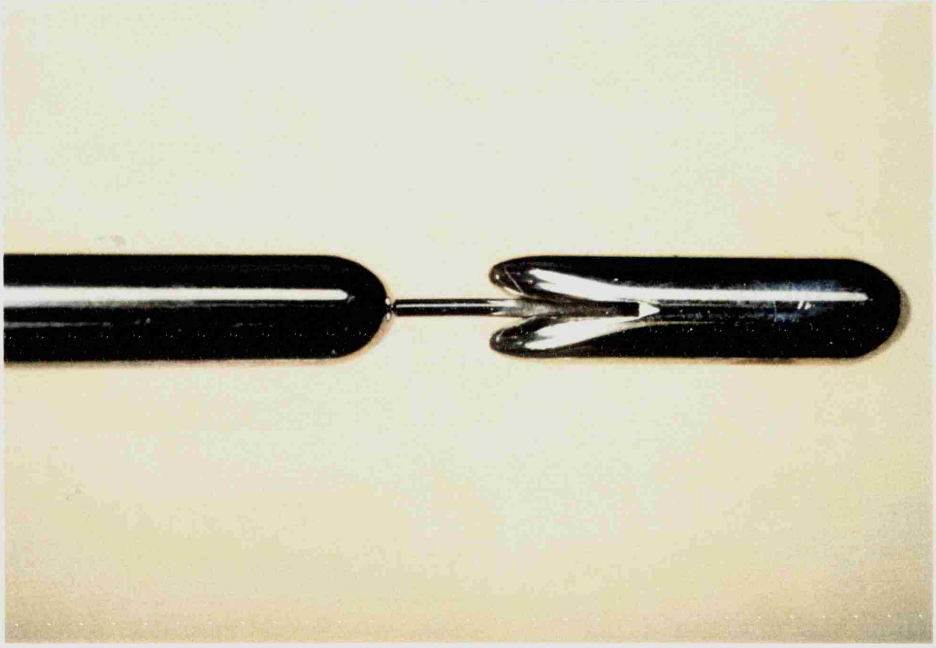


Figure 39. A 2 mm Hall valvulotome.

Figure 40. Photograph showing a 2 mm Hall valvulotome being removed from the distal end of a femoro-distal non-reversed vein graft.

The venous segment was cannulated and attached to a three way tap and a 20 mls syringe. The vein was slowly distended with agar to a physiological pressure of 100 mmHg (Figure 41). In the majority of cases the length of vein was between 1-2 cm in length, which often proved difficult to distend. The pressure was monitored by a NISSEI sphygamanometer connected to the three way tap by a 100 cm length of manometer tubing.

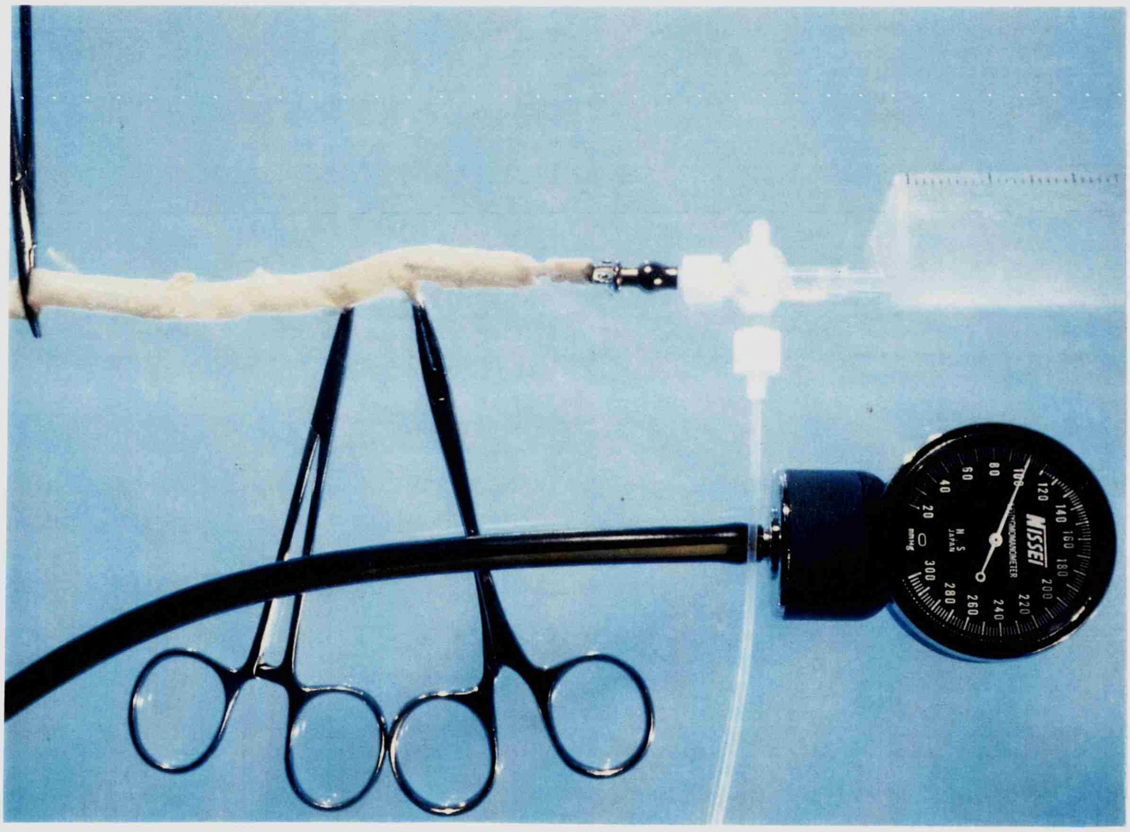


Figure 41. Method of venous distension using agar.

The agar was allowed to set and the vein fixed in 10% formal saline and sectioned at 0.5 cm intervals. Blocks were embedded in paraffin and 4 micron thick sections cut and stained with haemotoxylin and eosin, elastic Van Gieson and Masson trichrome. Some sections were also stained with a monoclonal antibody to desmin using the avidin-biotin immunoperoxidase technique.

The pre and post stripping specimens were also stained with a factor VIII specific antigen to quantify the degree of endothelial loss following valve stripping. Endothelial cell loss was calculated on the pre and post-stripping specimens by assessing the percentage of the luminal surface covered by endothelial cells (Figure 42 & 43).

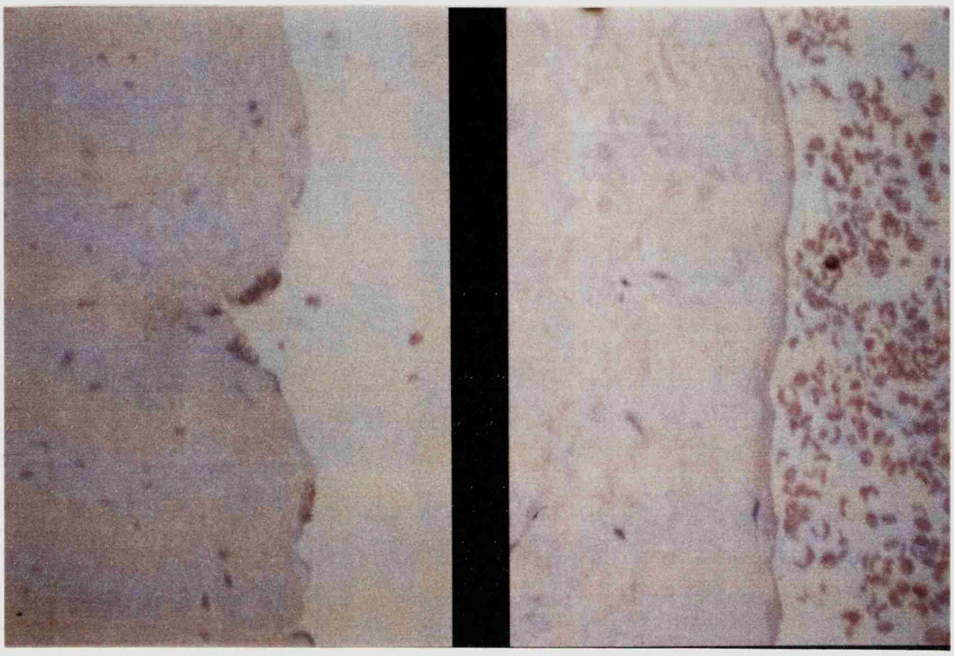


Figure 42. Haematoxylin and eosin stain. On the left is the pre-stripping specimen and on the right the post-stripping specimen.

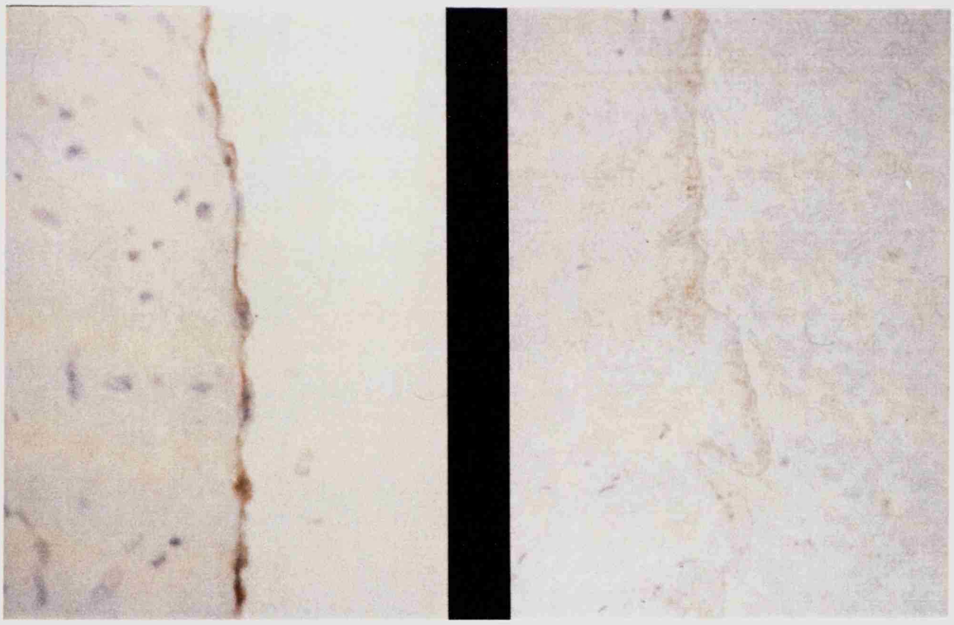


Figure 43. Factor VIII stain. On the left is the pre-stripping and on the right the post-stripping specimen.

Histology of the normal long saphenous vein.

The normal long saphenous vein has a thin intima covered by endothelium (Figures 44 and 45). It is separated from the media by a rudimentary internal elastic lamina. The media consist of two muscular layers, (i) the inner longitudinal and (ii) outer circular, the latter being the more prominent. The inner longitudinal muscle layer is thicker at the site of venous valves. The adventitia is composed of connective tissue and contains the vaso vasorum and occasionally a third longitudinal muscle layer.

Figures 44 and 45. On the left is a low power view of a normal LSV and on the right is a high power view showing a thin intimal layer. A thin longitudinal muscle layer and a thicker circular muscle layer.

Histological features.

In a pilot study five histological features were noted:

1. Intimal hyperplasia; (Diffuse and Focal), (Figure 46).
2. Medial longitudinal muscle hypertrophy and an increase in the intervening connective tissue, (Figure 47).
3. Circular muscle hypertrophy and an increase in intervening connective tissue, (Figure 48).
4. Luminal stenosis, (Figure 49).
5. The presence of a prominent outer longitudinal muscle layer between the circular coat and the adventitia.

Grading system.

A semi-quantitative histological grading system was used to assess the long saphenous vein. A scale of I to IV was used to grade;

1. intimal hyperplasia both focal and diffuse (figure 46)
2. longitudinal muscle hypertrophy (LMH) (figure 47)
3. circular muscle hypertrophy (CMH) (figure 48).

Grade I represented minimal change, II = mild, III = moderate and IV = severe. In the case of luminal stenosis grade I represented 0-25% narrowing, grade II 26-50%, grade III 51-75% and grade IV 76-100%. A series of examples are shown below (Figure 49).

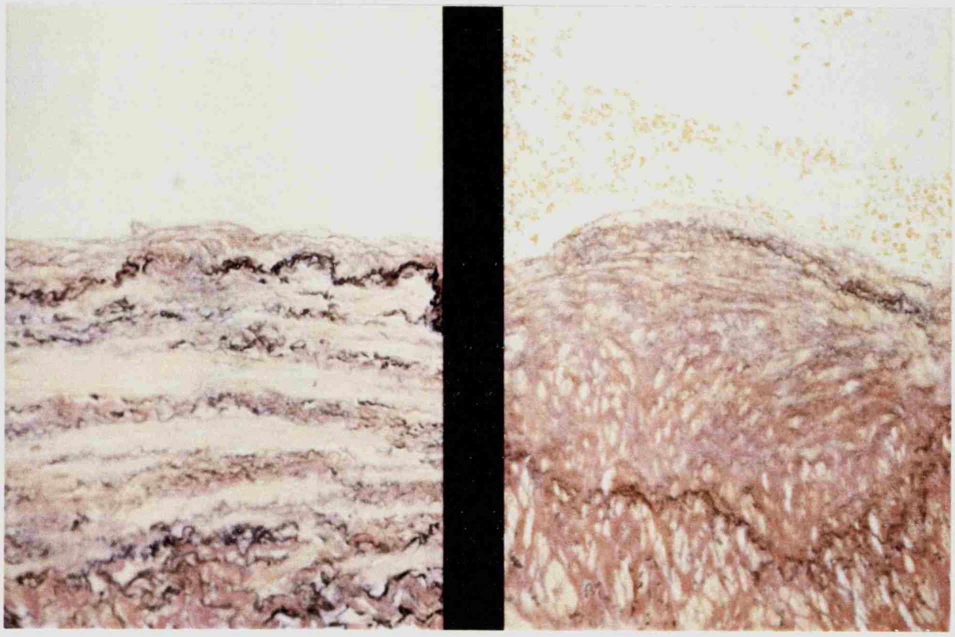


Figure 46. Photomicrograph showing grade I diffuse intimal hyperplasia on the left and grade IV focal intimal hyperplasia on the right.

Figure 47. Photomicrograph showing grade I longitudinal muscle hypertrophy (LMH) on the left and grade IV on the right.

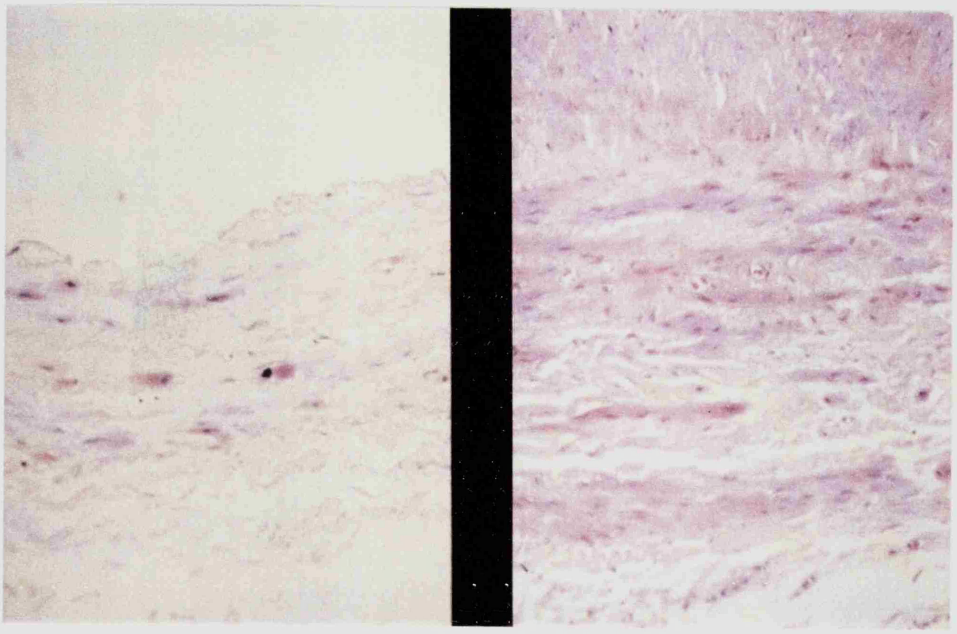


Figure 48. Photomicrograph showing grade I circular muscle hypertrophy on the left and grade IV on the right.

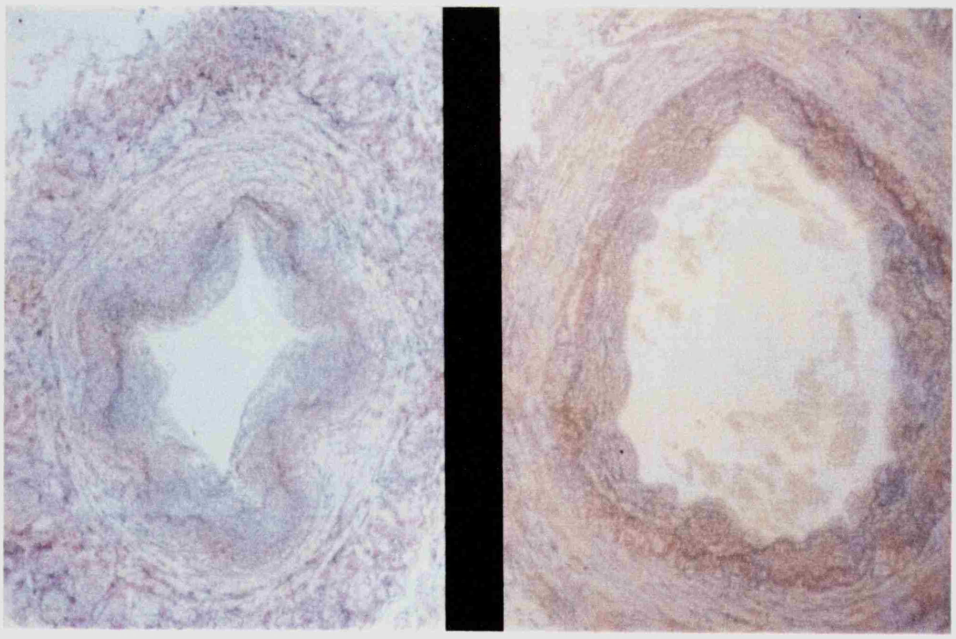


Figure 49. Photomicrograph showing grade I luminal stenosis on the left and grade IV on the right.

Electron microscopy (scanning and transmission).

A 0.5 cm piece of long saphenous vein was fixed in 4% glutaraldehyde / formaldehyde at a pH of 7.2. Dehydration took place through a series of graded ethanolic solutions and 100% acetone. Critical point drying in an EMSCOPE CPD 750. The specimens were then mounted on copper studs and subjected to light gold evaporation (approximately 300 nm thick). The specimens were then examined by Mr Peter Heap (Department of Anatomy, Bristol Medical School) at 40 and 80Kv in a JEOL 200 CX TEM scan analytical electron microscope fitted with a KEVEX 6000 X-ray energy spectrometer.

CHAPTER 7a.

RESULTS; ARTERIOGRAPHY.

Patients.

Eighty eight consecutive femoro-distal non-reversed vein grafts were performed in 57 men and 31 women of median age 71 years (range 41-87 years). All grafts were performed for critical ischaemia; 37 for rest pain and 51 for tissue necrosis. Twenty eight grafts were anastomosed to a single calf vessel, 9 to the tibioperoneal trunk and the remaining 51 to the distal popliteal artery.

Results

(a) Correlation between peripheral resistance and arteriogram scoring systems.

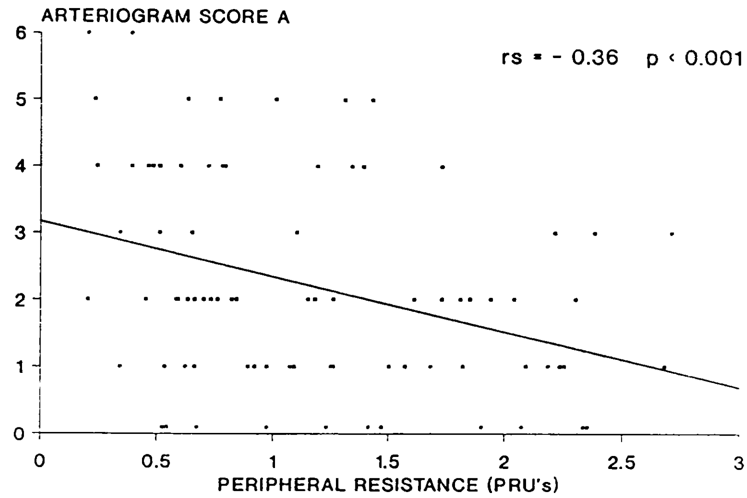
The arteriographic scoring systems A, B and C were correlated with measured PR at the time of femoro-distal bypass in 88 patients. There was a significant correlation between the arteriogram scoring systems A, B and C and the measured PR, (Table 8, Figures 50-52).

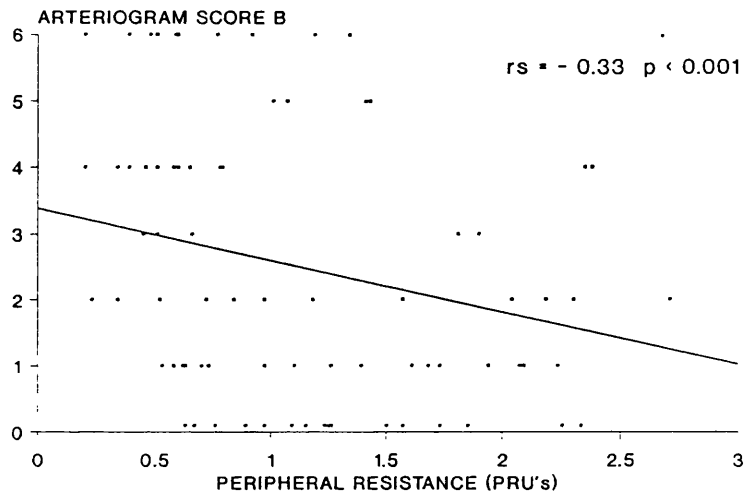
Table 8.

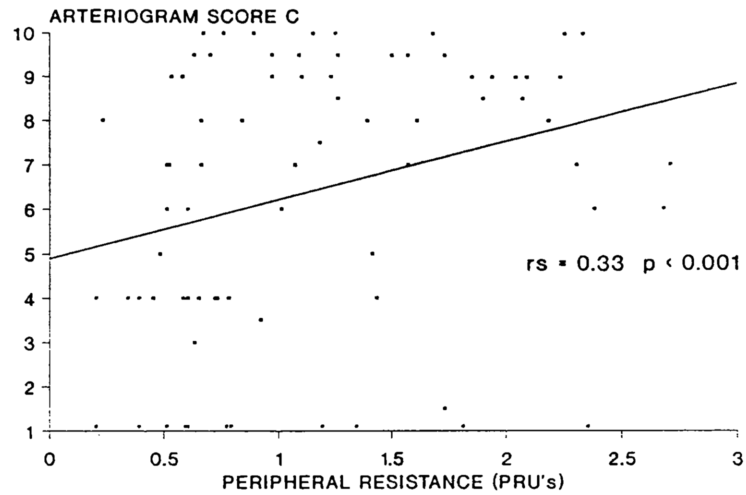
Correlation between PR and arteriogram scoring systems.

Correlation	SCORE A	SCORE B	SCORE C
PR r_s	-0.36^{***}	-0.33^{***}	0.33^{***}

Not Significant $^{+}$, $p < 0.05^{*}$, $p < 0.01^{**}$, $p < 0.001^{***}$







Figures 50-52. Correlation between PR and arteriogram scoring systems.

(b) Influence of intra-arterial digital subtraction arteriography on scoring systems.

During this consecutive series, IA DSA became available and was routinely used in the assessment of patients with critical ischaemia. Two groups were subsequently identified and analysed to assess the impact of IA DSA.

Group I Conventional arteriography only (n = 40).

Group II Intra-arterial digital subtraction angiography (n = 48).

In the conventional arteriogram group there was a poor correlation between the arteriogram scoring systems A, B and C and the measured peripheral resistance . With the introduction of IA DSA there were significant correlations between the arteriogram scoring systems A, B and C and the measured peripheral resistance. This was most marked in scoring systems B and C confirming the improved visualization of calf vessels using the IA DSA technique, (Table 9, Figures 53-58).

Table 9.

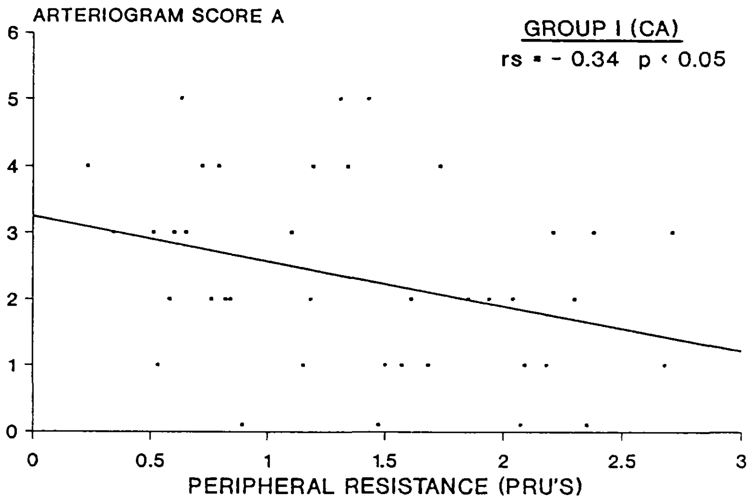
Influence of intra-arterial digital subtraction arteriography on scoring systems.

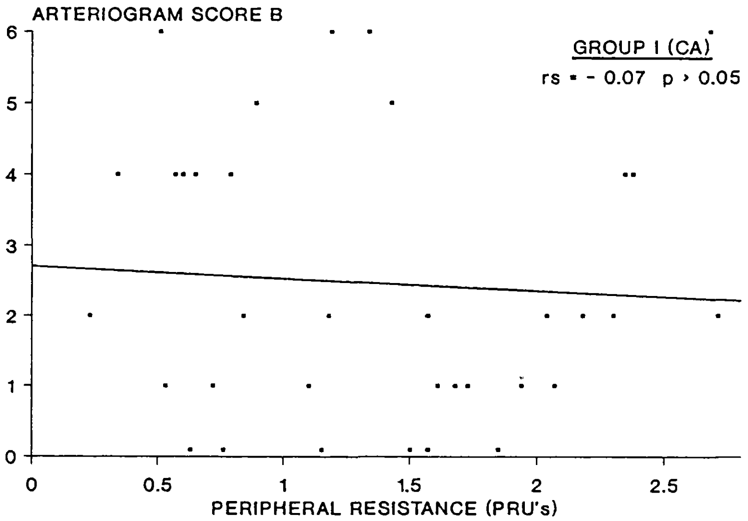
Groups	Correlation	SCORE A	SCORE B	SCORE C
I (CA)	PR r_s	-0.34*	-0.07+	0.13+
II (DSA)	PR r_s	-0.46***	-0.56***	0.55***

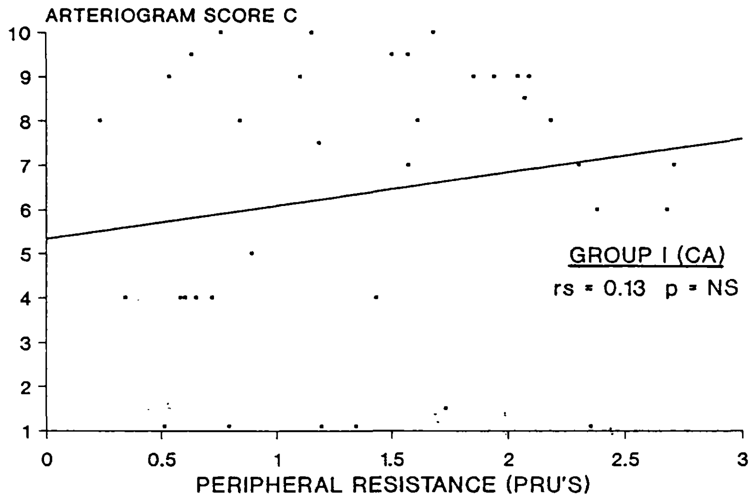
Group I = Conventional arteriograms (CA) only (n = 40), (See page 147).

Group II = IA DSA (n = 48), (See page 148).

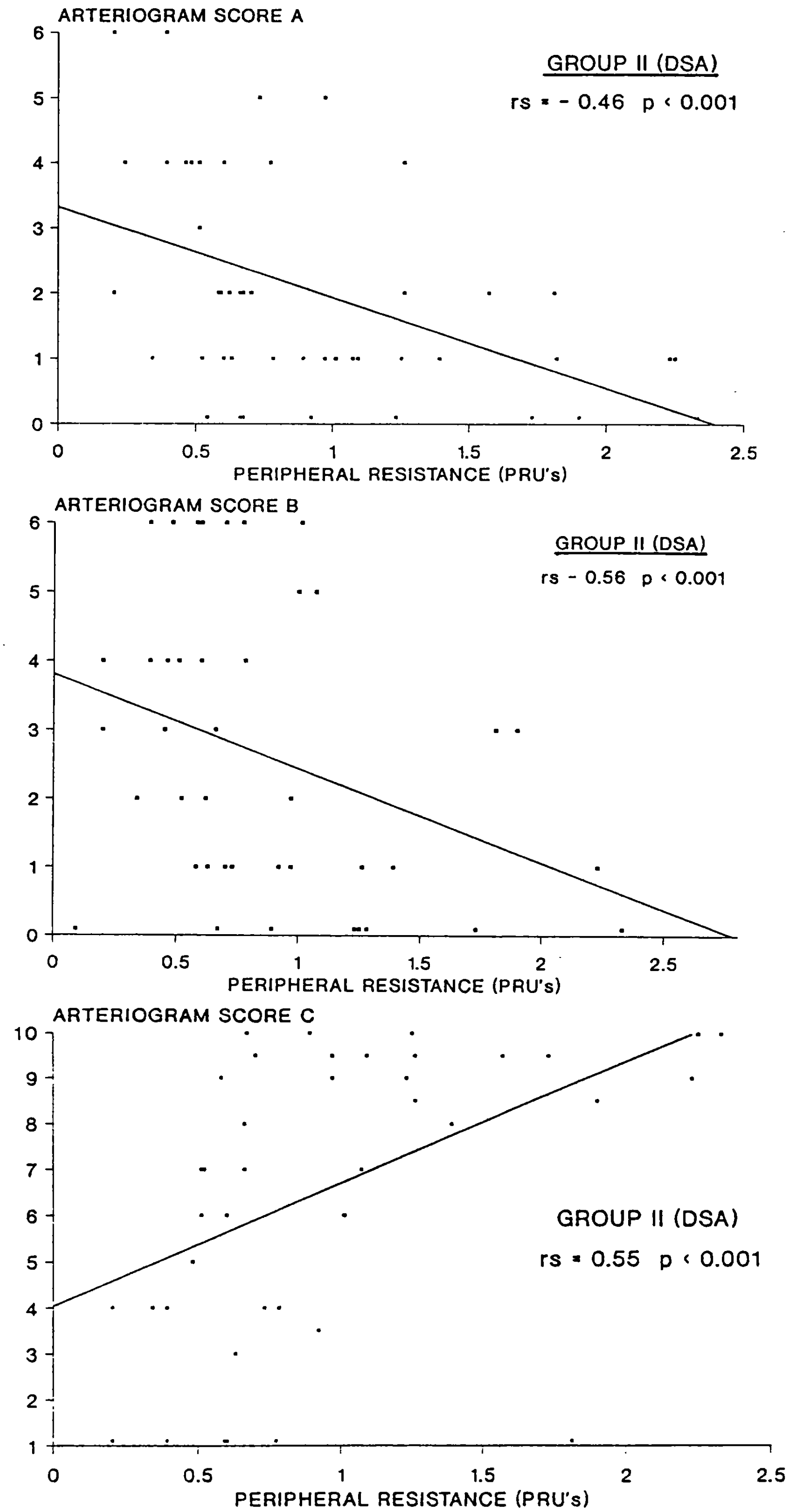
Not Significant +, $p < 0.05^{*}$, $p < 0.01^{**}$, $p < 0.001^{***}$







Figures 53-55. Influence of intra-arterial digital subtraction arteriography on scoring systems.



Figures 56-58. Influence of intra-arterial digital subtraction arteriography on scoring systems.

(c) <u>The role of IA DSA in determining the site of distal anastomosis.</u>

Groups I and II were analysed to assess the role of both conventional arteriography and IA DSA in determining the suitability of patients for either proximal (distal popliteal) or distal (single calf vessel) reconstruction.

(i) <u>Proximal (distal popliteal) reconstruction.</u>

The arteriogram scores A, B and C derived from the IA DSA views correlated better with the measured PR than with the scores from conventional arteriograms, (Table 10, Figures 59-64). In particular, scoring systems B and C correlated well with the measured PR.

Table 10.

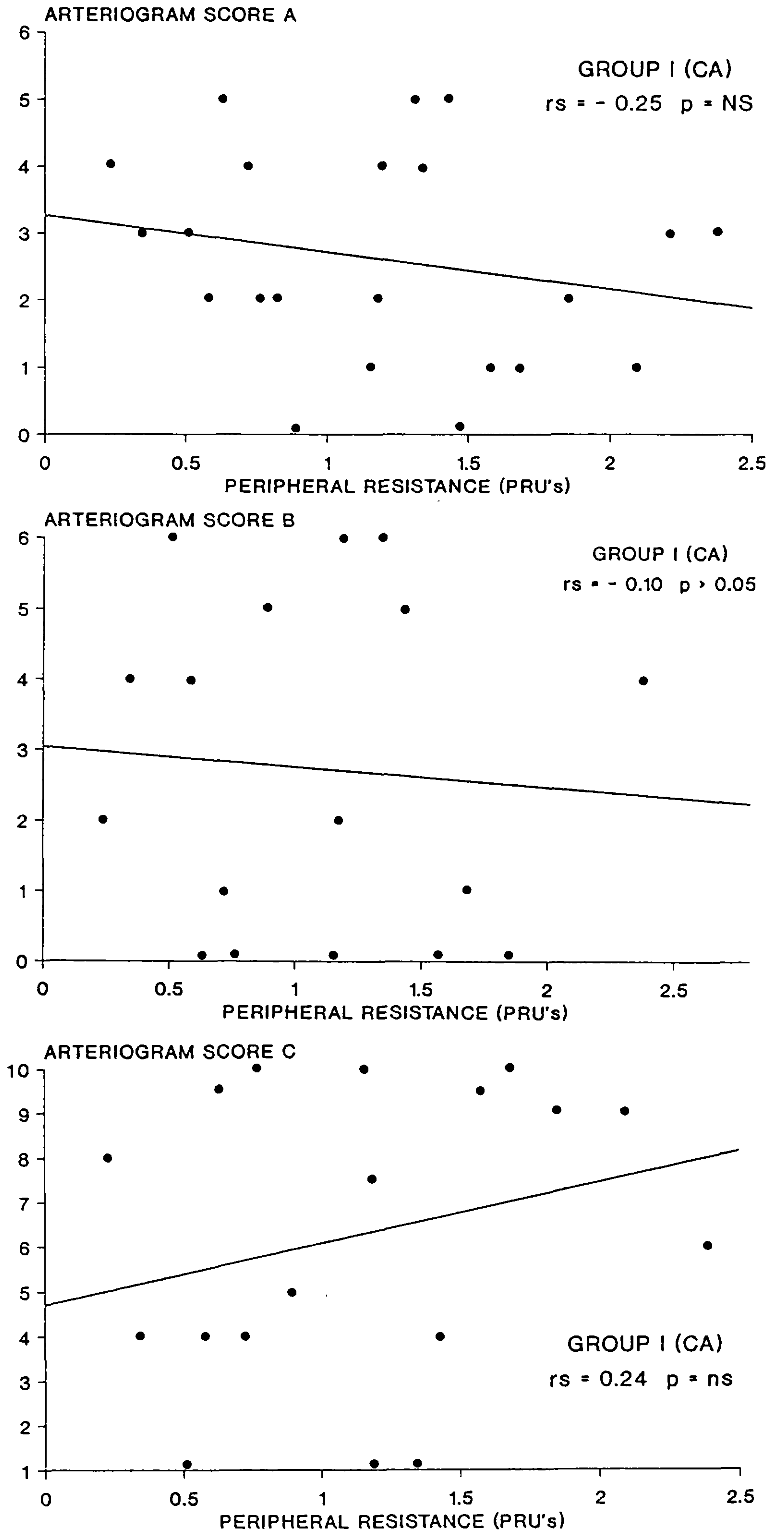
Correlation of PR with arteriographic scoring systems in reconstructions to the distal popliteal artery.

Groups	Correlation	SCORE A	SCORE B	SCORE C
I (CA)	PR r_s	-0.25 +	-0.10 +	0.24 +
II (DSA)	PR r_s	-0.43^{**}	-0.56^{***}	0.55^{***}

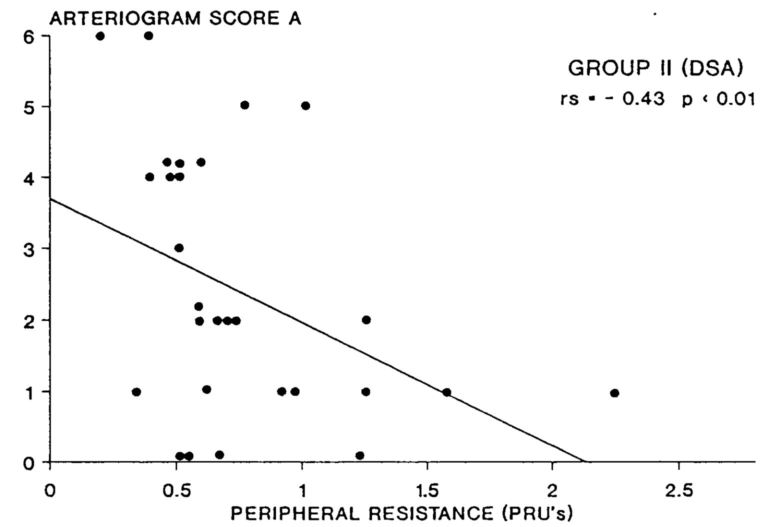
Group I = Conventional arteriograms (CA) only (n = 22), (See page 150).

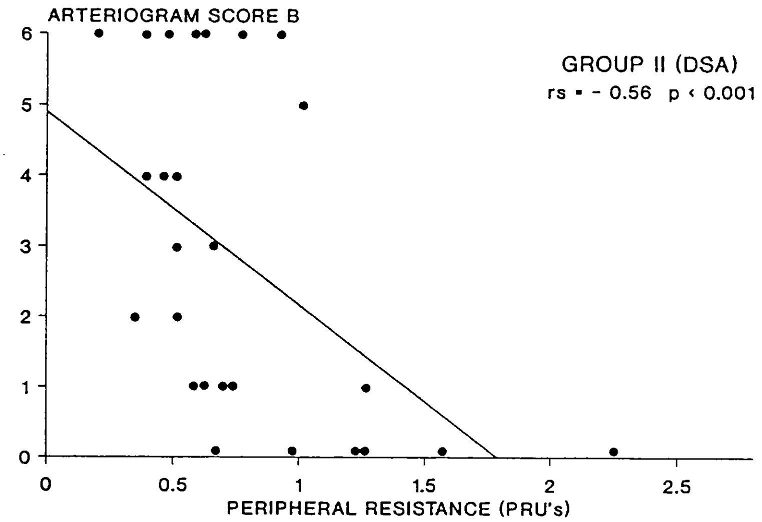
Group II = IA DSA (n = 29), (See page 151).

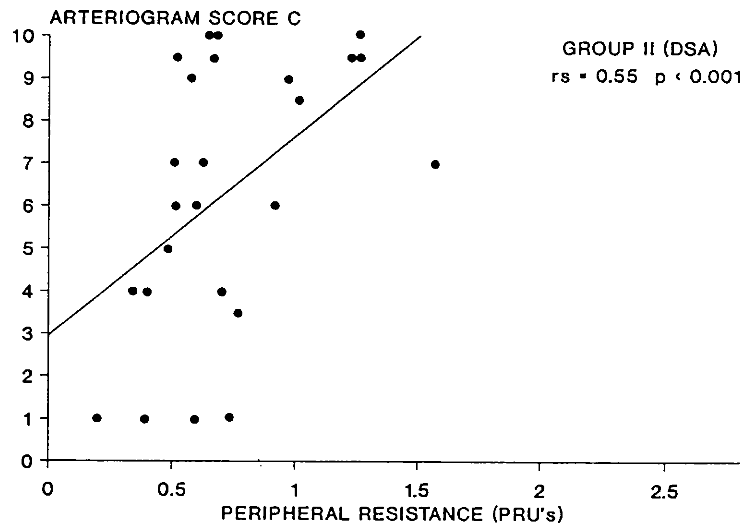
Not Significant +, $p < 0.05^{*}$, $p < 0.01^{**}$, $p < 0.001^{***}$



Figures 59-61. Correlation of PR with arteriographic scoring systems in reconstructions to the distal popliteal artery.







Figures 62-64. Correlation of PR with arteriographic scoring systems in reconstructions to the distal popliteal artery.

(ii) Distal (single calf vessel) calf reconstructions.

Neither conventional nor IA DSA derived arteriogram scores A, B and C correlated with the measured PR, (Table 11, Figures 65-70).

Table 11.

Correlation of PR with arteriographic scoring systems in reconstructions to single calf vessels.

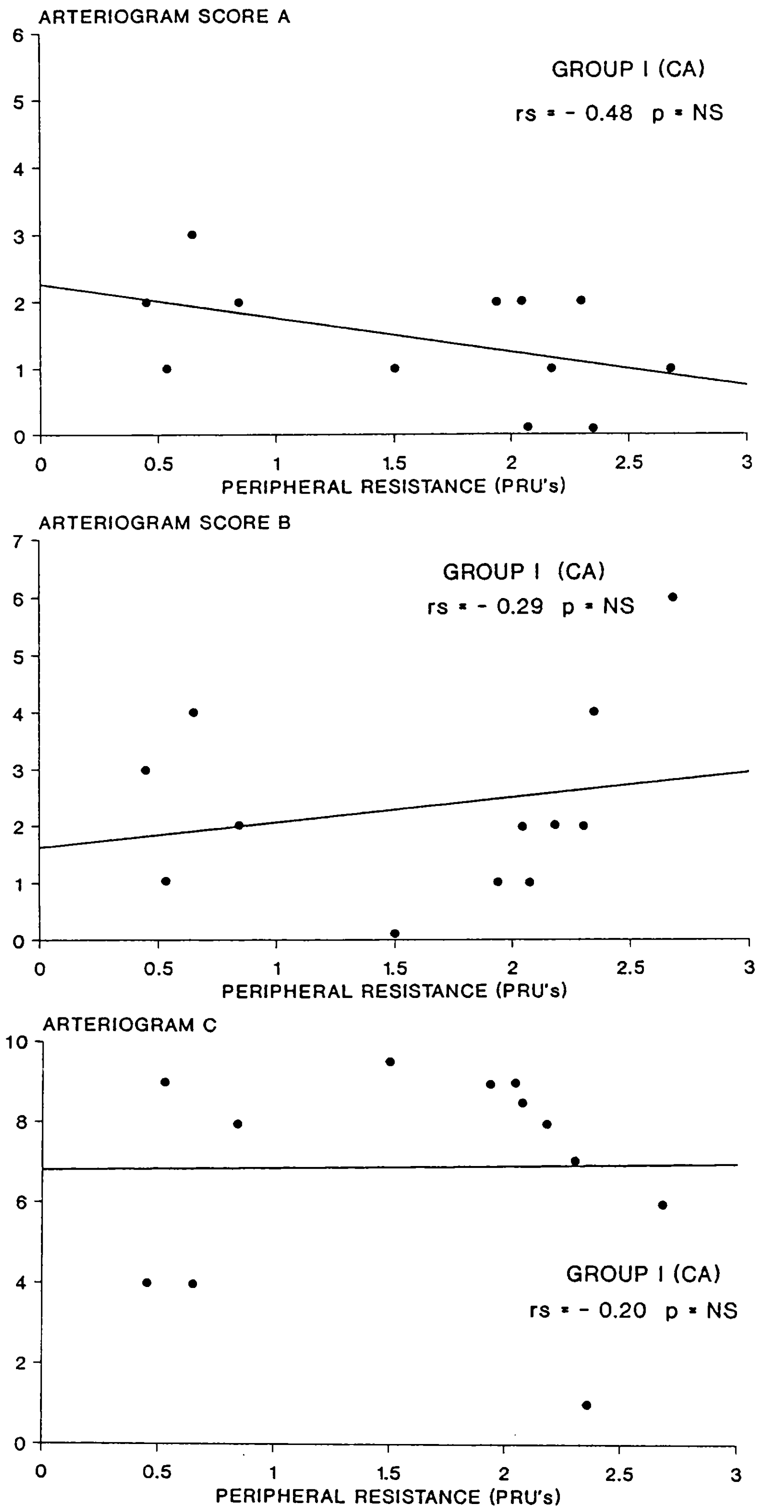
Groups	Correlation	SCORE A	SCORE B	SCORE C
I(CA)	PR r_s	-0.48 +	0.29 +	-0.20 +
II(DSA)	PR r_s	-0.28 +	-0.29 +	0.42 +

Group I = Conventional arteriograms (CA) only (n = 12), (See page 153).

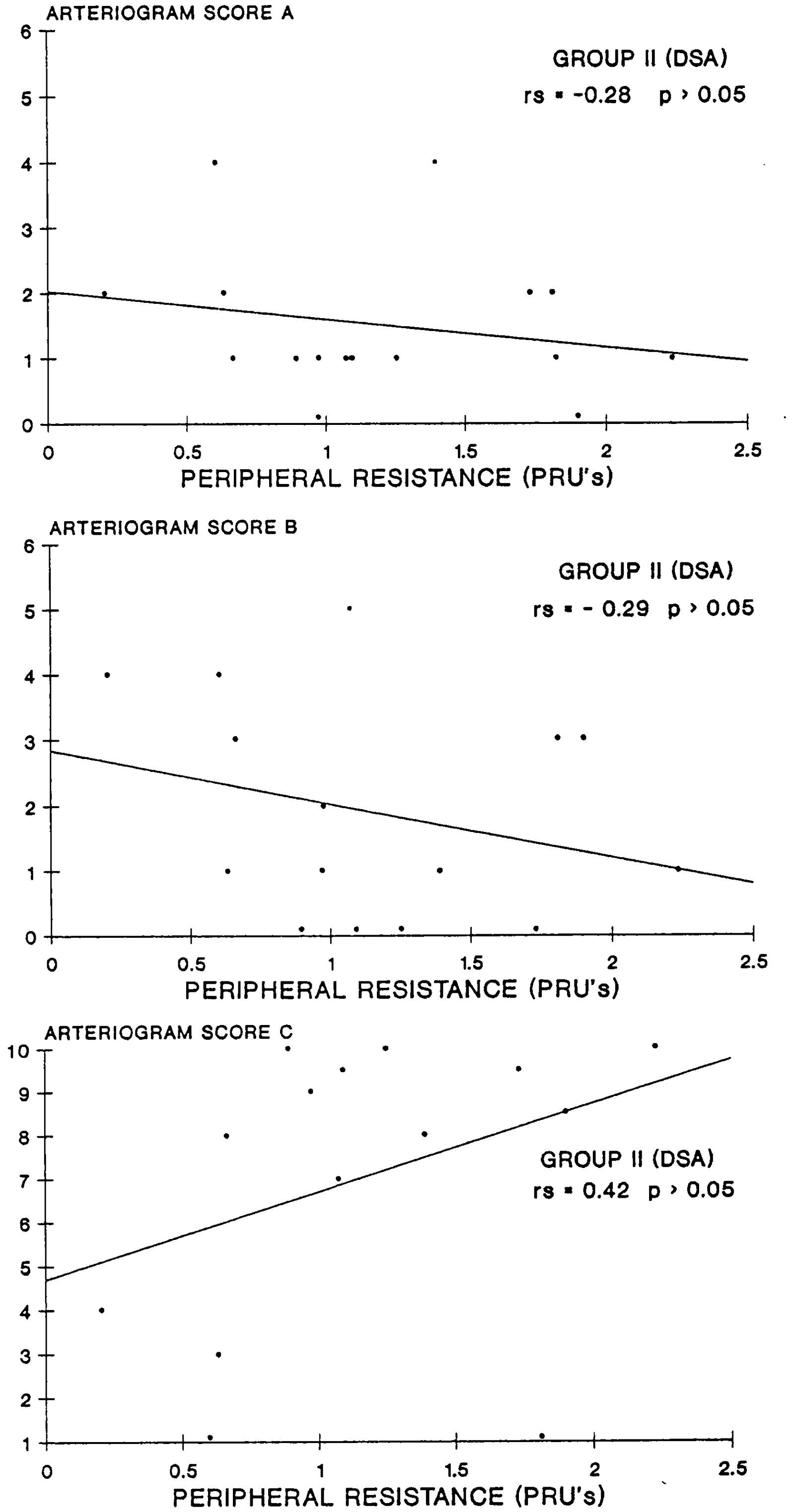
Group II = IA DSA (n = 16), (See page 154).

Not Significant +, $p < 0.05^{*}$, $p < 0.01^{**}$, $p < 0.001^{***}$

These results clearly reflects the limitation of arteriography, particularly in patients with severe multisegment disease with patent single calf vessels not in continuity with the distal popliteal artery.



Figures 65-67. Correlation of PR with arteriographic scoring systems in reconstructions to single calf vessels.



Figures 68-70. Correlation of PR with arteriographic scoring systems in reconstructions to single calf vessels.

(d) Graft outcome at one month

In the analysis of all 88 femoro-distal grafts the arteriogram scores A, B, and C were significantly higher in the successful grafts, (Table 12, Figures 71-73). But despite this there were 18 (29%) successful grafts in whom the pre-operative arteriogram scoring system A failed to show any significant runoff.

Table 12.

Graft outcome at one month, success vs failure using the arteriogram scoring systems A, B, and C. (Mann U Whitney test).

	SCORE A	SCORE B	SCORE C
Overall	$p < 0.001$	$p < 0.02$	$p < 0.04$

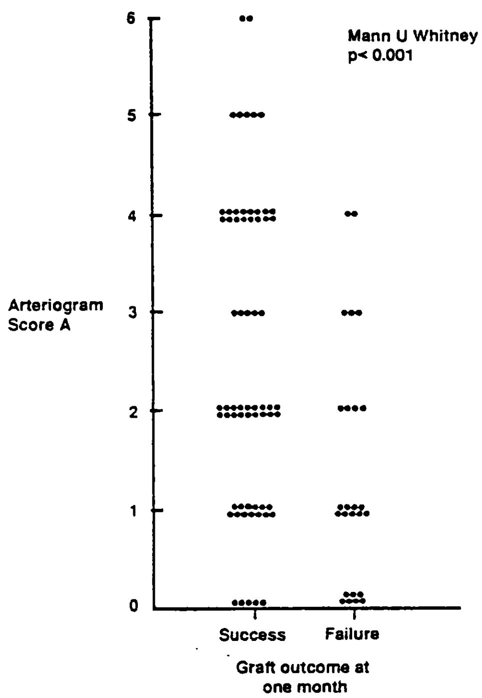


Figure 71. Graft outcome at one month, success vs failure using the arteriogram score A in group II (IA DSA).

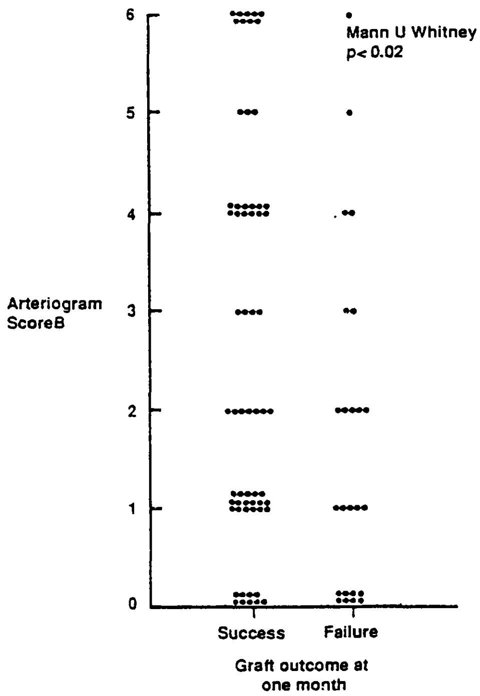


Figure 72. Graft outcome at one month, success vs failure using the arteriogram score B in group II (IA DSA).

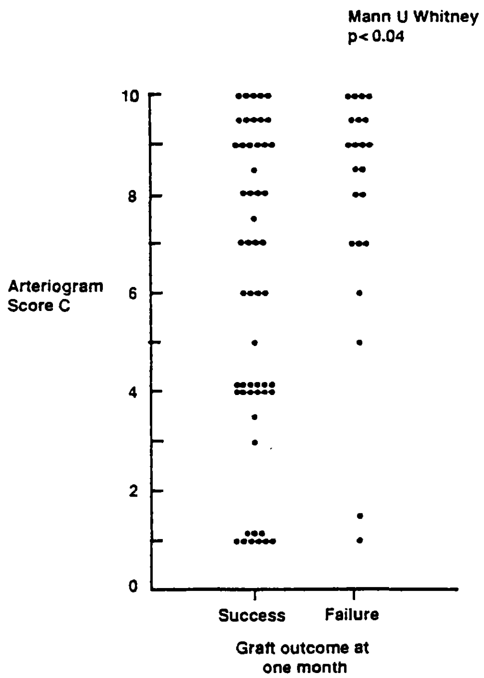


Figure 73. Graft outcome at one month, success vs failure using the arteriogram score C in group II (IA DSA).

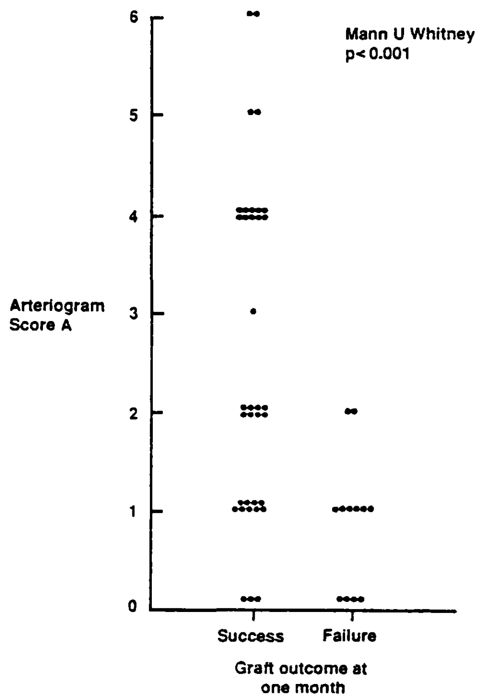
In view of the previous finding that IA DSA provided a better form of assessment of calf vessel runoff, the 48 femoro-distal grafts in group II were subdivided into (i) overall, (ii) distal popliteal and (iii) single calf vessel grafts. Using the same scoring systems, similar results were obtained (Tables 12 & 13, Figures 74-82). Successful grafts had better arteriogram scores than failed in the overall and distal popliteal groups. In contrast, the scores derived from the IA DSA in the single calf vessel group were unable to differentiate between success and failure at one month. This may well be a function of numbers and further studies are underway to refine the techniques of distal calf visualisation.

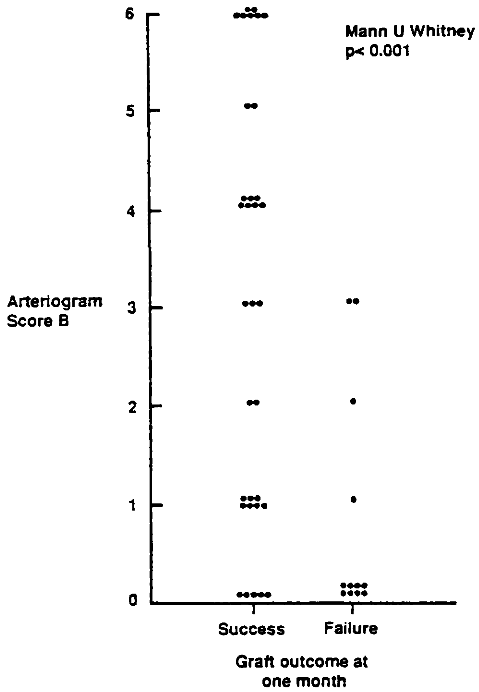
Table 13.

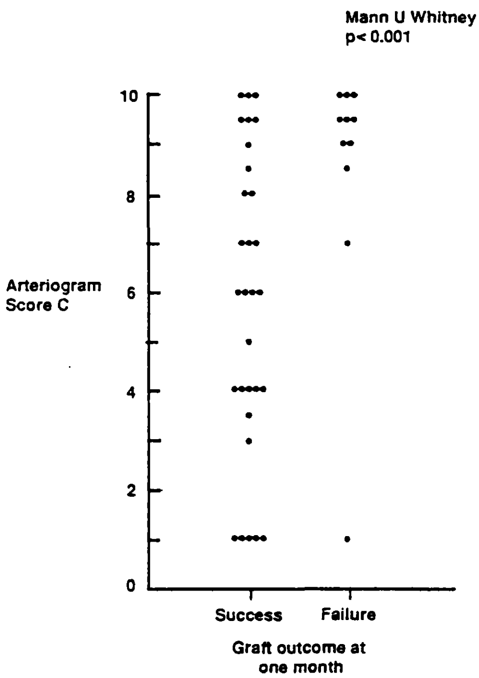
Graft outcome at one month (success vs failure), using the arteriogram scoring systems A, B, and C in Group II (IA DSA), (Mann U Whitney test).(See page 158-160).

	SCORE A	SCORE B	SCORE C
OVERALL	$p < 0.001$	$p < 0.001$	$p < 0.01$
DISTAL POP	$p < 0.05$	$p < 0.03$	$p > 0.05$
SINGLE CV	$p > 0.05$	$p > 0.05$	$p > 0.05$

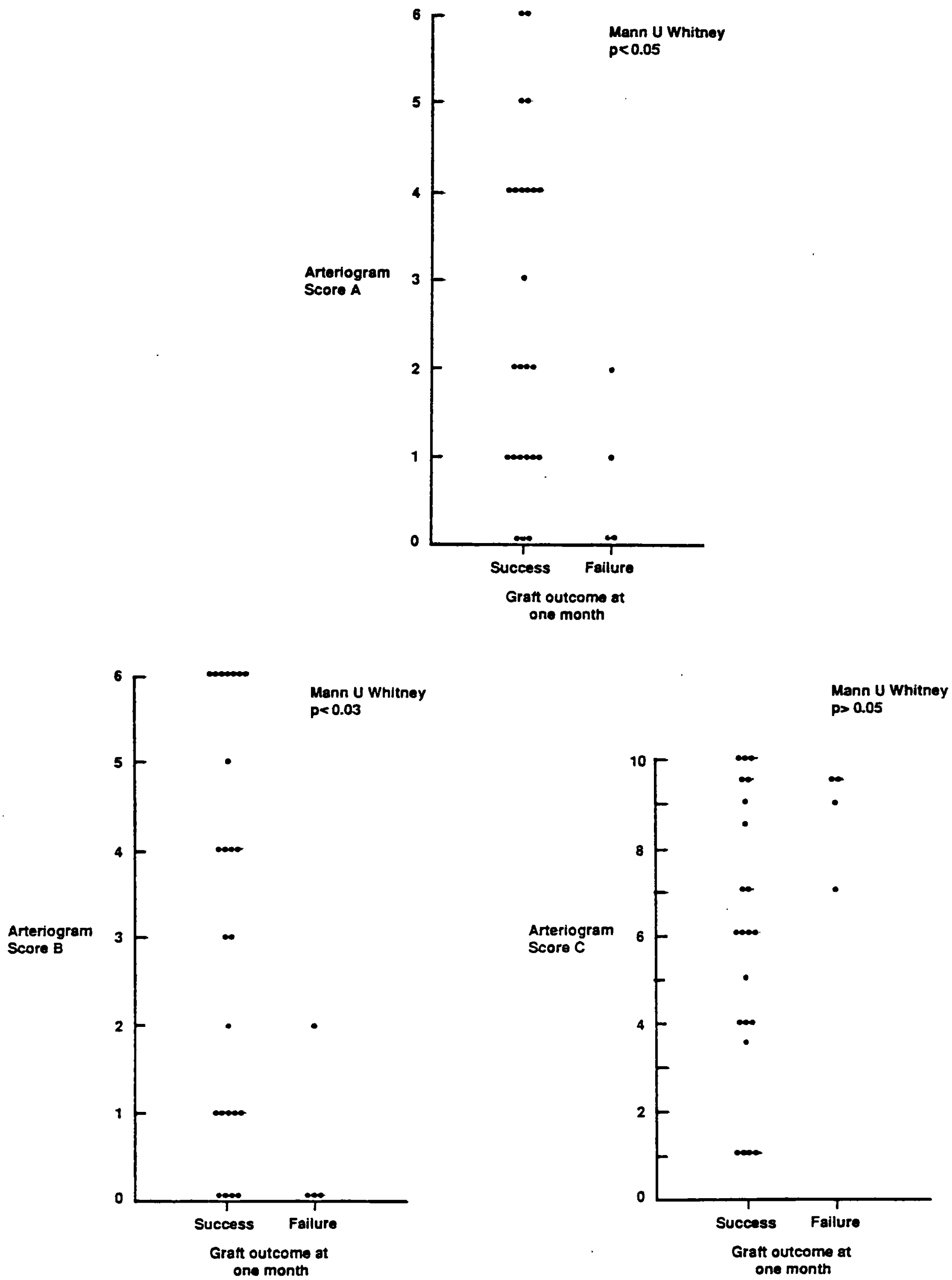
These results show considerable overlap between the arteriogram scores of succesful and failed grafts and highlights the inability of arteriography to predict the outcome of reconstruction. Patients should not therefore be denied the possibility of reconstruction on the basis of the pre-operative arteriogram and some alternative method of selection should be sought.



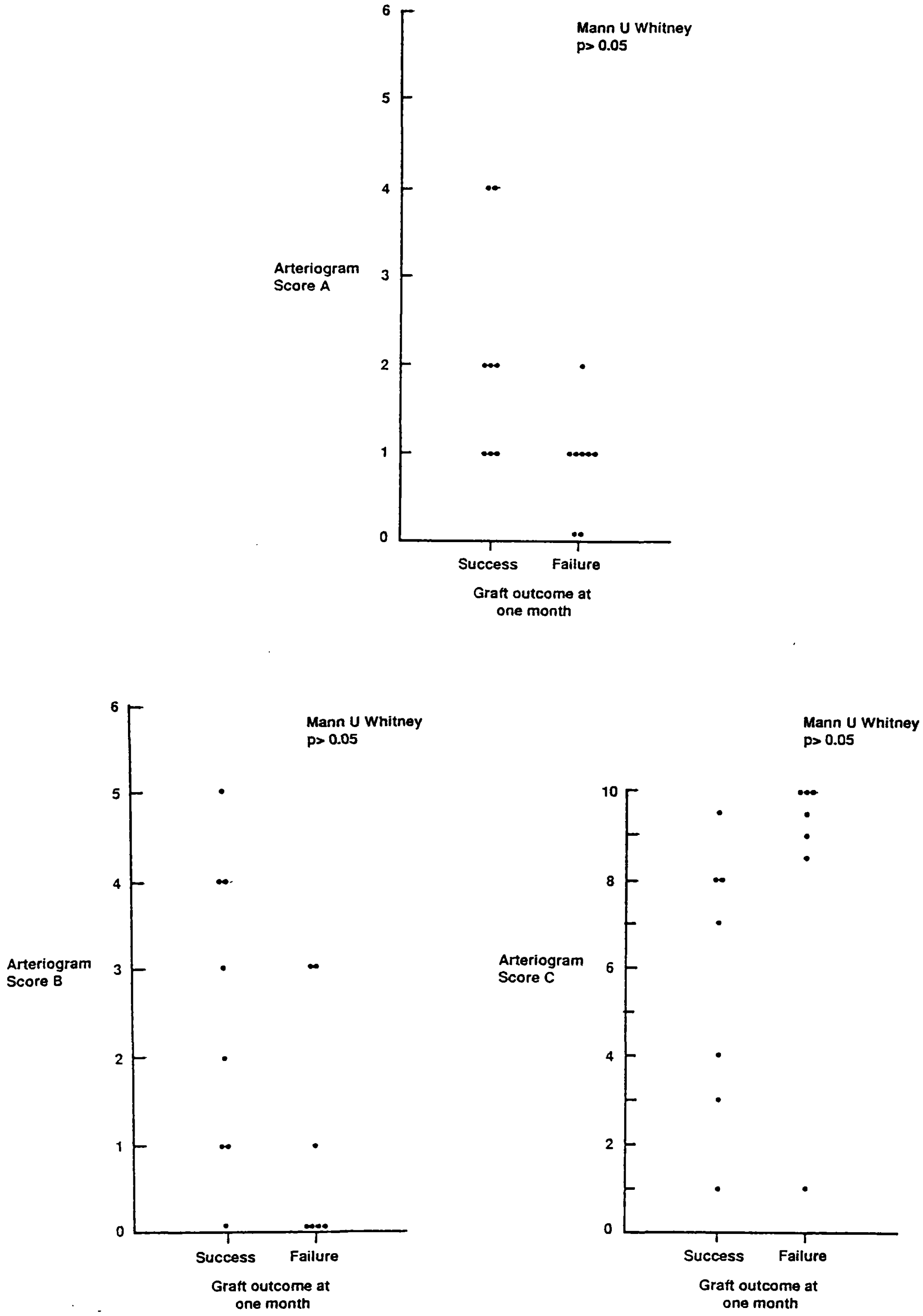




Figures 74-76. Graft outcome at one month (success versus failure), using the arteriogram scoring systems A, B and C in group II (IA DSA), (Overall).



Figures 77-79. Graft outcome at one month (success versus failure), using the arteriogram scoring systems A, B and C in group II (IA DSA), (Distal Pop).



Figures 80-82. Graft outcome at one month (success versus failure), using the arteriogram scoring systems A, B and C in group II (IA DSA), (Single CV).

(e) Arteriographic Predicted peripheral resistance.

Multiple linear regression analysis was used to derive a predicted resistance value on the basis of the pre-operative arteriogram. The calf vessels were scored independently of each other using scoring system B. The arteriogram subscores for the anterior tibial, posterior tibial and peroneal arteries (independent variables) were correlated against the measured peripheral resistance, (dependant variable) The pedal arch status was not included in the subscores, as this was not consistently visualised on the pre-operative IA-DSA. A series of equations were derived which best described the relationship between the pre-operative IA-DSA assessment of calf vessel and the measured peripheral resistance at various levels within the calf, (Table 14).

Using multiple linear regression analysis (MLR) the arteriogram subscores for the AT, PT, PER were correlated against the measured peripheral resistance for all 35 cases. Three peripheral resistance values were derived at different sites; (i) for a single calf vessel (R1), (ii) distal popliteal artery (R3) and (iii) irrespective of the level (R0), (Figure 81). There were insufficient numbers within the tibioperoneal group (R2) for analysis. These were then applied to a prospective series of 14 femoro-distal grafts. The individual arteriogram subscores are given in Table 14.

Table 14.

Predicted Peripheral resistance equations

$$R0 = 1.23 - 0.21(PT) - 0.08(AT) - 0.13(PER)$$

$$R1 = 1.84 - 0.11(PT) - 0.15(AT) - 0.49(PER)$$

$$R3 = 0.96 - 0.15(PT) - 0.05(AT) - 0.04(PER)$$

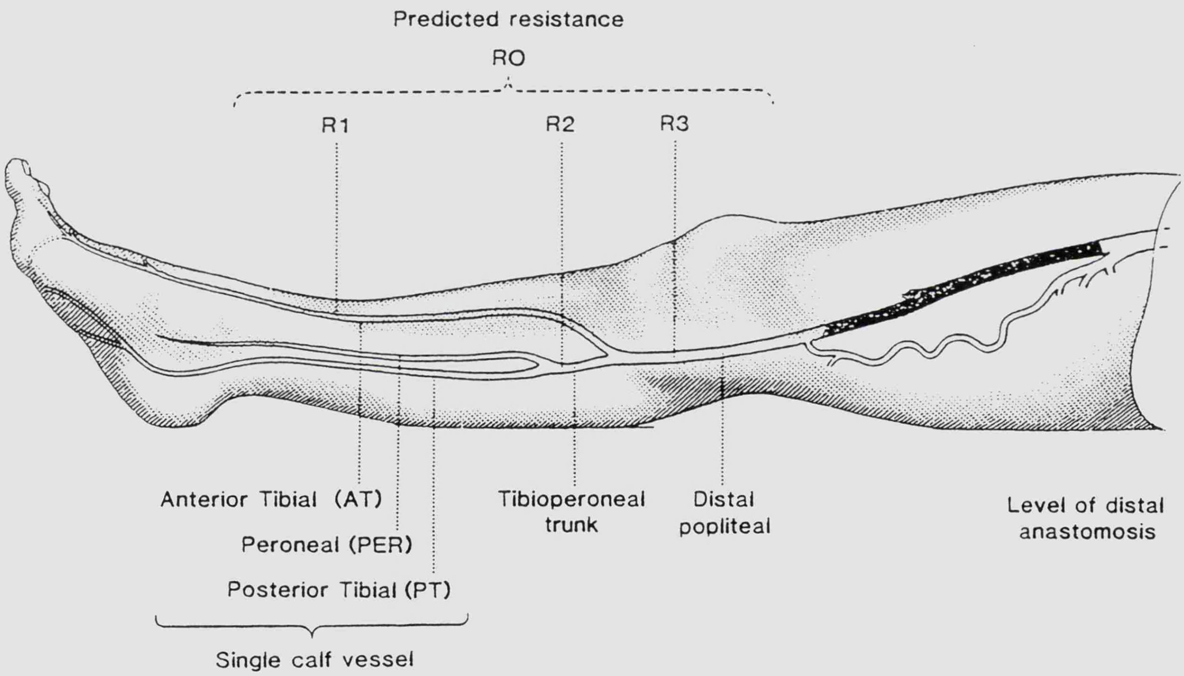


Figure 83.

Predicted peripheral resistance values at different levels in the calf.

Table 15.

Arteriographic subscores for grafts to a single calf vessel.

PTNO	AT	PT	PER	MPR	PPR
1	0	1	0	2.23	1.73
2	0	0	2	1.73	0.86
3	0	0	1	0.89	1.35
4	0	1	1	1.81	1.20
5	0	0	1	1.39	1.35
6	0	0	2	0.20	0.86
7	1	0	0	1.08	1.69
8	0	2	2	0.39	0.64
9	1	1	2	1.25	1.35
10	0	2	2	1.90	1.84

MPR = Measured peripheral resistance, PPR = predicted peripheral resistance.

Table 16.

Arteriographic subscores for grafts to the tibioperoneal trunk.

PTNO	AT	PT	PER	MPR
11	1	1	2	0.78
12	0	2	2	0.24
13	1	0	0	0.92

Table 17.

Arteriographic subscores for grafts to the distal popliteal artery.

PTNO	AT	PT	PER	MPR	PPR
14	0	2	0	0.59	0.66
15	2	2	2	0.39	0.48
16	0	2	2	0.51	0.58
17	0	2	2	0.51	0.58
18	0	0	2	0.73	0.88
19	2	1	1	0.60	0.63
20	1	1	0	0.70	0.76
21	0	0	1	0.83	0.92
22	1	2	2	1.01	0.53
23	0	0	2	0.66	0.88
24	0	1	2	0.51	0.73
25	0	2	2	0.92	0.58
26	0	0	0	0.97	0.96
27	0	0	0	1.34	0.96
28	1	0	0	1.25	0.91
29	0	0	0	0.54	0.96
30	0	2	2	0.44	0.58
31	2	1	1	0.39	0.63
32	1	0	0	0.58	0.91
33	0	0	1	1.73	0.92
34	1	1	0	1.26	0.76
35	0	1	0	0.30	0.81

There was good agreement between the predicted peripheral resistance value R3 (ie at the distal popliteal level) and the measured PR, limits of agreement -0.65 to 0.67, with a 95% confidence intervals of -0.17 to 0.18, (Figure 84).

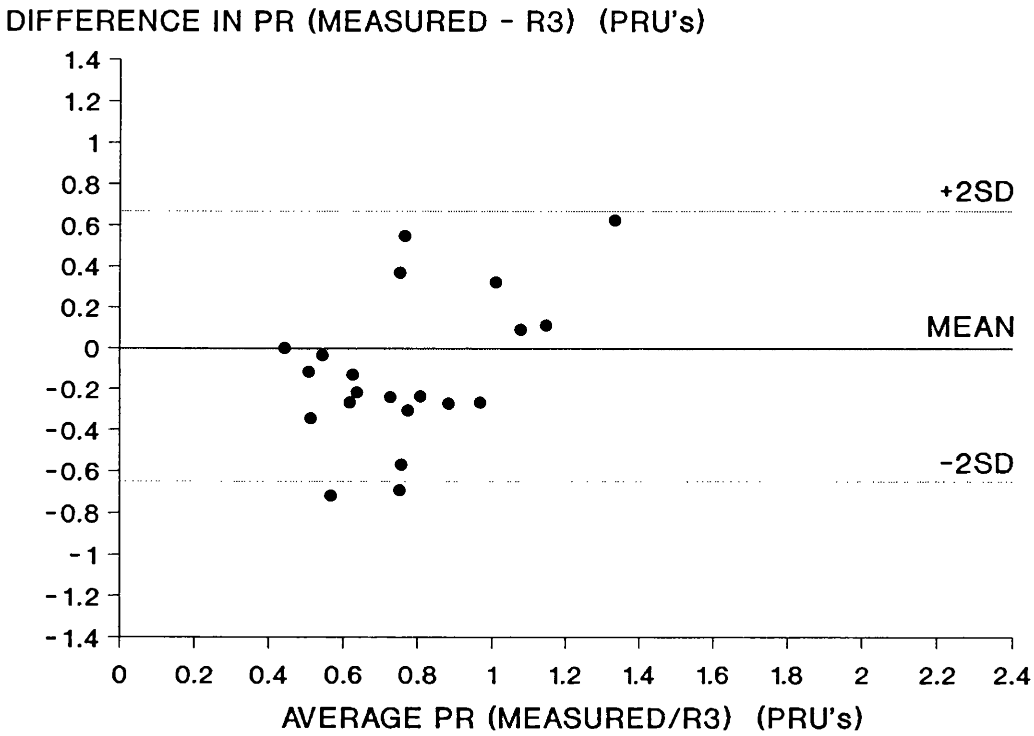


Figure 84.

Measurement of agreement; arteriographic predicted peripheral resistance R3 (Distal popliteal level).

In contrast there was poor agreement between the predicted PR value R1 and the measured PR, limits of agreement -1.04 to 1.04, with a 95% confidence interval of -0.52 to 0.52, (Figure 85).

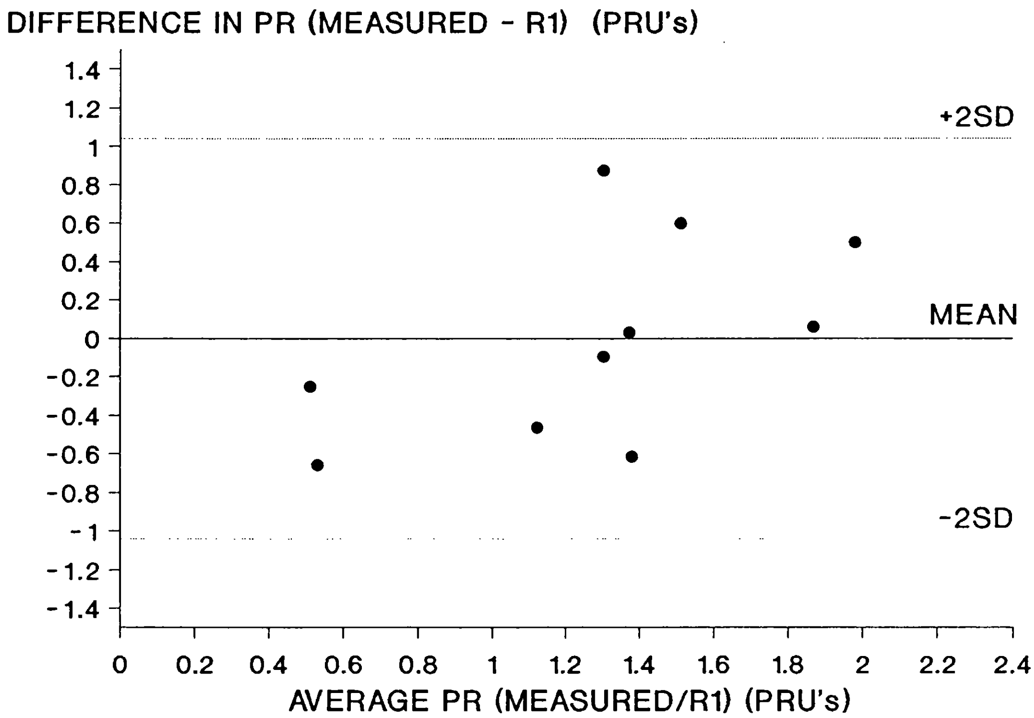


Figure 85.

Measurement of agreement; Arteriographic predicted peripheral resistance R1 (single calf vessel).

In the prospective series of 14 grafts, there was again a wide range of agreement between the predicted and measured PR, -1.25 to 0.59, with a 95% confidence interval of -0.72 to 0.06, (Figure 86).

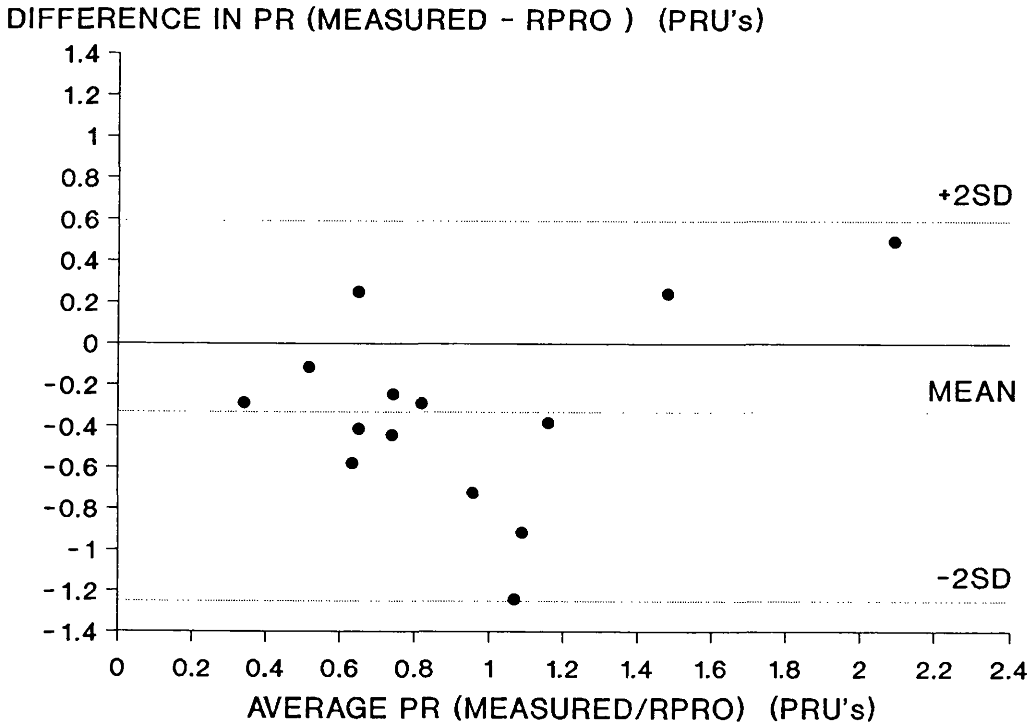


Figure 86.

Measurement of agreement; Arteriographic predicted peripheral resistance, prospective series.

These results suggest that a predicted PR value can be obtained for the distal popliteal level which will accurately predict the operative findings. In the case of more distal grafts the R1 equation is inaccurate and cannot be relied upon as a method of selecting patients for femoro-distal reconstruction.

Discussion

Conventional arteriography has been the definitive investigation in patients with critical ischaemia, the decision to perform surgery being based upon the visualization of an adequate runoff. In patients with a single calf vessel, continuity with the pedal arch is a decisive factor in both short and long term patency (Imparato, Kim, Madayag et al 1973, O'Mara, Flinn, Neiman et al 1981 and Simms 1988). Unfortunately, in the presence of multisegment disease and poor myocardial function, visualisation of calf vessel runoff and pedal arches using arteriography may prove impossible. While the introduction of IA DSA has resulted in better vessel resolution with a lower contrast load, it still may not show very distal patent calf vessels. Peripheral resistance, on the other hand, has recently been shown to be of predictive value in the per-operative assessment of patients for femoro-distal bypass (Ascer, Veith, Morin et al 1984, Ascer, Veith, Flores-White et al 1987 and Parvin 1987), but this is an intra-operative technique and does not allow pre-operative selection of patients.

In an attempt to improve the predictive value of arteriography, various scoring systems have been devised, the simplest being a grading of 0-3, one point being given for each patent calf vessel (Shearman, Gwyn, Curran et al 1986b, LaMorte, Menzoian, Sidawy et al 1985 and Rutherford, Flanigan, Gupta et al 1986). LaMorte found this simple scoring system to be of little predictive value in terms of the peripheral resistance measured at the time of surgery. The poor correlation between the arteriogram score and the peripheral resistance was attributed both to the inability of the scoring system to differentiate between good and bad vessels, and to the assumption that all three calf vessels contributed equally to the overall peripheral resistance. On the basis of these criticisms, LaMorte devised a new scoring system which took the pedal arch into account in the overall determination of peripheral resistance. This produced a better correlation with peripheral resistance (r = 0.61). One criticism against the addition of an arch score is that some centres may not have the equipment, technical expertise, or time to visualise these vessels.

In an attempt to standardise the use of arteriographic scoring systems in reporting runoff, the ad hoc Committee (SVS/ISCVS) on reporting standards devised a novel method of assessing runoff (Rutherford, Flanigan, Gupta et al 1986). The runoff was graded at the site of the proposed distal anastomosis. This grading system took into account the vessel chosen for the anastomosis, the severity of disease, patency of the arch if applicable and a base resistance. Nevertheless, Peterkin et al (1988) reported that the SVS/ISCVS scoring system correlated poorly with the measured peripheral resistance ($r = 0.30$; $p < 0.01$), although it was improved by weighting the individual calf vessel by means of multiple linear regression.

In the present study three separate arteriogram scoring systems were correlated with PR. In the analysis of all 88 grafts there were poor correlations between all three arteriogram scoring systems and PR. The introduction of IA DSA, however, produced an overall improvement in the visualization of the proximal calf vessels with subsequent improved correlation between the arteriogram scores and PR. The better correlations with systems B and C probably reflect superior methods of scoring. In system B the assessment was based on the first 5 cms of the calf vessel and in system C the grading was based at the level of the distal anastomosis. Although system C may be theoretically more attractive, system B is easier to apply and produces a similar correlation with PR. In the distal calf reconstructions the arteriogram scores derived from both the conventional and IA DSA films failed to correlate with the measured PR. These results highlight some of the limitations of arteriography scoring in patients with patent distal calf vessels not in continuity with the popliteal artery.

The use of IA DSA in combination with conventional arteriography improved visualisation of calf vessels, particularly in the proximal calf. An aggressive approach to the arteriographic demonstration of these vessels must be tempered by consideration of the problems related to increasing dose of contrast medium. In most patients this is not a problem when using IA DSA but may be so when using conventional arteriography.

Although there were poor correlations between the measured peripheral resistance and the arteriogram scoring systems, all three produced significantly higher scores in the successful grafts. There were however a number of patients with successful grafts at one month in whom the pre-operative arteriogram failed to show any real evidence of calf vessel runoff capable of supporting a graft. Almost 30% of the 88 femoro-distal grafts studied had incomplete visualisation of the distal runoff. Clearly there is a need for a more predictive test of calf vessel runoff. Of the grafts that failed with arteriogram scores of 2 or more all were due to technical errors at the time of surgery.

The use of multiple linear regression enabled the relative importance of each vessel to be assessed and this is reflected in the different coefficients. In the case of the R3 equation the peroneal artery has a low weighting factor and implies that it does not communicate much to the overall resistance of the leg where there is proximal disease. In contrast the peroneal artery is weighted highly in the R1 equation and this may reflect the fact that the artery communicates with the pedal arch in severe disease. The anterior tibial artery is consistently weighted highly and suggests that it is linked to a low resistance bed. The base line resistance value of approximately 1 in the R1 and R0 equations implies that the graft should be successful. The equations do not take into account the effect of a large collateral supply on the overall base line resistance. This will be of more significance in grafts to an isolated popliteal segment with peri-geniculate anastomoses. In the case of isolated patent calf vessel the presence of a well developed collateral circulation is rare.

Using multiple linear regression to derive a predicted PR value there was good agreement between the predicted (R3) and measured PR at the level of the distal popliteal artery. At the level of the single calf vessel there was poor agreement between the predicted and measured PR such that arteriography was a poor predictor of PR.

These findings are supported by Peterkin et al 1988 who showed that the more distal the graft the worse the correlation between the scoring system and the predicted peripheral resistance (Above knee fem-pop $r = 0.85$ $p < 0.001$ versus below knee fem-pop $r = 0.43$ $p < 0.01$). The inclusion of an arch score may well improve the correlation particularly in the single calf vessel group. Since the study has been completed the radiological department has increased its experience in arch visualisation techniques and now makes it a realistic proposition to include the arch score into the equation.

Summary

Arteriography is the conventional investigation of choice in patients with critical ischaemia to select the site for the distal anastomosis of a femoro-distal bypass. Several arteriographic scoring systems have been devised in an attempt to quantify the runoff. Intra-operative peripheral resistance measurements have been proposed as better predictors of early graft patency. Eighty-eight consecutive femoro-distal bypass grafts were studied using conventional and intra-arterial digital subtraction arteriography (IA DSA) and peripheral resistance (PR) measurement. Three widely used arteriographic scoring systems were used to grade the arteriographic runoff. There were significant correlations between the scoring systems and the measured PR. IA DSA improved the correlation between the arteriogram scoring systems and the measured PR in the distal popliteal artery, but not in single calf vessels. **Selection of patients for proximal calf vessel reconstruction may be based upon arteriography but distal reconstruction should not be denied to patients who have no evidence of runoff on either conventional arteriography or IA DSA.**

CHAPTER 7b.

RESULTS: PULSE GENERATED RUNOFF.

Patients.

Thirty-five consecutive patients (25 men and 10 women) undergoing non-reversed vein femoro-distal bypass for critical ischaemia were studied. Their median age was 70 years (range 54-86). Twenty two grafts were performed to the distal popliteal artery, 3 to the tibioperoneal trunk and 10 to a single calf vessel. All patients underwent non-invasive assessment before surgery including ankle pressures and a PGR study. An IA DSA was obtained in all cases.

Statistics

The comparison between the PGR, PGR/ARCH scores and the measured PR were evaluated statistically using the Spearman rank (r_S) correlation test. Multiple linear regression analysis was used to derive a predicted resistance value. The PGR subscores for the anterior tibial, posterior tibial, peroneal and pedal arch (independent variables) were correlated against the measured peripheral resistance (dependant variable). A series of equations were derived which best described the relationship between the non-invasive PGR assessment of the calf vessels and the measured peripheral resistance. The predicted PR was compared with the measured PR using measurements of agreement described by Bland and Altman (1986), rather than correlation coefficients as the latter does not reflect agreement between the two methods of PR measurement. In this situation the null hypothesis is that neither method is linearly related. The probability of this is small and so a high correlation does not necessarily reflect agreement.

Results

Measured Peripheral Resistance

There was a reasonable correlation between the PGR score and the measured peripheral resistance for all 35 grafts $r_S = -0.39$, $p < 0.02$ (Table 18, Figures 87-92). The correlation improved with the addition of the arch score (PGR/ARCH), $r_S = -0.44$, $p < 0.01$.

Table 18.

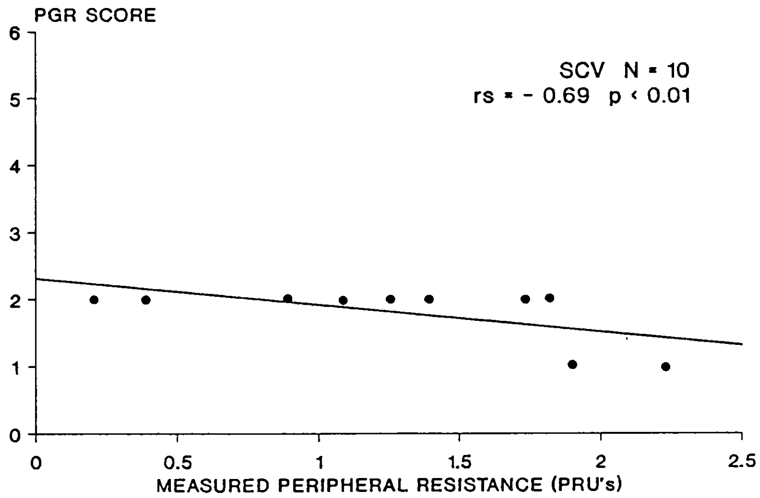
PGR and PGR/ARCH scores correlated against the measured peripheral resistance.

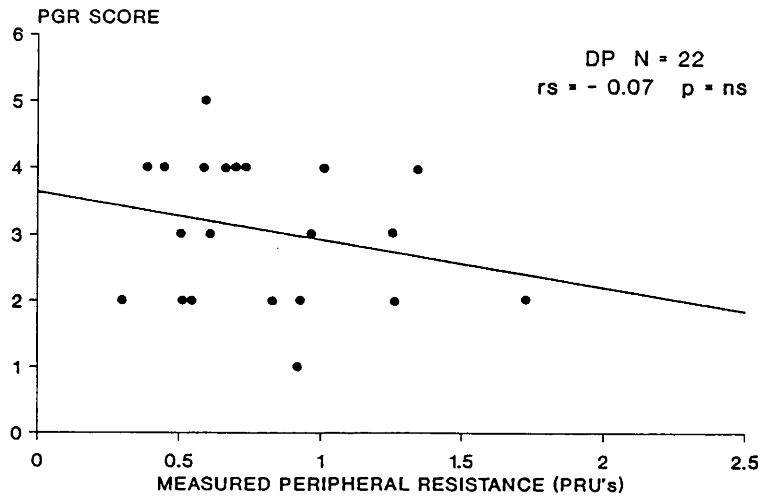
Correlation PR (rs)	Overall (N=35)	DP (N=22)	SCV (N=10)
PGR	-0.39^{**}	-0.07^{+}	-0.69^{**}
PGR/ARCH	-0.44^{**}	-0.08^{+}	-0.88^{***}

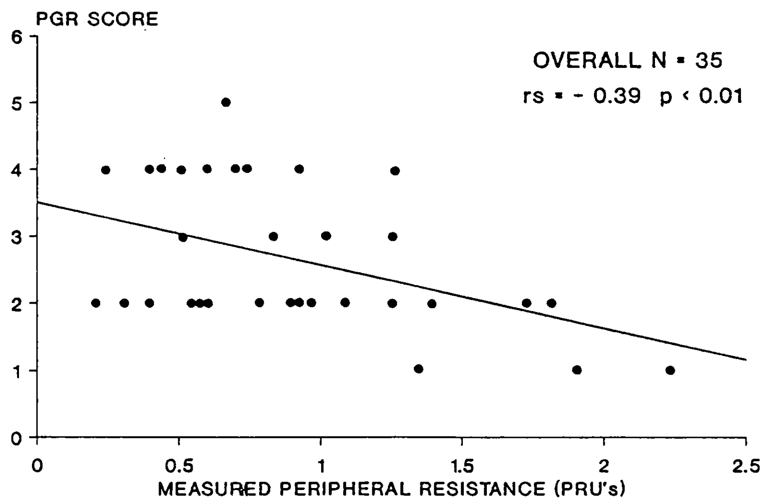
Not significant = $^{+}$, $p<0.05^{*}$, $p<0.01^{**}$, $p<0.001^{***}$.

DP = Distal popliteal, SCV = single calf vessel.

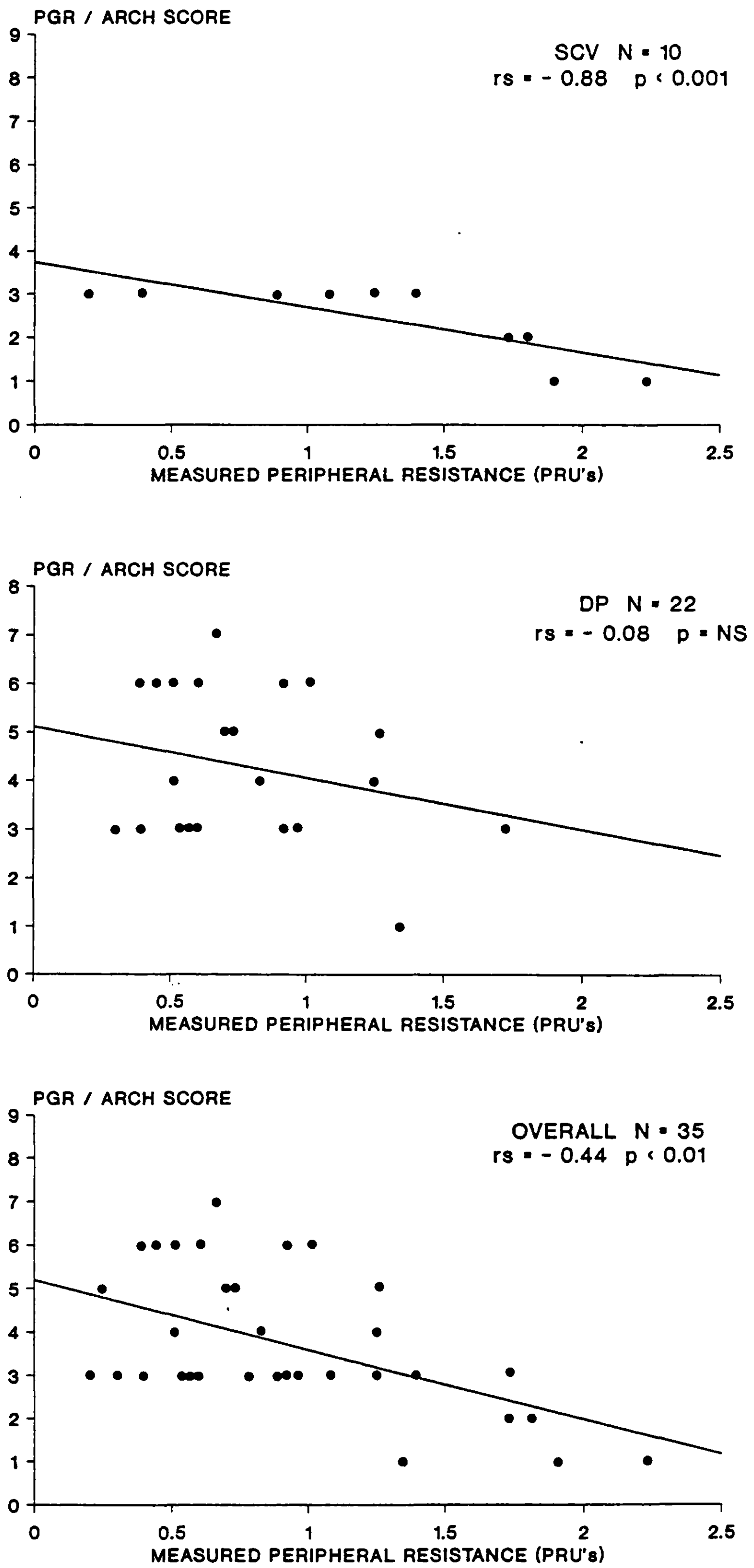
In the distal popliteal group, PGR failed to correlate with the measured peripheral resistance, reflecting the inability of PGR to recognise proximal calf vessel disease. In the single calf vessel group there was a significant correlation between the PGR score and the measured peripheral resistance $r_S = -0.69$, $p < 0.025$. This improved with the addition of the arch score $r_S = -0.88$, $p < 0.001$.







Figures 87-89. PGR scores correlated against the measured peripheral resistance.



Figures 90-92. PGR/ARCH scores correlated against the measured peripheral resistance.

PGR Predicted Peripheral Resistance

Using multiple linear regression (MLR) the PGR calf vessel scores for the AT, PT, PER and ARCH score were correlated against the measured peripheral resistance. Three peripheral resistance values were derived at different sites (i) for a single calf vessel (R1), (ii) distal popliteal artery (R3) and (iii) irrespective of the level (R0). There were insufficient numbers to analyse in the tibioperoneal artery group (Figure 93).

Figure 93.

Predicted peripheral resistance equations using multiple linear regression analysis.

$$R1 = 2.97 - 0.90(PT) - 0.57(AT) - 0.63(PER) - 0.77(ARCH)$$

$$R3 = 1.46 - 0.005(PT) - 0.15(AT) - 0.04(PER) - 0.34(ARCH)$$

$$R0 = 1.02 + 0.02(PT) - 0.13(AT) + 0.2(PER) - 0.14(ARCH)$$

R1 = Single calf vessel grafts.

R3 = Distal popliteal Grafts.

R0 = Overall, irrespective of the level of the anastomosis.

PT = Posterior tibial

AT = Anterior tibial

PER = Peroneal

ARCH = Arch score

Table 19.

PGR subscores for grafts to a single calf vessel.

PTNO	AT	PT	PER	ARCH	MPR	PPR
1	0	1	0	0	2.23	2.07
2	0	0	2	0	1.73	1.71
3	0	0	2	1	0.89	0.94
4	2	0	0	0	1.81	1.83
5	0	0	2	1	1.39	0.94
6	0	0	2	2	0.20	0.17
7	2	0	0	1	1.45	1.06
8	0	2	0	1	0.39	0.4
9	0	0	2	1	1.10	0.94
10	0	1	0	0	1.90	2.07

MPR = Measured peripheral resistance, PPR = predicted peripheral resistance.

Table 20.

PGR subscores for grafts to the tibioperoneal trunk.

PTNO	AT	PT	PER	ARCH	MPR
11	0	1	0	1	0.78
12	0	0	2	1	0.24
13	2	0	2	1	0.92

Table 21.PGR subscores for grafts to the distal popliteal artery.

PTNO	AT	PT	PER	ARCH	MPR	PPR
14	2	2	0	1	0.59	0.92
15	2	0	1	1	0.39	0.62
16	2	2	1	2	0.51	0.79
17	2	2	0	2	0.51	0.79
18	0	2	0	1	0.73	0.66
19	1	1	1	2	0.60	0.52
20	1	2	0	1	0.70	0.66
21	2	0	0	1	0.83	0.82
22	1	2	0	1	1.01	0.69
23	2	2	0	1	0.66	0.72
24	2	2	0	2	0.51	0.79
25	0	0	1	0	0.92	1.18
26	2	2	0	1	0.97	0.62
27	0	2	2	2	1.34	1.22
28	2	0	0	1	1.25	0.64
29	0	2	0	1	0.54	0.62
30	0	2	0	1	0.44	0.52
31	0	2	1	1	0.39	0.52
32	2	0	0	1	0.58	0.92
33	2	2	0	2	1.73	0.92
34	2	2	0	2	1.26	0.64
35	2	0	0	1	0.30	0.62

The use of multiple linear regression to derive a predicted PR value resulted in a better agreement with the measured PR, especially in grafts to a single calf vessel. This suggests that the combined use of PGR and the MLR equations may improve patient selection for femoro-distal bypass.

Table 22.

Level of agreement between the predicted and measured peripheral resistance.

	R0 (N=35)	R1 (N=10)	R3 (N=22)
Mean Difference	-0.01	0.01	-0.007
+2SD	0.81	0.39	0.59
-2SD	-0.83	-0.41	-0.60
95% Confidence Intervals	-0.15 +0.13	-0.16 +0.14	-0.14 +0.126

There was good agreement between the predicted resistance R1, R3 and R0 and the measured PR at the time of surgery (Table 24). In particular there was good agreement between the predicted resistance in the single calf vessel group (R1) and the measured PR, limits of agreement -0.41 to +0.39, 95% confidence interval -0.16 to +0.14 (Figure 94).

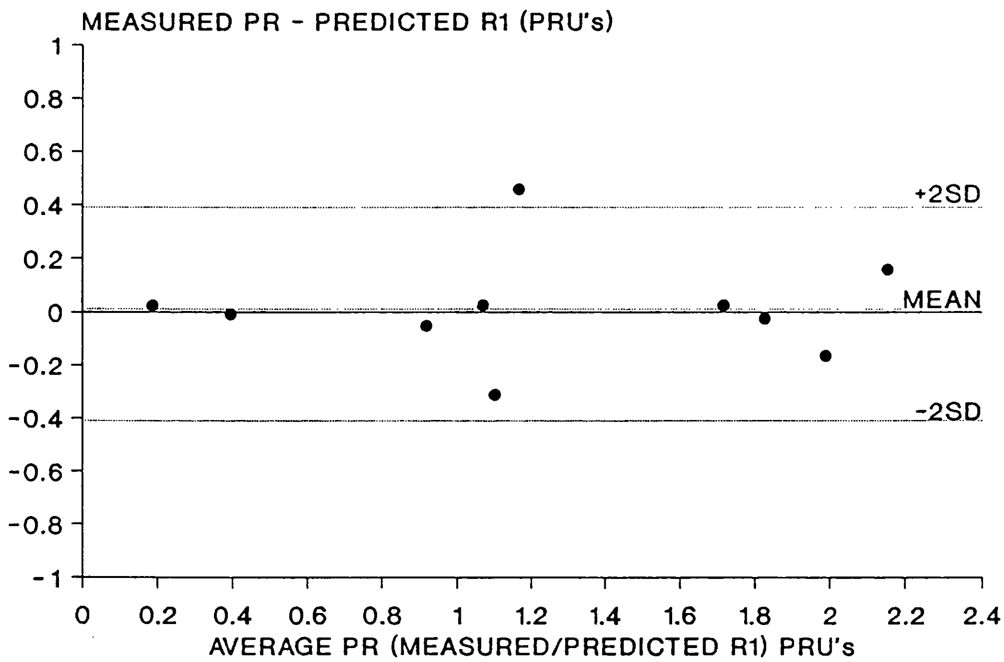


Figure 94. Agreement between the predicted resistance value R1 and the measured PR in a series of 10 femoro-distal grafts.

In the distal popliteal group R3, weighting of the individual calf vessels produced good agreement between the predicted and measured PR, 95% confidence interval -0.14 to 0.126 but with wider limits of agreement -0.60 to +0.59, (Figure 95).

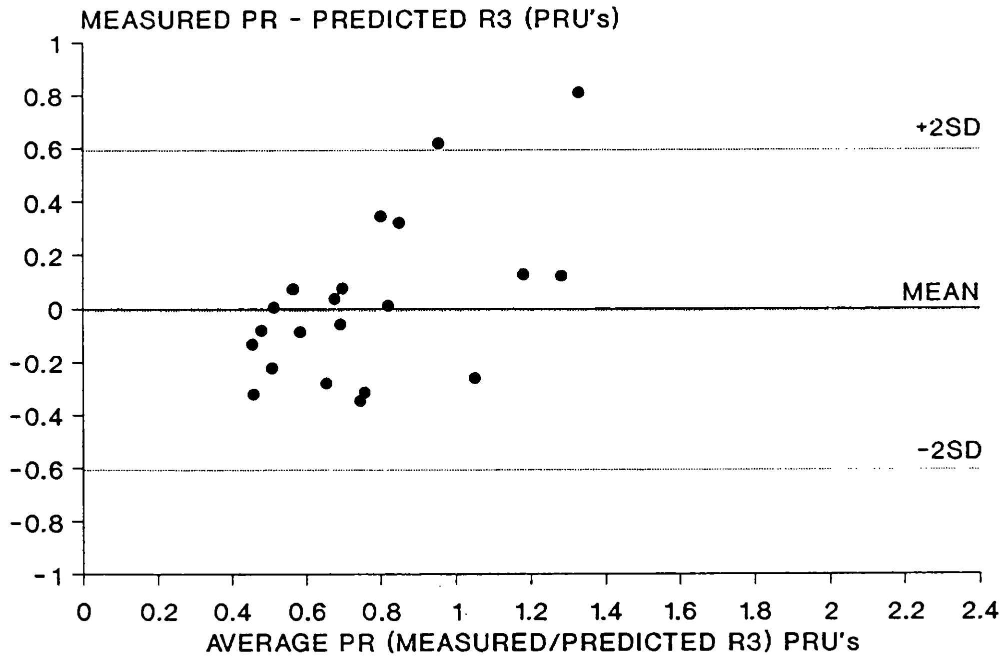


Figure 95. Agreement between the predicted peripheral resistance value R3 and the measured PR in a series of 22 femoro-distal vein grafts.

Prospective Series

The equations R1 and R3 were then validated in a prospective series of 14 non-reversed vein femoro-distal grafts. There was good agreement between the predicted and measured PR, 95% confidence interval -0.26 to +0.15 (Figure 96).

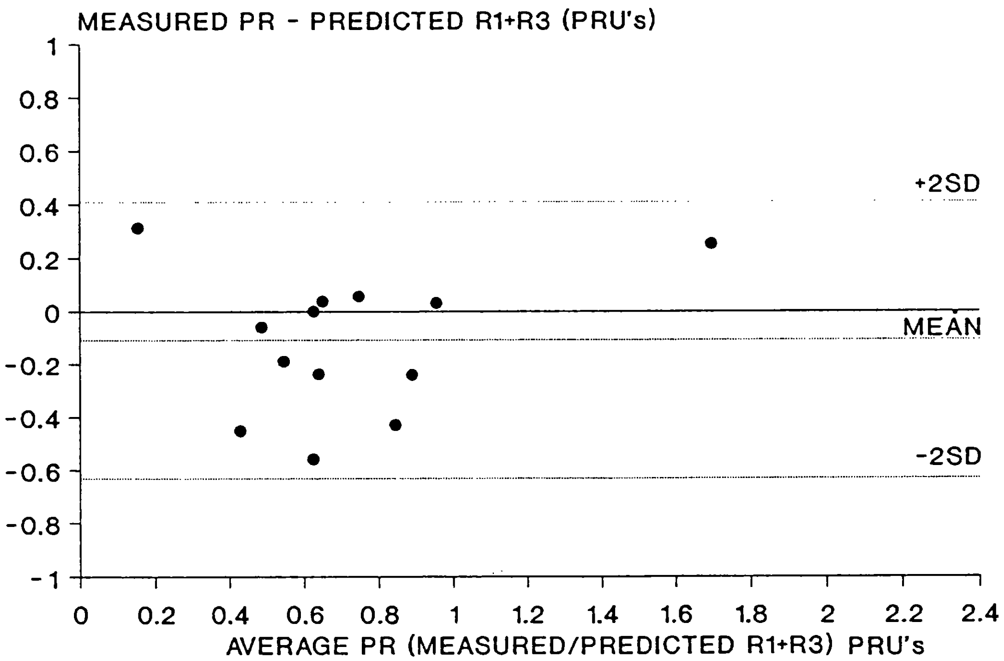
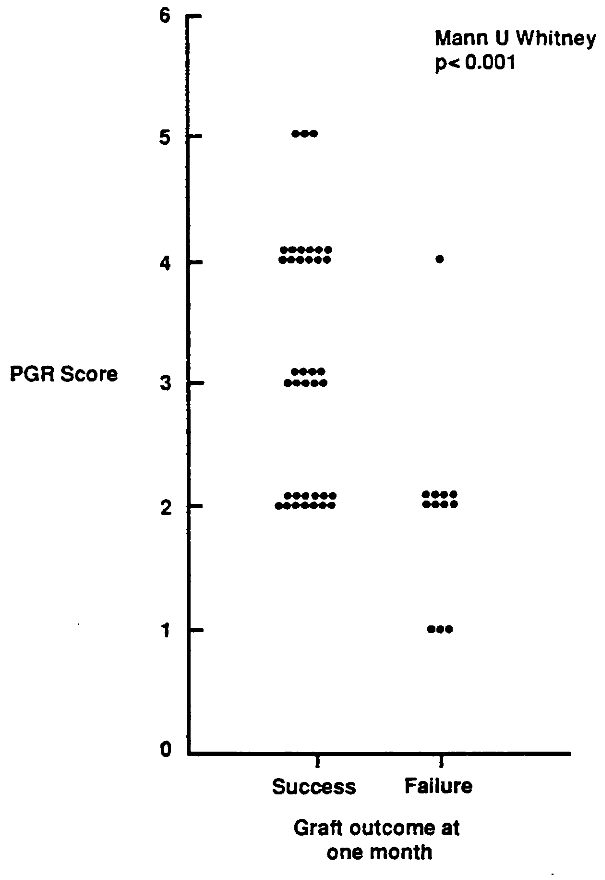
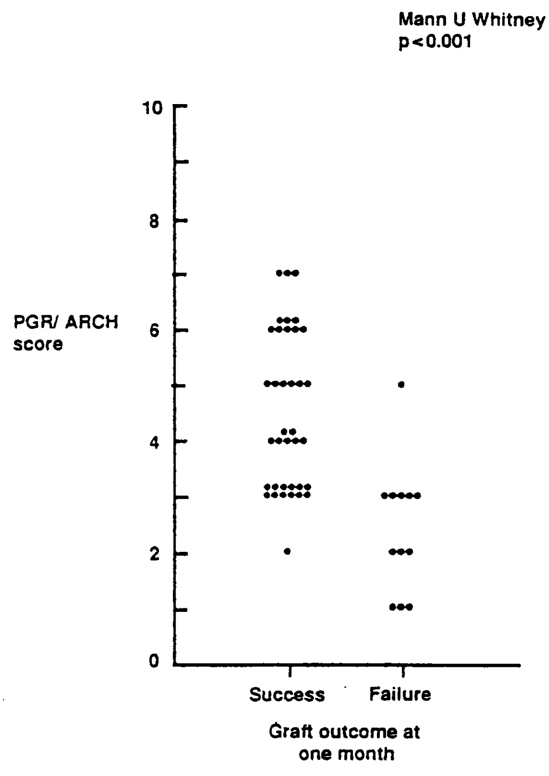


Figure 96. Agreement between the predicted peripheral resistance value RPRO (R1 + R3) and the measured PR in a prospective series of 14 femoro-distal grafts.

Outcome at one month.

The successful grafts at one month had a significantly higher PGR and PGR/ARCH score than the failed grafts. In contrast to the arteriogram scores, the successful grafts all had a PGR score of two or more. Similar results was obtained for the PGR/ARCH score, all but one of the successful grafts had a score of 3 or more. The one femoro-distal graft with a score of 2, failed at six months and the patient subsequently underwent an amputation.





Figures 97-98. Outcome at one month, PGR and PGR/ARCH scores.

Discussion

The recent trend towards more distal reconstructions has highlighted the inadequacy of conventional arteriography and shown a need for better assessment of distal calf vessels. Failed reconstructions result in higher amputation sites, increased morbidity, mortality, poor quality of life and wasted resources (Szilagyi, Hageman, Smith et al 1979, Dardik, Kahn, Dardik et al 1982, Sethia, Berry, Morrison et al 1986).

The pre-operative prediction of subsequent graft function is usually based upon a combination of arteriographic and ultrasound data (Cutler, Thompson, Kliensasser et al 1976, Dean, Yao, Stanton et al 1975, Corson, Johnson, LoGerfo et al 1978, Samson, Gupta, Veith et al 1985). Pre-operative transcutaneous oxygen tension, pulse volume recordings have been evaluated, but are of poor predictive value (Kram, Appel and Shoemaker 1988, Clyne, Ryan, Webster et al 1982).

More recently several authors have reported the value of intra-operative peripheral resistance measurements (Parvin, Evans and Bell 1986, Beard 1987, Ascer, Veith, Morin et al 1984). This appears to be a better predictor of both short and long term graft patency (Ascer, White-Flores, Veith, et al 1987) than other methods including arteriography.

Menzoian et al (1985) reported that a simple arteriographic scoring system based on the number of patent calf vessels failed to predict the measured peripheral resistance. More sophisticated scoring systems have graded the severity of calf vessel disease and the presence of a patent pedal arch and have shown good correlation with the measured peripheral resistance (LaMorte, Menzoian, Sidawy et al 1985). In the same study LaMorte used multiple linear regression to derive a predicted resistance based on the arteriographic subscores. In a retrospective study of 39 patients the predicted resistance correlated significantly with the measured PR ($r = 0.78$ $p < 0.001$).

Careful Doppler examination may identify patent calf vessels and pedal arches not seen on conventional arteriography (Simms 1988, Campbell, Fletcher and Hands 1986). Campbell et al 1986 reported that 35% of vessels judged to be occluded on arteriography had normal or damped Doppler signals.

PGR generates a new pulse wave which can be detected at the ankle if the vessel is patent. Semi-quantitative analysis of the waveform allows a score to be derived for each calf vessel. In this study PGR correlates reasonably well with the measured peripheral resistance. The addition of the ARCH score, as with the arteriographic scoring systems, improves the correlation with measured peripheral resistance. In contrast to arteriography, pedal arch assessment using PGR is easy to perform, repeatable and gives some functional information.

The poor correlation between PGR and PR in the distal popliteal grafts may be attributable to several factors. The PGR cuff was placed at the level of the distal popliteal and tibioperoneal arteries. The augmented flow at the ankle must therefore represent calf vessel patency between the cuff and the ankle. Positioning of the cuff above the knee may have allowed proximal calf vessels to be evaluated, but this was not studied. In the below knee position, the PGR system only assesses the individual calf vessels and not their proximal connections.

In the majority of arteriographic scoring systems no account is taken of the relative contributions of each vessel to the overall resistance. Because of the difficulties involved in the visualization of the pedal arches this is often discounted from the score.

In this study PGR was used to assess both calf vessel and pedal arch patency. In an attempt to assess the relative contributions of the calf vessels to the overall peripheral resistance, multiple linear regression analysis was used. This examines the linear relationship between a dependant variable eg peripheral resistance and two or more independent variables eg PGR subscores, by determining an equation which best describes the relationship. A series of regression coefficients are derived which weight the independent variables .

In all three equations (R1, R3, R0) the ARCH coefficient appears to be a major determinant of peripheral resistance. On the basis of this, continuity between the calf vessel and the pedal arch is clearly an important factor in overall peripheral resistance. In single calf vessel grafts, the absence of the arch produces a predicted peripheral resistance value of greater than 1 which in our experience is rarely compatible with a successful bypass.

In the R0 equation the peroneal artery has a high positive coefficient consistent with a high resistive bed. This finding was previously reported by LaMorte who noted that on arteriography the peroneal coefficient approached zero. These results may reflect that in the normal lower leg the peroneal artery does not usually communicate directly with the pedal arch.

In the R1 equation all 3 vessels (AT, PT, PER) have similar coefficients. The weighting of the peroneal artery supports the finding that in severe disease, particularly where there is an isolated patent calf vessel, the peroneal artery is often relatively disease free and in continuity with the pedal arches (Dardik, Ibrahim, Sprayregen et al 1976, Dardik, Ibrahim and Dardik 1979).

Calf vessel continuity with the pedal arch is an important determinant of peripheral resistance which has been correlated well with successful femoro-distal reconstructions. A non-invasive PR measurement can now be derived from PGR using MLR which can predict the operative PR. We would recommend that patients be selected for calf vessel exploration on the basis of a PGR and non-invasive peripheral resistance measurement rather than arteriographic appearance alone. This is a simple, inexpensive, non-invasive test of calf vessel runoff, which can be applied to all patients with critical ischaemia.

Summary

The measurement of peripheral resistance is a useful technique for predicting the outcome of femoro-distal bypass. In an attempt to non-invasively predict peripheral resistance Pulse Generated Runoff (PGR) was used to assess thirty-five consecutive patients undergoing femoro-distal non-reversed vein bypass for critical ischaemia. The PGR sub-scores (anterior tibial (AT), posterior tibial (PT), peroneal (PER) and pedal arch (ARCH)) were correlated against the measured peripheral resistance. Using multiple linear regression (MLR) three resistance values were derived for run-off at different levels; (i) a single calf vessel (R1), (ii) distal popliteal artery (R3), and (iii) irrespective of the level (R0). There was good agreement between the predicted resistances R0, R1 and R3 and the measured peripheral resistance. In the single calf vessel group (R1) the limits of agreement (-0.41 to +0.39) and 95% confidence intervals (-0.16 to + 0.14) with the measured peripheral resistance were better than the R0 and R3 groups. These levels of agreement are small enough to replace the measured PR with the predicted PR method. Using the appropriate resistance equation in a further prospective series of 14 cases, there was agreement between the predicted and measured peripheral resistance, limits of agreement -0.67 to +0.41, 95% confidence intervals -0.26 to +0.15.

These results confirm the value of PGR in the assessment of critical ischaemic limbs particularly those with a single patent calf vessel. Calf vessel continuity with the pedal arch appears to be a major determinant of peripheral resistance, particularly in the isolated calf vessel group. A non-invasive resistance value can be derived which will predict the intra-operative peripheral resistance and should help predict subsequent graft outcome.

CHAPTER 7c.

RESULTS: PEDAL ARCH ASSESSMENT

Patients.

A consecutive series of forty nine patients (33 men and 16 women) undergoing non-reversed femoro-distal vein grafts for critical ischaemia were studied. Their median age was 70 with a range of 49-86 years. Twenty nine grafts were performed to the distal popliteal artery (12 proximal and 17 distal), 3 to the tibioperoneal trunk and 16 to a single calf vessel.

All patients underwent non-invasive assessment prior to femoro-distal bypass. This included Doppler ankle pressures, ankle/brachial indices, calf pulse volume recordings (PVR's) and a PGR study.

Statistical analysis.

Methods of agreement described by Bland and Altman (1986) was used to compare the PGR derived pedal arch score with the IA DSA findings. The pre and per-operative haemodynamic results were expressed as a mean with 95% confidence intervals. A Kruskal-Wallis one way analysis of variance for non-parametric data was first carried out and then a Mann-Whitney U test used to compare the individual groups. Cumulative graft patency and limb salvage rates were calculated on an SSPS statistical package. A Lee-Desu non-parametric test was used to compare the three arch groups with right censored data.

Results.

Forty nine non-reversed femoro-distal vein grafts were analysed. Twenty six grafts were performed for gangrene, 8 for rest pain with ulcers and 15 for rest pain. There were 15 immediate failures (< 30 days), of which 10 were in the gangrene group. This gave a primary patency rate of 69%. Three grafts were successfully revised giving a secondary patency rate of 76%.

Arch Status.

Thirteen (27%) patients had a complete pedal arch, 30 (61%) an incomplete arch and 6 (12%) an occluded arch on pre-operative PGR mapping.

Post-operative IA DSA views of the pedal arches were obtained in 16 cases and showed a good agreement with the PGR assessment of the pedal arch; limits of agreement -0.94 to 0.82, 95% confidence interval -0.3 to +0.23. These results reflect excellent agreement between the two methods of assessment (Figure 99).

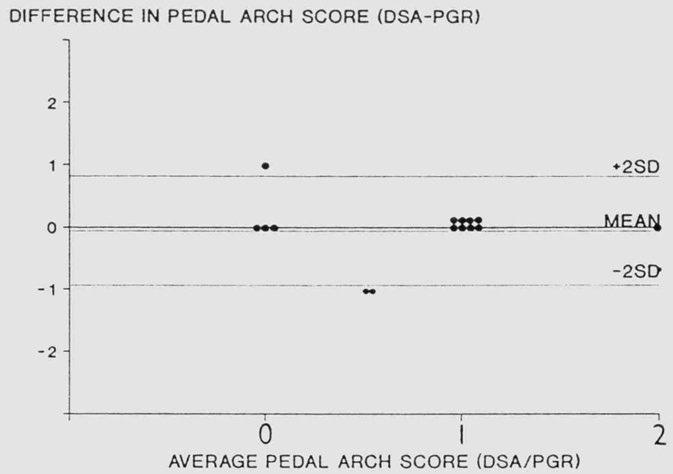


Figure 99. Method of agreement between the PGR and IA DSA derived pedal arch scores.

The pre and per-operative haemodynamic parameters were analysed with respect to the pedal arch status; complete, incomplete and occluded, thus giving three groups for analysis.

Pre-operative haemodynamic assessment.

There was no significant difference between the three groups in the pre-operative Doppler ankle pressures, ankle/brachial indices, calf PVR amplitude and upstroke time (Table 23).

Table 23.

Pedal arch status versus pre-operative haemodynamic parameters

	Complete (N=13)	Incomplete (N=30)	Occluded (N=6)
Ankle Systolic	50.4	60.2	67.7
pressure mmHg	(36.9-63.9)	(51.8-68.6)	(8.2-127)
ABI	0.37	0.40	0.47
95% CI	(0.28-0.46)	(0.36-0.44)	(0.11-0.83)
PVR amplitude	5.6	3.3	2.62
95% CI	(0.6-10.6)	(1.87-4.73)	(0.18-5.06)
PVR upstroke	340	351	313
95% CI	(274-406)	(313-389)	(200-426)

Results expressed as a mean with 95 confidence intervals in brackets.

In contrast there was a significant difference in the PGR scores between all three groups, ($p < 0.001$). The complete pedal arch group had a significantly higher PGR score compared to the occluded group, (Figure 98).

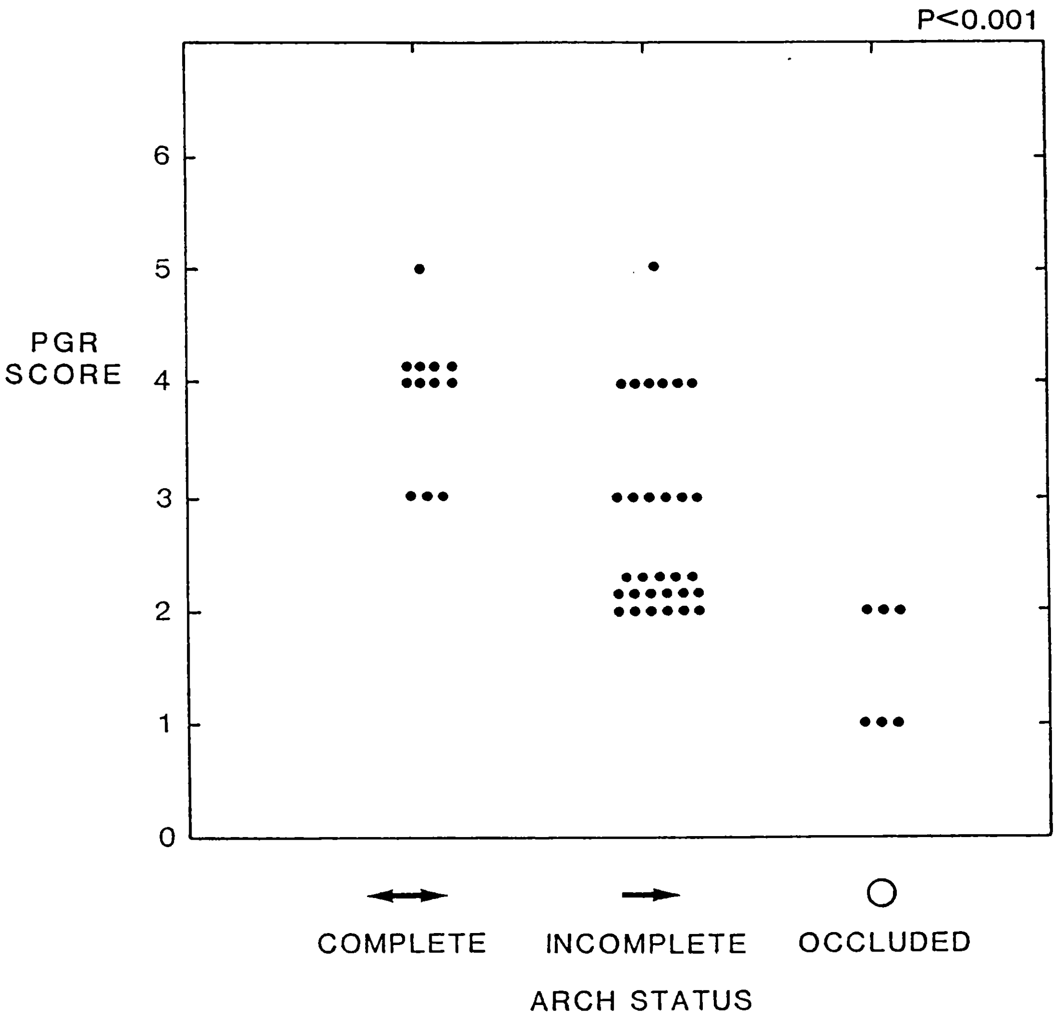


Figure 100. PGR score in the three pedal arch groups.

On the pre-operative IA DSA, there was a significant difference in the arteriographic run-off between the three groups, ($p < 0.02$), in particular between the complete and occluded arch groups ($p < 0.001$), (Figure 101).

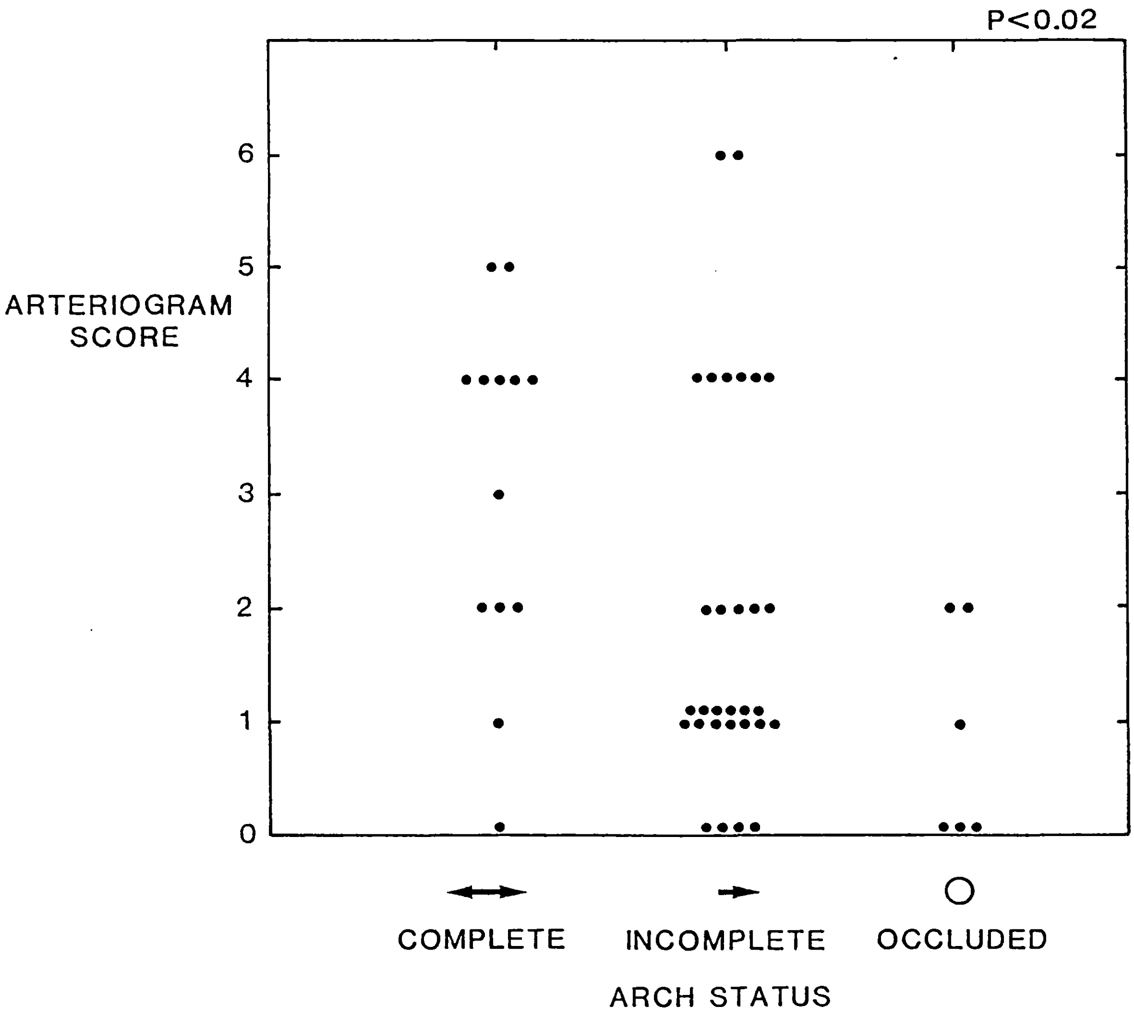


Figure 101. Pre-operative arteriogram score in the three pedal arch groups.

Per-operative haemodynamic assessment.

There was a significant difference in the peripheral resistance between the three groups ($p < 0.02$), (Table 24).

Table 24.

Pedal arch status versus per-operative haemodynamic parameters.

Complete	Complete (N=13)	Incomplete (N=30)	Occluded (N=6)
PR	0.62 (0.47-0.77)	0.83 (0.67-0.99)	1.66 (0.99-2.33)
GF1	122 (72 - 172)	120 (91 - 149)	61 (17 - 105)
GF2	205 (122 - 288)	173 (136 - 210)	71 (14 - 128)
GR1	0.65 (0.41-0.89)	0.80 (0.56-1.05)	1.44 (0.49-2.39)
GR2	0.38 (0.23 - 0.53)	0.55 (0.34-0.76)	1.27 (0.24-2.3)

Results expressed as a mean with 95% confidence intervals in brackets.

PR = Peripheral Resistance (PRU's).
GF1 = Graft flow at rest (mls/min).
GF2 = Graft flow after papaverine hydrochloride (mls/min).
GR1 = Graft resistance at rest (PRU's).
GR2 = Graft resistance after papaverine hydrochloride (PRU's).

The peripheral resistance was significantly lower in patients with a complete arch compared to those with an occluded arch ($p < 0.001$), (Figure 102).

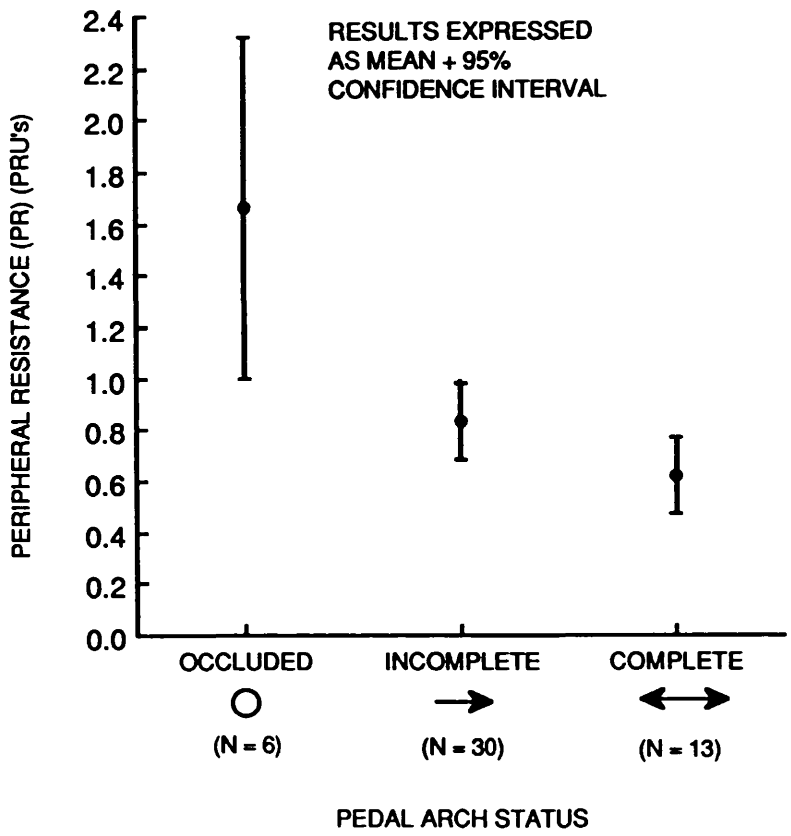


Figure 102. Peripheral resistance at the time of calf vessel exploration in the three arch groups.

On completion of the graft, there was no significant difference in both graft flow and resistance at rest between the three arch groups ($p > 0.05$). The administration of papaverine hydrochloride resulted in a significant difference between the three arch groups both in terms of graft flow (GF_2) and resistance (GR_2), ($p < 0.05$ and $p < 0.02$ respectively), (Figures 103 and 104). Subsequent analysis revealed no significant difference between the complete and incomplete arch groups. In contrast, grafts with a complete arch had a significantly higher flow rates and a lower peripheral resistance than the occluded arch group.

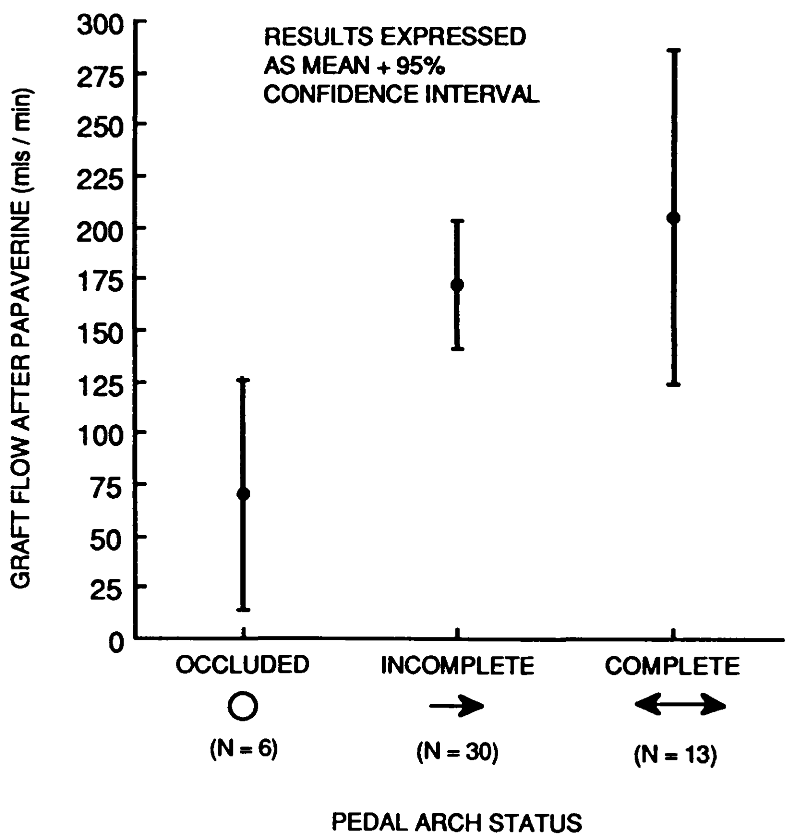


Figure 103.

Post papaverine graft flow (GF2) in the three pedal arch groups.

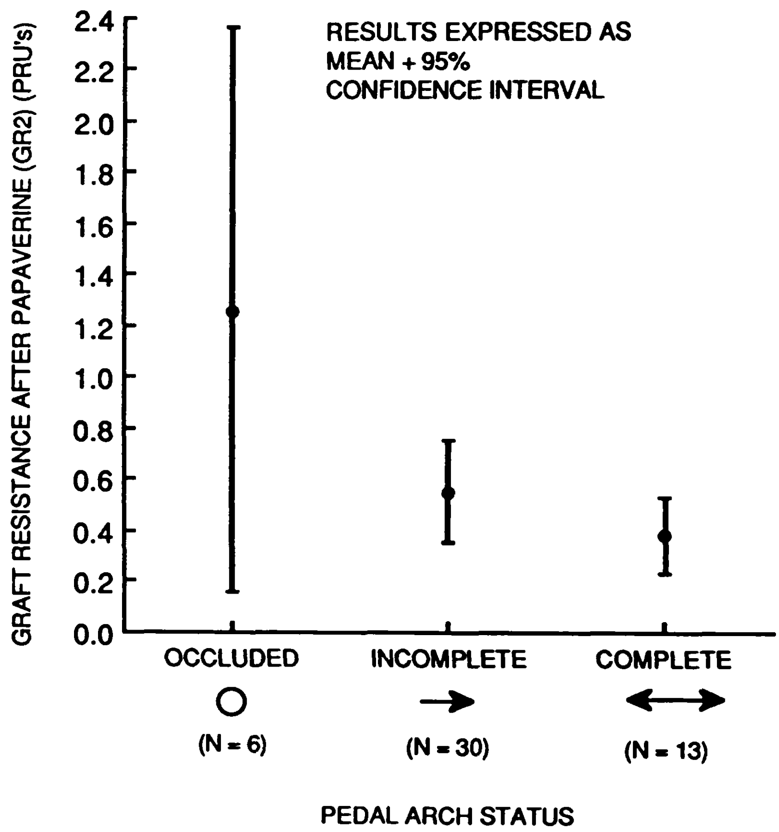


Figure 104.

Post papaverine graft resistance (GR2) in the three pedal arch groups.

Outcome at one month.

A significant difference was noted in the outcome between those grafts with a complete and occluded arch, $p < 0.001$ (Fishers exact probability test). All but one of the grafts with an occluded arch failed, the remaining distal graft failed at six months. Seven out of the 30 grafts with an incomplete arch failed, of which 4 may have been due to missed technical errors. In contrast none of the complete arch grafts failed.

Long term follow-up.

There was a significant difference in the cumulative graft patency rates between the three arch groups (complete, incomplete and occluded), Lee-Desu $p < 0.0002$, (Figure 105). Although the numbers were small, all the grafts with a complete pedal arch were patent at six months. The twelve month patency rates for the incomplete and occluded arches were 66% and 0% respectively. Similar results were obtained for limb salvage (Figure 106). Grafts with complete, incomplete and occluded arches had six month limb salvage rates of 100%, 76% and 0% respectively, Lee-Desu $p < 0.00001$.

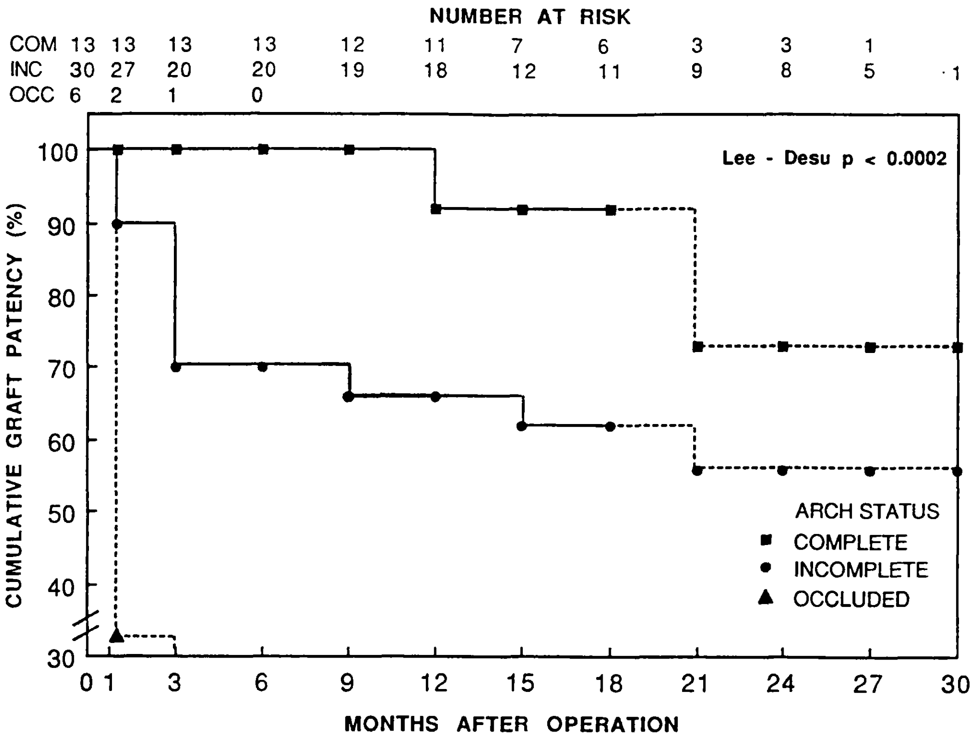


Figure 105. Cumulative graft survival for the three arch groups.

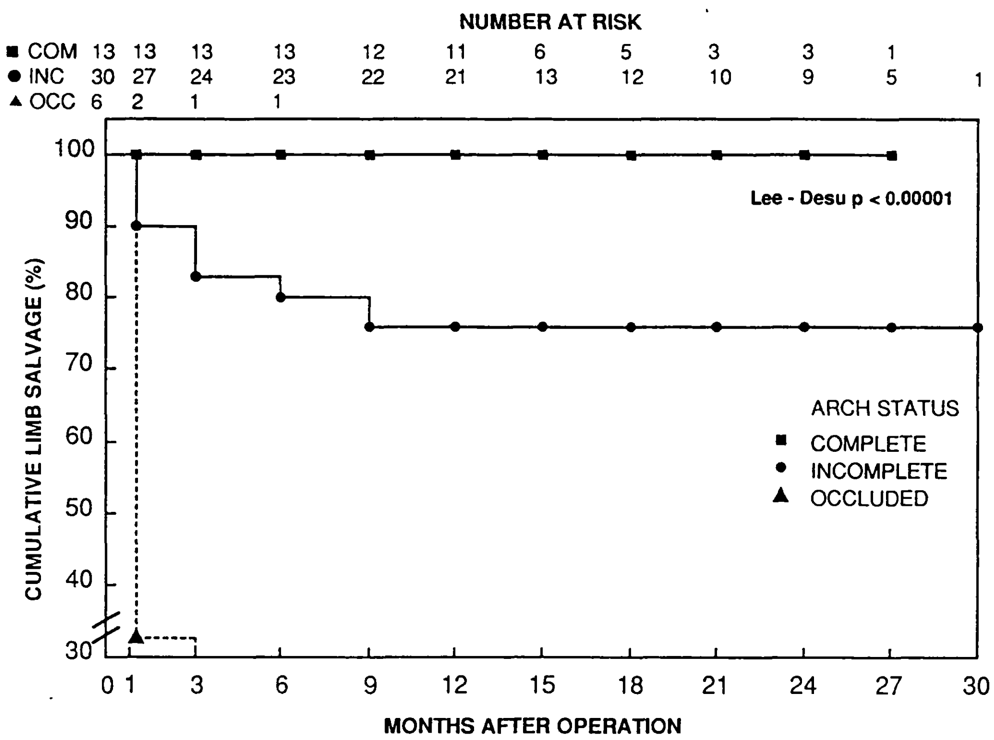


Figure 106. Cumulative limb salvage for the three arch groups.

Discussion

The use of pre-bypass and completion arteriography has highlighted the importance of pedal arch patency in successful femoro-distal bypass (O'Mara, Flinn, Neiman et al 1981, Scarpato, Gembarowicz, Farber et al 1981, Flanigan, Williams, Keifer et al 1982). Klimach and Charlesworth 1983 reported significantly higher graft patency rates in grafts with a patent pedal arch .

The pre-operative identification of the pedal arch has previously been confined to a combination of arteriography and Doppler ultrasound both of which may be unsatisfactory.

Conventional arteriography may fail to demonstrate the pedal arches as a result of multisegment disease and poor peripheral perfusion. Several techniques have been reported to improve the pre-operative visualization including IA-DSA (Turnipseed, Detmer, Berkoff et al 1982), occlusive cuff hyperaemia (Kahn, Boyer, Moran and Callow 1968), limb exercise (Boijsen and Dahn 1965) and vasodilators (Jacobs and Hanafee 1967), but none are entirely successful.

Pre-bypass operative arteriography offers an alternative method of calf vessel run-off and pedal arch assessment. However it may still miss patent distal vessels and does not allow the clinician the opportunity to plan surgery.

In this study, pre-operative IA DSA was initially used to assess the calf vessel and pedal arch runoff. The generation of a new pulse wave with PGR has been shown to be a better predictor of outcome than arteriography. The post-operative IA DSA views of the pedal arch correlate extremely well with the pre-operative PGR map and confirm the applicability of this technique in the assessment of the pedal arches.

In 1981 Roedersheimer et al reported the pedal arch patency test using simple

Doppler ultrasound. Simms in 1988 reported the value of this technique in the pre-operative evaluation of patients for femoro-distal bypass. In 38% of cases no arch signal could be detected and in a further 10% no calf signal could be obtained. He observed that following successful bypass, five of the six grafts with a persistent pedal arch occlusion failed. In contrast those with a complete pedal arch were all patent at 12 months. He concluded that selection for femoro-distal bypass could be based upon the findings of the Doppler ultrasound and the POA.
Recent studies have reported the predictive value of peripheral resistance in successful femoro-distal bypass (Ascer, Veith, Morin et al 1984, Parvin 1987). Few studies have investigated the influence of the pedal arch patency on haemodynamic parameters. Dardik et al 1978 reported no difference in the resting flow rates between intact and deficient arches. However the augmented flow rates with papaverine were significantly higher in the intact arch group. In contrast, Harris and Campbell 1983 in a study on adjuvant distal arteriovenous shunts in femoro-tibial bypass reported a significant difference in the resting flow rates between an intact and occluded pedal arch.

In this study, peripheral resistance and flow were measured at rest and after the administration of papaverine hydrochloride.

The peripheral resistance measured at the time of calf vessel exploration was significantly different between the three groups. Grafts to an occluded pedal arch had a significantly higher peripheral resistance, of which all but one failed within 30 days of the operation. On completion of the graft, no significant difference was noted in graft flow or resistance. The administration of papaverine hydrochloride resulted in a significant increase in blood flow and a concomitant drop in the peripheral resistance in grafts with either an incomplete or occluded arch. No such changes were observed in the occluded arch group. This poor haemodynamic response to papaverine hydrochloride is a reflection of the severity of distal disease in the proximal grafts and a smaller runoff bed in the more distal grafts.

There have been several advocates for the use of adjuvant arteriovenous fistulas and this may represent a appropriate group of patients. The use of potent peripheral vasodilators, eg prostacyclins may be beneficial not only in the occluded but also the incomplete pedal arch limbs.

Although there were small numbers in the long term follow-up, a significant trend was identified. Grafts to an occluded arch had an extremely poor prognosis and may require alternative management.

These results confirm the importance of the pedal arch in successful femoro-distal bypass and the measurement of peripheral resistance as good predictors of graft patency and likelihood of long term success. PGR in combination with the pedal arch patency test of Roedershemier is a good predictor of pedal arch integrity.

Higher flow rates and lower peripheral resistances were noted in patients with a complete pedal arch.

Grafts to occluded pedal arches all failed within six months requiring amputation.

PGR assessment of the pedal arch is a simple technique and provides additional information which is important in the selection of patients for femoro-distal grafts.

Further prospective studies are required to evaluate (i) the effect of pedal arch status on per-operative haemodynamic factors, in particular the occluded group, (ii) the place of AV fistulas in patients with an incomplete or occluded arch and (iii) the place of vasodilators eg prostacyclin analogues or epidural infusions in the management of grafts to the occluded pedal arch.

CHAPTER 7d.

RESULTS; LONG SAPHENOUS VEIN SCANNING

Patients.

Forty seven patients underwent a pre-operative vein scan. There were 31 men and 15 women with a median age of 71, range 51-86 years.

Results.

Vein size.

There was a progressive decrease in the size of the long saphenous vein down the leg, with a mean of 5.26 mm. at the saphenofemoral junction to 2.89 mm. at the level of the medial malleolus, (Table 25), (Figure 107).

Table 25.

Duplex long saphenous vein size (mm.)

	Mean	95% Confidence Intervals.
SFJ	5.26	(4.9-5.62)
Midthigh	4.39	(4.09-4.69)
Knee	3.60	(3.28-3.92)
Midcalf	3.03	(2.77-3.29)
Medial Malleolus	2.89	(2.73-3.05)

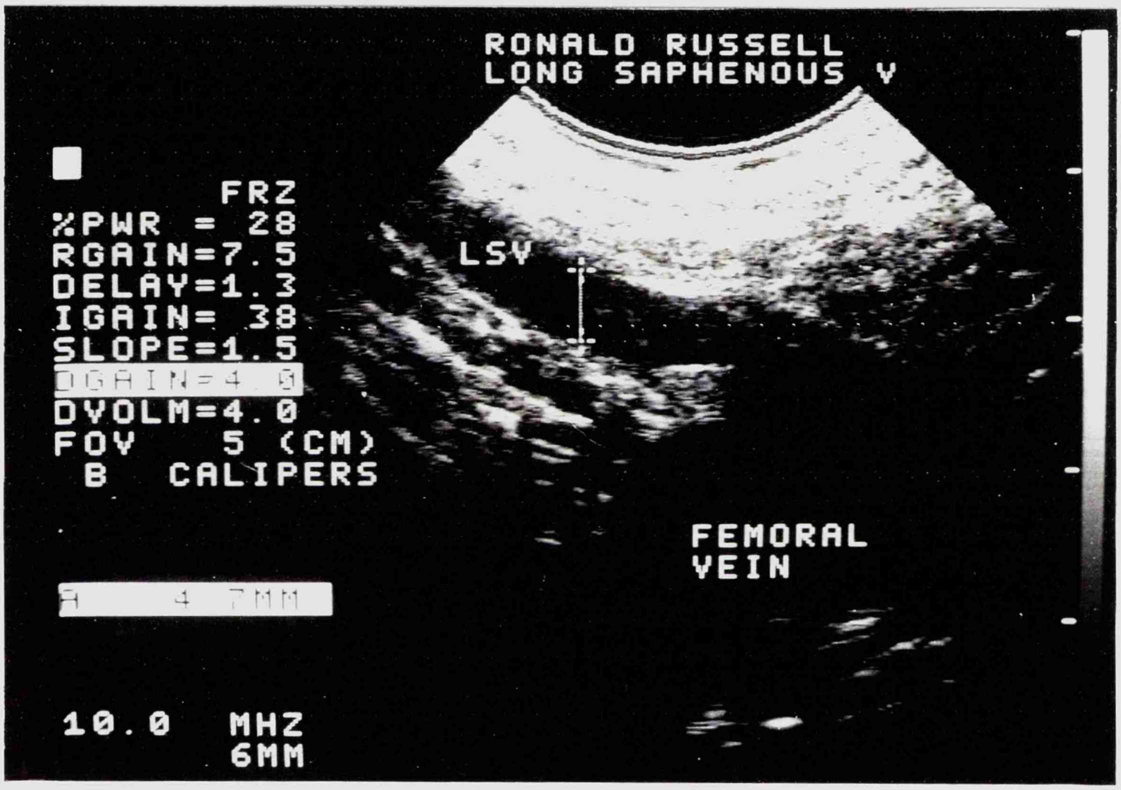


Figure 107. Long saphenous vein size on duplex scanning.

In the vast majority of cases (91%), the long saphenous vein was of a sufficient size to allow the passage of a 2 mm. Hall valvulotome. In the remaining cases, alternative sources of vein were sought, eg contralateral long saphenous, short saphenous and or arm vein.

Duplex versus Operative measurement of long saphenous vein size.

The pre-operative assessment of LSV size by (i) Duplex alone and (ii) PGR assisted were compared to the operative measurement of graft size at the proximal and distal anastomoses using the methods of agreement described by Bland and Altman (1986), (Table 26).

Table 26.

Measurement of agreement of vein size (mm.) between duplex imaging and operative measurement.

	Proximal		Distal	
	Duplex	Duplex/PGR	Duplex	Duplex/PGR
MD	-0.11	-0.45	-0.19	0.06
LOA	-2.41	-2.35	-2.73	-1.92
	+2.19	+1.45	+2.35	+2.04
95% CI	-0.41	-0.73	-0.57	-0.24
	+0.19	+0.17	+0.19	+0.36
95% CI UL	+1.89	+1.21	+1.97	+1.51
	+2.49	+1.69	+2.73	+2.57
95% CI LL	-2.70	-2.59	-3.11	-2.45
	-2.12	-2.11	-2.35	-1.39

MD = Mean Difference, LOA = Limits of agreement, CI = Confidence interval. CI UL = Confidence interval for the upper limit of agreement. CI LL = Confidence interval for the lower limit of agreement. There was good agreement between the duplex and operative measurement of vein size, the mean difference ranging between -0.45 and 0.06 mm. The limits of agreement and 95% confidence intervals are given in Table 26.

At the proximal anastomosis the limits of agreement were -2.41 to 2.19 mm with 95% confidence interval of -0.41 to 0.19 mm. (Figure 108).

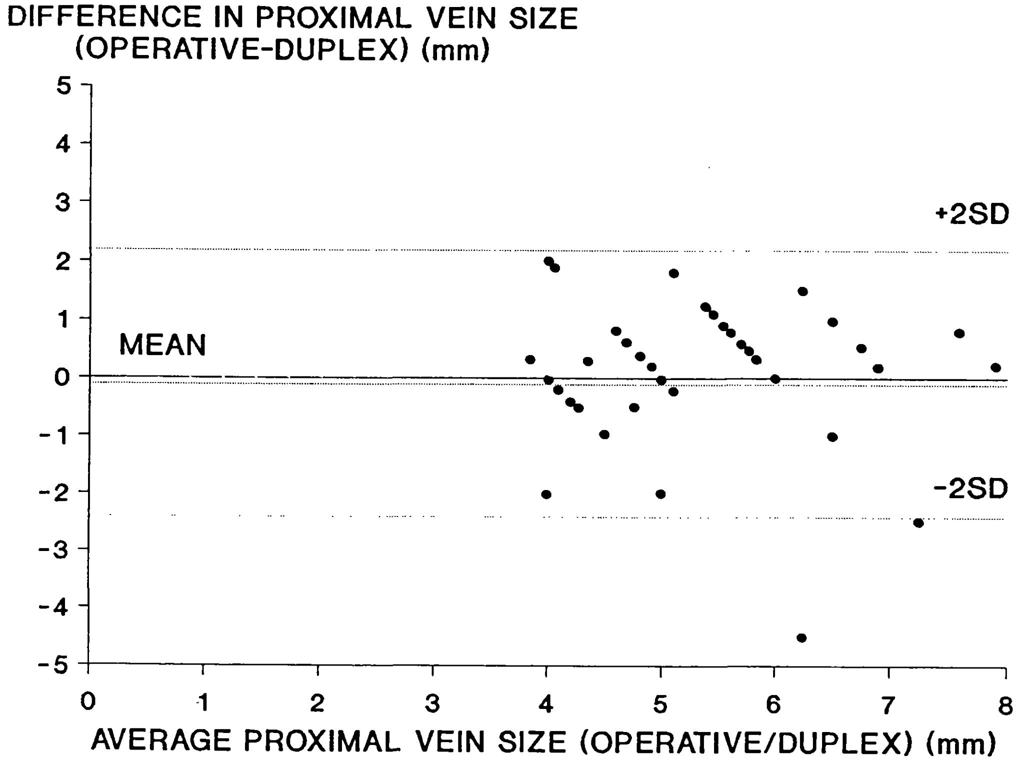


Figure 108.

Proximal vein anastomosis, measurement of agreement between Duplex imaging and operative vein size.

No additional benefit in terms of predicting vein size was obtained with the PGR assisted vein scanning at the proximal graft anastomosis. In fact PGR seem to overestimate the size of the vein in the majority of cases.

Similar results were obtained at the distal anastomosis, the limits of agreement were -2.73 to 2.35 with 95% confidence intervals of -0.57 to 0.19, (Figure 109). By contrast, there was better agreement between the duplex/PGR and operative assessment of vein size at the site of the distal anastomosis.

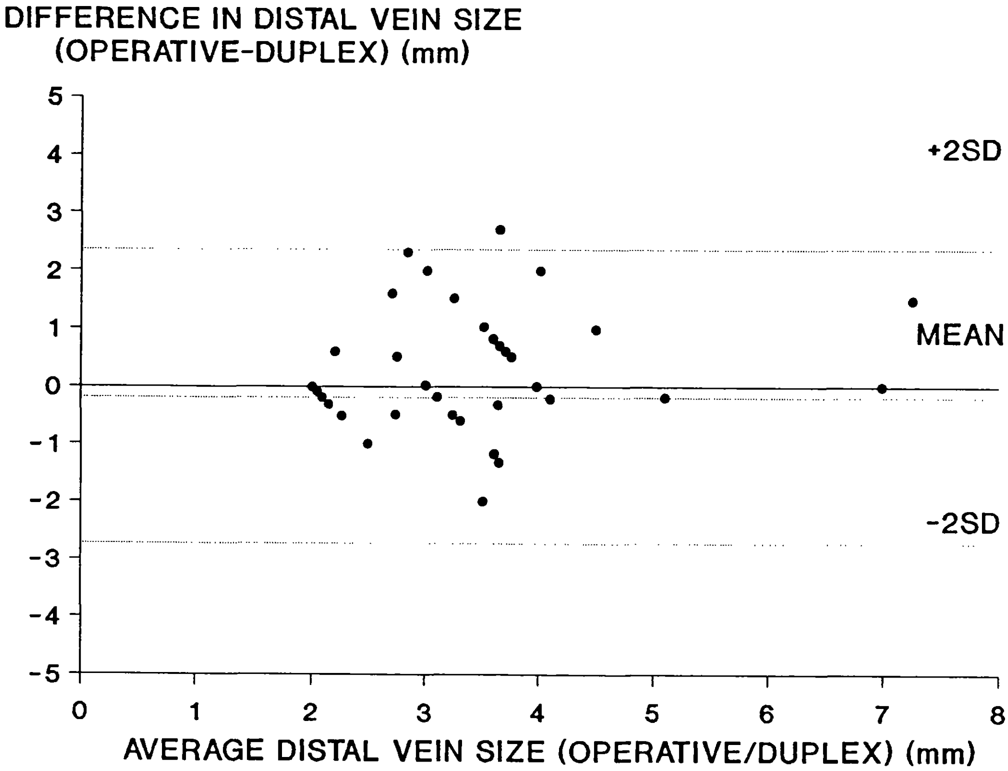


Figure 109.

Distal vein anastomosis. Measurement of agreement between Duplex imaging and operative vein size.

Suitability of the LSV for reconstruction.

At the time of duplex vein assessment the LSV was graded 0 to 3. Grades 0 and 1 were considered suitable for reconstruction and 2 to 3 inadequate. Of the 47 long saphenous veins assessed, 41 were considered adequate for femoro-distal bypass surgery on the basis of the duplex scan report. One patient was found to have an inadequate vein at the time of surgery. Six patients were considered to have inadequate long saphenous veins on duplex scanning and of these 3 were confirmed at the time of surgery (Table 27).

Table 27.

Suitability of the LSV for femoro-distal reconstruction.

		OPERATIVE ASSESSMENT	
		0-1	2-3
DUPLEX	0-1	40	1
	2-3	3	3

The sensitivity of duplex scanning was 95% and specificity of 75%. The predictive value of an adequate vein on duplex scanning was 97.5%.

Wound Infections.

Between September 1984 and November 1986, 100 femoro-distal grafts had been performed for critical ischaemia. During this time there were 12 reported wound infections. In contrast there was only one wound infection in those patients who had undergone pre-operative LSV mapping, (Table 28). This was a infected lymph leak in an obese diabetic lady.

Table 28.

Pre-operative vein mapping versus wound infection.

		PRE-OPERATIVE LSV MAPPING	
		YES	NO
WOUND INFECTION	YES	1	12
	NO	46	88

X^2 with Yates correction = 5.187, $p < 0.05$.

A significant difference in wound infections was noted during the period of LSV scanning, how much importance one attaches to this result is open to question and only a randomised study will answer the question. During the period of study all the LSV's were accurately located and there was no need to undermine the skin flaps to locate the LSV.

Discussion

The superiority of the LSV over prosthetic material for infrageniculate arterial reconstruction is well established. The wide variations in LSV utilisation rate has highlighted the need for improved pre-operative assessment. Between 20-30% of patients are reported to have an inadequate or absent LSV. Alternative sources of vein should be sought prior to surgery. This approach will prevent trauma following venesection, maintain superior limb salvage rates and improve utilisation of theatre resources. In the past LSV imaging was limited to venography which confirmed patency and provided limited information about it's course, tributaries and varicosities. Venography was later abandoned as a pre-operative investigation as experimental and clinical evidence highlighted the potential side effects of contrast media on vascular endothelium. The recent introduction of low osmolality contrast media has alaid some of the earlier fears but the technique fails to (i) identify duplex and triplex LSV systems, (ii) accurately assess vein size and (iii) confirm continuity between thigh and calf.

Duplex imaging of the LSV on the other hand is a safe and easy to perform technique. It provides information about (i) vein size, (ii) patency, (iii) course, (iv) the presence of duplex/triplex venous systems and (v) identifies venous tributaries and valves. The disadvantage of the technique is that there is a considerable learning curve. In most institutions, duplex scanning is undertaken by either an experienced ultrasonographer or a research fellow. During this study, the early scans took between 60 and 90 minutes to complete, considerable difficulties were encountered around the knee joint, where the LSV was often diseased, and any amount of surface pressure would lead to distortion of the venous image. The combined use of PGR and Duplex imaging shortened the scan time to 30 minutes. The combined technique provided the operator with a pulsatile signal which could be detected if the LSV was patent and in continuity between calf and thigh. Although difficult to quantify the relative distensibility of the vein could be assessed using the PGR system, in particular the LSV was found to be relatively non-distensible around the knee joint.

Duplex imaging confirmed the natural taper of the LSV with a mean external diameter of 5.26 mm. at the saphenofemoral junction and 2.89 mm. at the level of the medial malleolus. The majority of the veins were between 2.77 and 3.29 mm. at the site of the proposed distal anastomosis. This is probably an underestimate of the real size as the veins were more readily compressible in the calf than the thigh.

Previous studies have correlated duplex assessment of vein size with the "apparent" Gold standard operative measurement. The latter is inappropriate as the LSV undergoes marked spasm during harvesting. As a result we chose to use the completed graft external diameter after the administration of 30 mg of papaverine hydrochloride, in the hope of avoiding any marked venous spasm. Correlation coefficients were not used to compare vein size by the two methods as this would have been inappropriate (Bland and Altman 1986). Using the methods of agreement no benefit in terms of predicting proximal vein size was accrued with PGR. At the distal anastomosis, the mean difference between the operative and PGR assisted duplex measurement of vein size was much less (0.06 compared to -0.19), but both had wide limits of agreement. Ninety five percent of the measurements were within 0.5mm suggesting that Duplex imaging was a reasonable predictor of vein size and hence suitability for femoro-distal reconstruction.

A semi-quantitative grading system encompassing vein size and quality was used to identify suitable veins for femoro-distal reconstruction retrospectively. Patency of the LSV was confirmed by a transmitted PGR signal and the detection of flowing intraluminal echoes. In partial or complete occlusions, the PGR signals were often damped or absent. The veins were often difficult to image as the intraluminal thrombus produced an echogenic pattern similar to that of the surrounding tissues. Thick walled veins were identified by a thick echogenic layer on B-mode and semiquantified on M-mode.

Using the semi-quantitative grading system, duplex imaging identified suitable veins with a sensitivity of 95% and a specificity of 75%. The predictive value of an adequate vein on duplex scan being 97.5%. In those cases where the LSV was inadequate, alternative sources of vein were sought including; short saphenous, cephalic, basilic and the contralateral LSV.

In all cases the pre-operative LSV mapping was correct and there was no need to undermine the skin flaps. In addition it enabled two groups of surgeons to work simultaneously mobilising the vein proximally and distally. This is reflected in the wound infection rate during the study. Although there were significantly more wound infections prior to Duplex imaging of the LSV, it would require a randomised study to confirm the benefits of pre-operative LSV mapping.

Since the introduction of duplex imaging, the non-reversed vein technique (Beard, Wyatt, Scott et al 1989) has been modified. The full length exposure of the LSV has been abandoned in favour of multiple skin bridges. This is particularly important in patients undergoing femoro-distal reconstructions, where lymphatic disruption around the knee joint leads to marked calf swelling.

In summary duplex imaging of the LSV is an accurate method of assessing the vein suitability for femoro-distal reconstruction and enables accurate marking of the LSV with the reduction of skin flap undermining, wound and graft infection.

CHAPTER 7e

RESULTS;PER-OPERATIVE HAEMODYNAMIC MONITORING.

Patients.

Forty nine femoro-distal grafts were studied, of which 15 failed within the first month. Three of these grafts were successfully revised. This gave a primary patency rate of 69% and a secondary patency rate of 76% at one month. The cause of the 12 failures are listed in Table 29.

Table 29.

Failed Grafts

1. High retrograde flow, severe distal disease.
2. Technical error, distal intimal flap.
3. Poor vein, femoro-distal (SCV) graft.
4. Technical error, calcified anterior tibial vessel.
5. Poor vein, femoro-distal graft.
6. Technical error, missed proximal valve.
7. Unknown
8. Unknown
9. Severe postoperative hypertension, blown proximal anastomosis
10. Poor vein
11. Severe distal disease, Buergers Disease
12. Acute ischaemia, extensive collaterals, no runoff.

Results.

Outcome at one month

The haemodynamic parameters (PR, GF1, GF2, GR1, GR2 and RF) were then analysed with respect to the outcome at one month. Success at one month was determined by the following; (i) a patent graft on either Duplex or arteriography, (ii) a rise in the ankle/brachial index of > 0.25 and (iii) an improvement in the patients symptoms. All three had to be present for the graft to be deemed successful.

The results are expressed as means with a 95% confidence interval and the statistical tests used were Kruskal Wallis and Mann U Whitney test.

There was no significant difference in the initial PR measurement at the time of calf vessel exploration, (Table 30, Figure 110). On completion of the graft there was a significant difference in both flow and resistance both at rest and after the administration of 30 mg of papaverine hydrochloride, (Table 30, Figures 111 and 112).

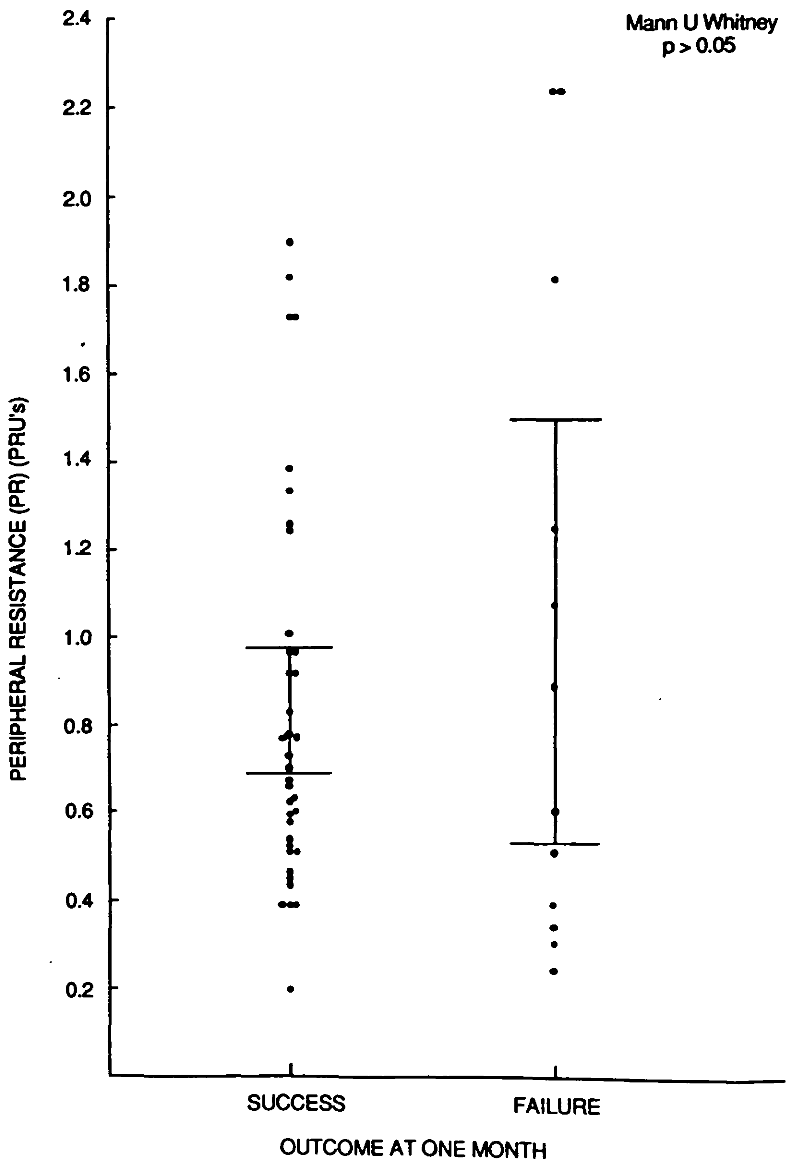


Figure 110.

Outcome at one month; Peripheral resistance at the time of calf vessel exploration.

Bars = 95% Confidence intervals.

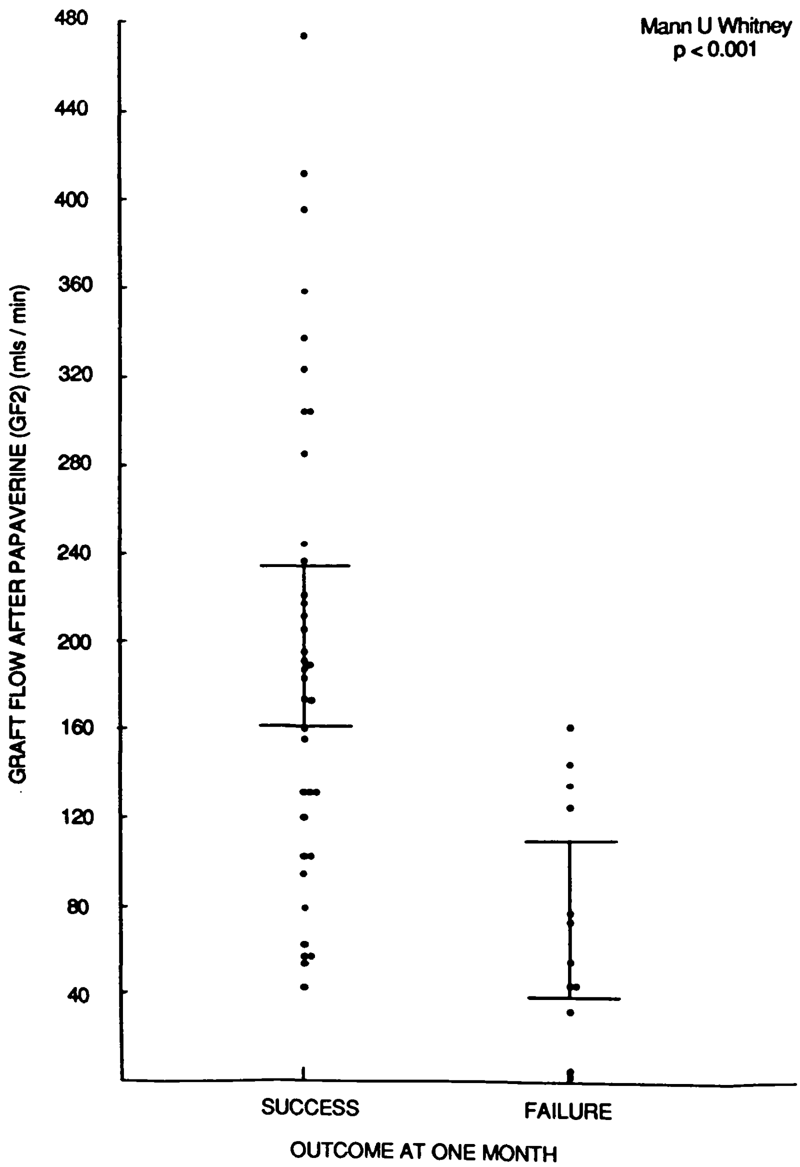


Figure 111.

Outcome at one month; Graft flow (GF2) after papaverine.

Bars = 95% Confidence intervals.

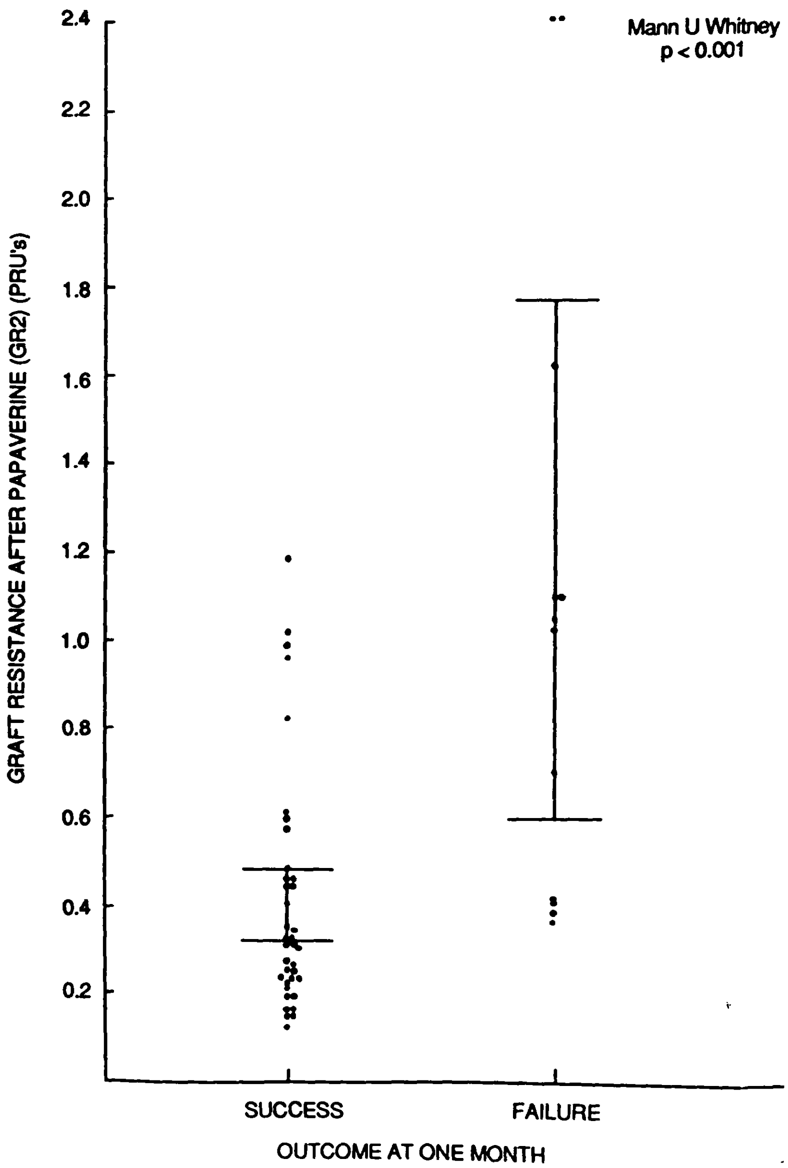


Figure 112.

Outcome at one month; Graft resistance (GR2) after papaverine.

Bars = 95% Confidence intervals.

Table 30.

Outcome at one month versus haemodynamic parameters

	SUCCESS	FAILURE	P	95%CI
PR	0.84	0.99	P>0.05	(-0.28 to +0.49)
	(0.69-0.99)	(0.53-1.45)		
GR1	0.63	1.46	P<0.001	(+0.22 to +1.20)
	(0.51-0.75)	(0.87-2.05)		
GR2	0.40	1.1 8	P<0.001	(+0.17 to +0.87)
	(0.32-0.48)	(0.59-1.77)		
GF1	132	57	P<0.001	(-113 to -27.0)
	(106-158)	(29-85)		
GF2	199	75	P<0.001	(-172 to -55.0)
	(162-236)	(40-110)		
RF	5	11	P>0.05	(0 to 11)
	(2.2-7.8)	(0.1-21.9)		

Results expressed as a mean + 95 CI. P = Mann U Whitney test.

PR =	Peripheral Resistance	(PRU'S)
GR1 =	Graft Resistance at rest	(PRU's)
GR2 =	Graft Resistance after Papaverine hydrochloride	(PRU's)
GF1 =	Graft flow at rest	(mls/min)
GF2 =	Graft flow after Papaverine hydrochloride	(mls/min)
RF =	Retrograde flow	(% of total Graft Flow)

Criteria for a successful graft at one month

In this prospective study the criteria for success; a PR of < 1 PRU after the administration of papaverine hydrochloride and a retrograde flow of < 33%, had a sensitivity of 95% and a specificity of 67%. The predictive value of the parameters being 90%. Four grafts failed with a PR < 1 PRU and or a RF < 33%. One patient had a missed proximal valve, one had uncontrolled post-operative hypertension and blew the proximal anastomosis and subsequently thrombosed his graft. One patient presented with an acutely ischaemic leg with angiographic evidence of knee collaterals but no distal runoff and the last a patient with Buergers disease. The remaining graft failures are detailed in table 29.

Level of distal anastomosis and its effect on haemodynamic parameters.

The haemodynamic parameters were analysed with respect to the level of the distal anastomosis (Table 31). There was no difference in the peripheral resistance between the grafts anastomosed to (i) the proximal popliteal , (ii) distal popliteal and (iii) a single calf vessel.

Table 31.

Level of distal anastomosis versus haemodynamic parameters

	PP	DP	SCV/TPT	P
PR	0.67	0.86	0.98	NS
GF1	142	138	73	P < 0.001
GF2	289	183	101	P < 0.001
GR1	0.52	0.56	1.29	P < 0.001
GR2	0.25	0.38	0.98	P < 0.001

Results expressed as a mean + 95% CI.

Statistical Analysis: Kruskal Wallis and Mann U Whitney.

PR = Peripheral Resistance

GR1 = Graft Resistance at rest

GR2 = Graft Resistance after Papaverine hydrochloride

GF1 = Graft flow at rest

GF2 = Graft flow after papaverine hydrochloride

PP = Proximal Popliteal

DP = Distal Popliteal

SCV = Single Calf Vessel

Grafts to the proximal and distal popliteal arteries had similar measurements of GF1, GF2, GR1, GR2. The only exception were grafts to the proximal popliteal which had a significantly higher flow after the administration of papaverine compared with grafts to the distal popliteal artery (Figure 113). By contrast, grafts to the tibioperoneal trunk or a single calf vessel had significantly higher resistance (GR1 and GR2) and lower flows (GF1 and GF2).

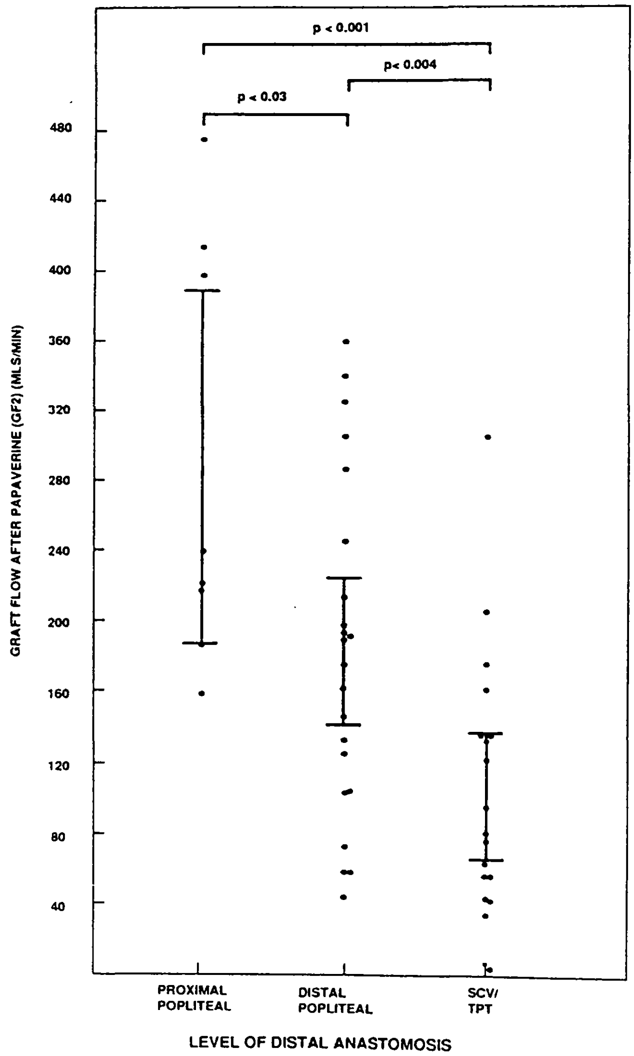


Figure 113.

Graft flow after papaverine hydrochloride (GF2) (mls/min) versus the level of the distal anastomosis.

<u>*Arteriographic runoff and haemodynamic parameters.*</u>

The arteriographic runoff was divided into three groups, (i) poor (0-1), (ii) moderate (2-3) and (iii) good (4-6). The total scores had been calculated on the basis of the arteriogram scoring system A (Chapter 6a). There was no significant difference between the arteriographic runoff groups and (i) peripheral resistance and (ii) graft flow before papaverine. In the presence of good runoff on arteriography, there was a significantly higher flow rate and lower peripheral resistance. This was most noticeable in graft resistance after papaverine (Figure 114).

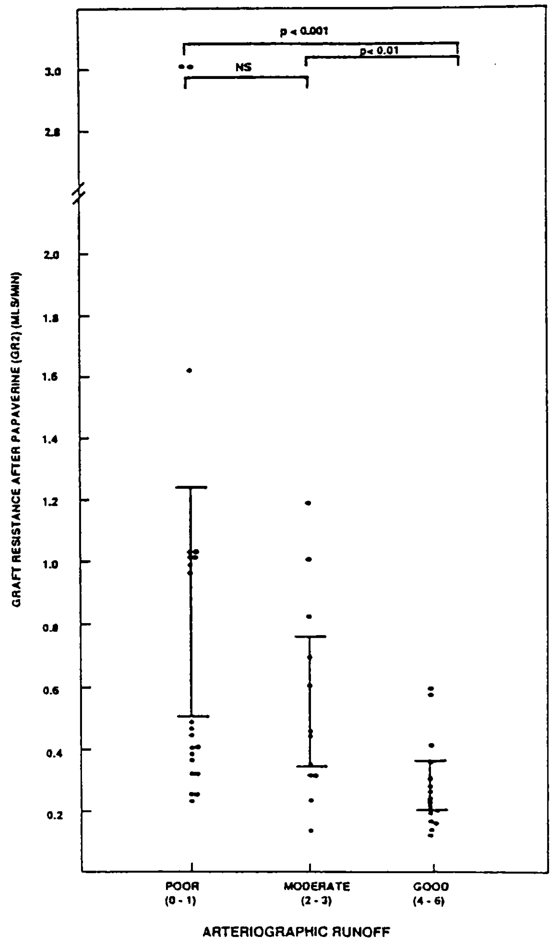


Figure 114.

Graft resistance after papaverine versus arteriographic runoff.

Table 32.

Arteriographic runoff versus haemodynamic parameters.

	Poor (0-1)	Moderate (2-3)	Good (4-6)	P
PR	0.84	0.95	0.87	NS
GF1	88	113	148	NS
GF2	124	167	229	$P < 0.02$
GR1	1.12	0.76	0.52	$P < 0.05$
GR2	0.86	0.55	0.27	$P < 0.001$

Results expressed as a mean + 95% CI.

Statistical Analysis: Kruskal Wallis and Mann U Whitney.

PR	=	Peripheral Resistance	(PRU'S)
GR1	=	Graft Resistance at rest	(PRU's)
GR2	=	Graft Resistance after Papaverine hydrochloride	(PRU's)
GF1	=	Graft flow at rest	(mls/min)
GF2	=	Graft flow after Papaverine hydrochloride	(mls/min)

Discussion.

To date there is a large volume of literature on both flow and peripheral resistance during femoro-distal bypass. The reluctance to incorporate haemodynamic monitoring in reconstructive vascular surgery may have been due to the problems encountered with electromagnetic flowmeters. These were often expensive, time consuming and required additional personal. The Doppler flowmeter used in this study had been designed with those facts in mind. It is easy to use, inexpensive and can be operated by the surgeon in charge of the case.

Beard (1987) reported that the initial infusion peripheral resistance was able to identify those grafts that would fail in the early post-operative period. In this study, peripheral resistance at the time of calf vessel exploration did not discriminate between success and failure at one month. This may have been due to a subtle change in the clinical practice of the unit. In the light of the early PGR work (Beard 1987) , it became apparent that grafts with a PGR score of < 2 did not succeed, and this may account for the lack of discrimination. This is supported by the fact that in Beard's work the infusion PR in the successful grafts was 1.15 compared to 0.84 in this study. Similar results were found in the failed grafts with a infusion PR of 2.22 in Beard's study compared to 0.99.

Despite this result, the infusion peripheral resistance remains a useful haemodynamic measurement. It confirms that the vessel identified on PGR is suitable for reconstruction and will identify the correct level for the distal anastomosis. In addition, if there is gross discrepancy between the infusion peripheral resistance and the graft resistance after papaverine, it is highly suggestive of a technical error, and the graft should be re-explored.

The criteria for success (GR2 $<$ 1 PRU and a RF $<$ 33%) was derived from a multidiscriminant analysis of 47 non-reversed femoro-distal vein grafts (Beard 1989). This had a sensitivity of 97% and a specificity of 83% for a successful graft. These results, in a prospective evaluation of the criteria for success, confirm its applicability. The lower specificity may be accounted for by a number of grafts which failed due to a technical error rather than a high outflow resistance tract.

In the light of the higher attrition rate of below knee femoro-popliteal grafts, it was surprising not to find a significant haemodynamic advantage in the above knee grafts. These findings are similar to those reported by Parvin (1987). Similar results were noted in correlation between arteriographic runoff and flow and peripheral resistance. Not surprisingly grafts to a limited outflow tract (TPT/SCV) had a higher peripheral resistance and a lower graft flow. This raises the question as to what should constitute a cut-off value between reconstruction and amputation. In the past, Parvin et al (1987) have suggested a cut-off level between 1000 mPRU and 1500 mPRU, which is similar to that reported by Ascer, Veith, Morin et al (1984) of 1.2 mmHg/ml/min.

Clearly there needs to be further work to elucidate the "normal" peripheral resistance for a (i) proximal popliteal, (ii) distal popliteal, (iii) tibioperoneal trunk, (iv) upper third single calf vessels and (iv) distal third single calf vessels. This sort of information should allow surgeons to accurately locate the distal anastomosis, thus avoiding the problems of graft thrombectomy with or without a graft extension. In the situation of a high peripheral resistance despite the administration of papaverine, there may be a role for adjuvant dAVF and the use of newer pharmacological agents eg PGI2 analogues.

The role of haemodynamic monitoring in the identification of technical errors has yet to be fully established. In this study, one intact valve and one distal intimal flap were missed. Completion on-table arteriography has been advocated, but may still miss some of these lesions. The current development of small and steerable vascular endoscopes may prove to be a superior method of identification of technical errors.

CHAPTER 7f

RESULTS; LONG SAPHENOUS VEIN MORPHOLOGY

Patients.

Fifty consecutive patients undergoing non-reversed femoro-distal vein bypass for critical ischaemia were studied. There were 33 men and 17 women with a median age of 71 years, range 31-86 years.

Results.

Light Microscopy

In this study none of the veins were normal.

Intimal hyperplasia.

These lesions consisted of desmin positive smooth muscle cells embedded in collagen tissue. Two types of lesion were identified; (1) Diffuse and (2) Focal. In type 1 the smooth muscle cells were laid in a uniformly concentric manner and were not associated with an underlying muscle layer abnormality (Figure 115). In the type 2 lesion, the focal deposits were similar to early atherosclerotic plaques (Figure 116). The internal elastic lamina was often disrupted and replaced by a rudimentary layer. In the majority of cases the intimal lesion was associated with a thickened longitudinal muscular layer.

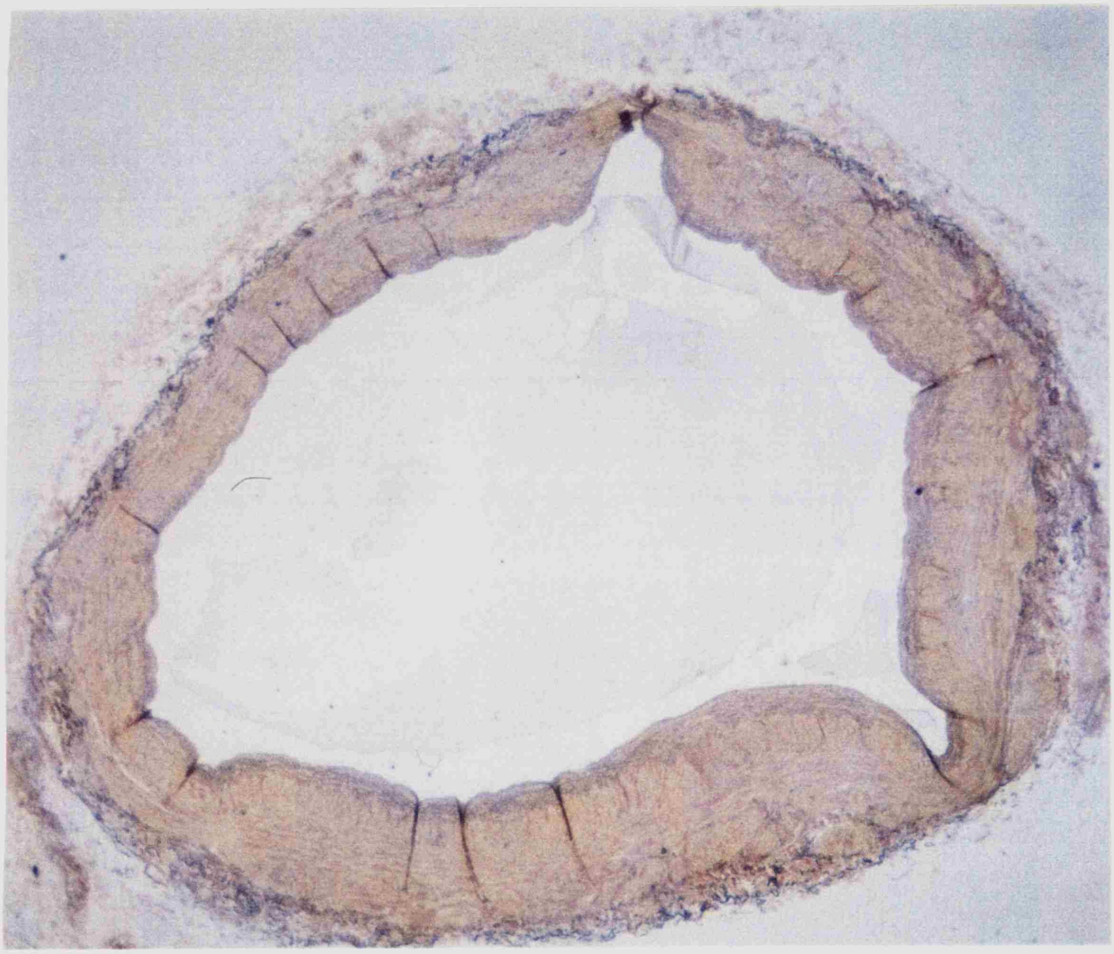


Figure 115. Stain Elastic Van Gieson. Photomicrograph showing an example of mild diffuse intimal hyperplasia.

Figure 116. Stain Elastic van Gieson. Photomicrograph showing an example of severe focal intimal hyperplasia. The internal elastic lamina is partially preserved in the upper aspect of the specimen (arrowed). Large plaques are seen projecting into the vessel lumen which is considerable decreased in diameter, despite adequate distension with agar.

Of the 50 patients studied, 31 showed evidence of mild diffuse intimal hyperplasia (Figure 114). In contrast 24 patients had areas of moderate focal intimal hyperplasia (Figure 117).

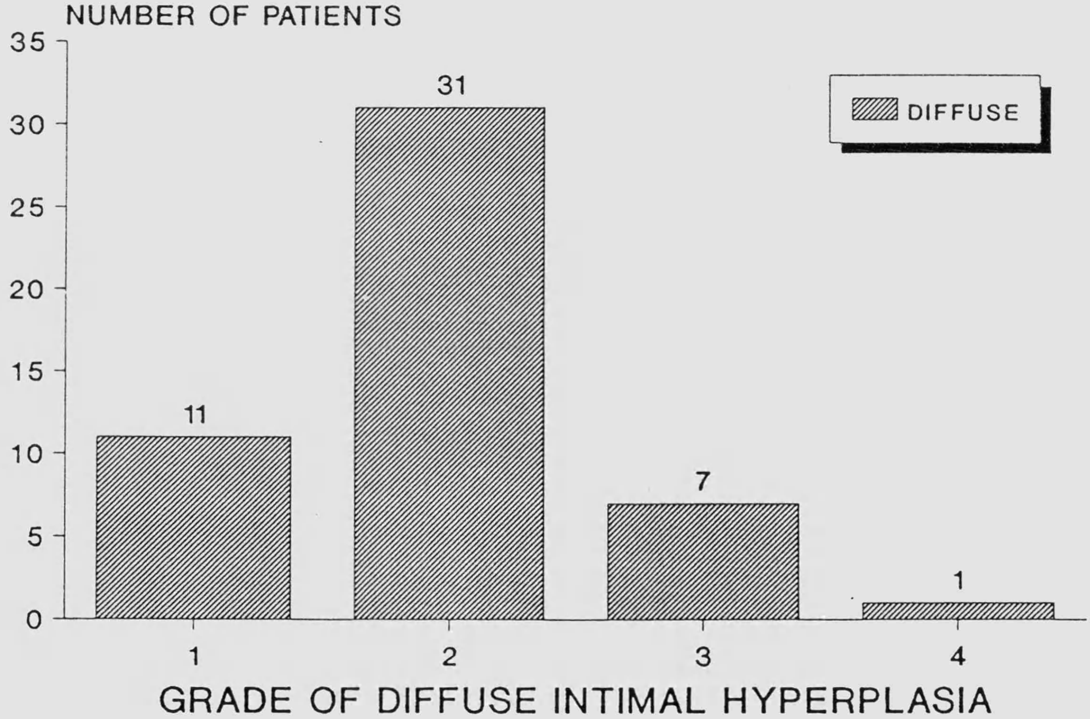


Figure 117. Histogram showing the grades of diffuse intimal hyperplasia.

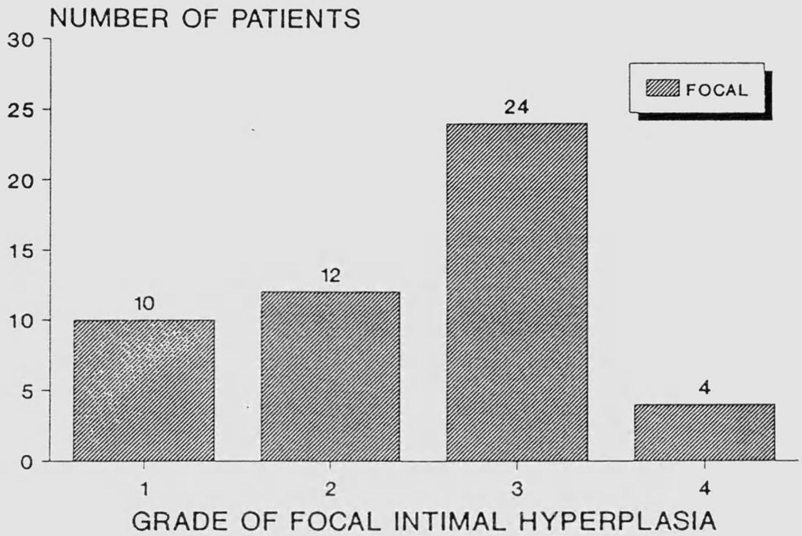


Figure 118

Histogram showing the grades of focal intimal hyperplasia.

<u>*Luminal stenosis*</u>

The vast majority of patients had no significant reduction in the internal diameter of the vessel lumen. Of the 50 patients studied, eight had a greater than 50% stenosis of the vessel lumen, despite adequate distension of the vein with agar (Figure 119).

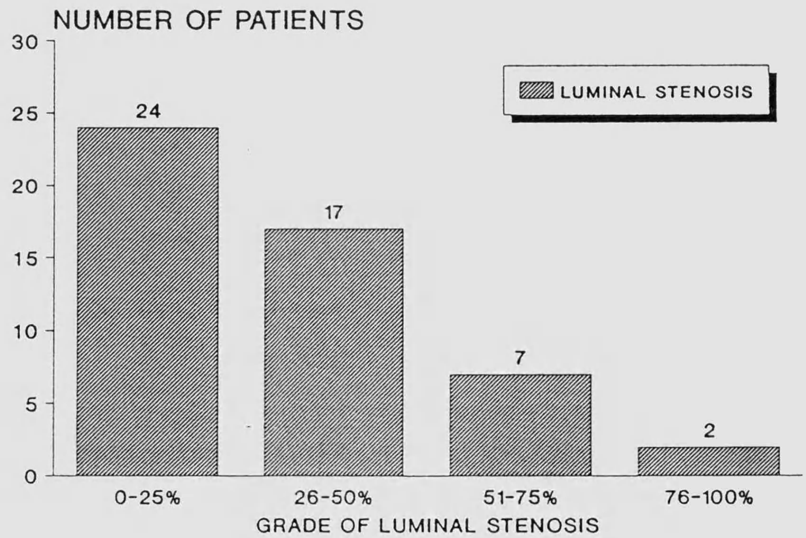


Figure 119.

Histogram showing the grades of luminal stenosis.

Muscle layers.

There was a wide range of muscle layer changes. In the majority of cases there was evidence of mild to moderate muscular hypertrophy in the longitudinal and circular layers (Figure 120). On several occasions the intense muscle hypertrophy gave the impression of migration of the smooth muscle cells from the underlying media into the intimal layer.

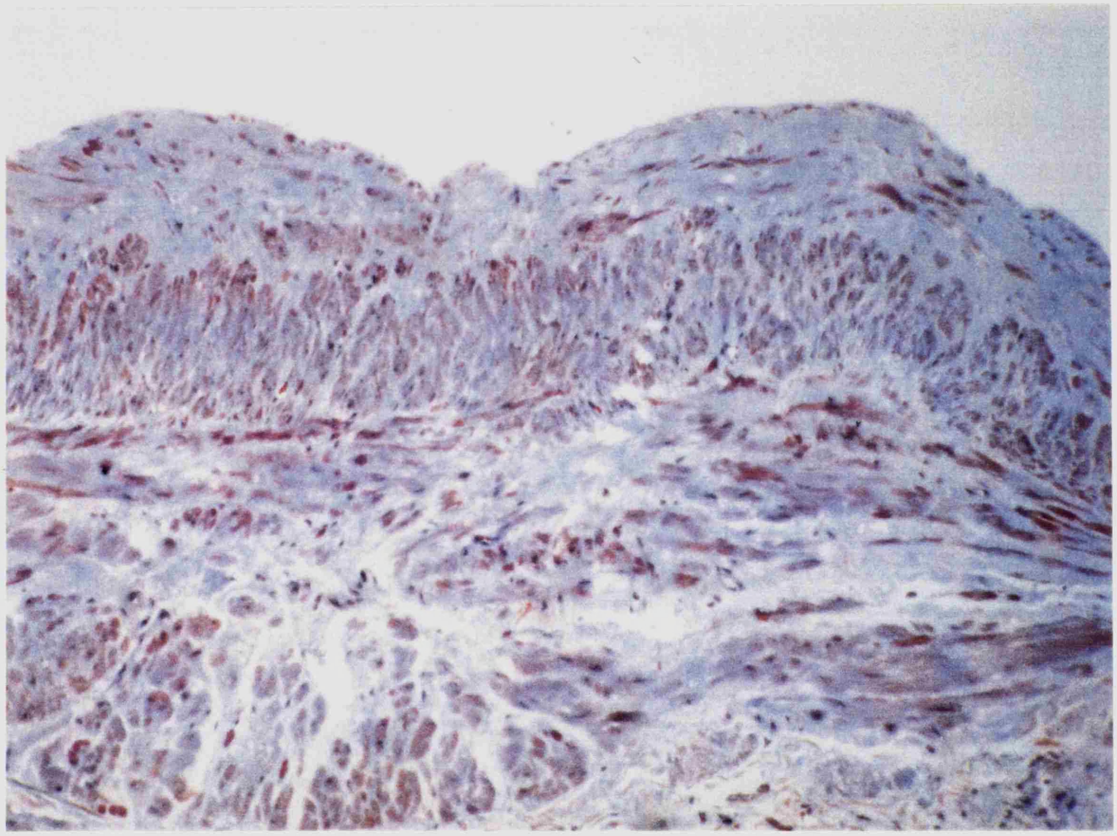


Figure 120.

Masson trichrome stain. Longitudinal muscle hypertrophy with smooth muscle migration from the media into the intimal layer.

In addition to the muscle hypertrophy there were areas of muscle fibrosis within the longitudinal and circular layers which were not quantified in this study.

Longitudinal muscle hypertrophy.

Only one patient had a normal complement of muscle fibres. Twenty five of the patients had evidence of mild muscle hypertrophy (Figure 121).

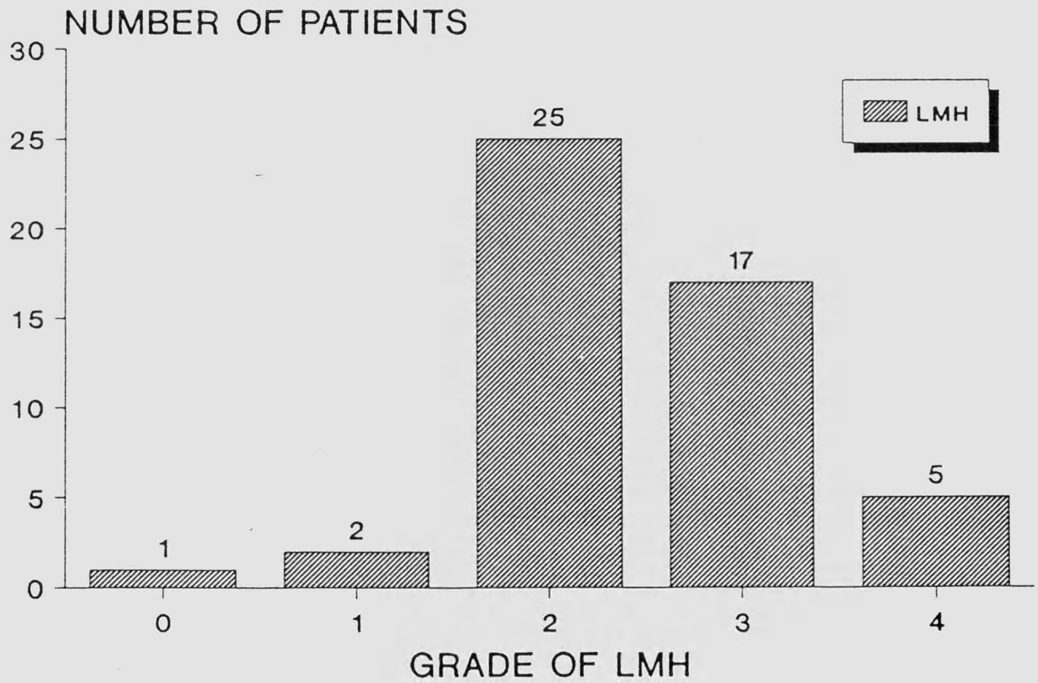


Figure 121.

Longitudinal muscle hypertrophy (LMH), Histogram showing the distribution of disease.

Circular muscle hypertrophy.

Four patients had no evidence of muscle hypertrophy. Half of the patients had evidence of moderate to severe circular muscle hypertrophy (Figure 122).

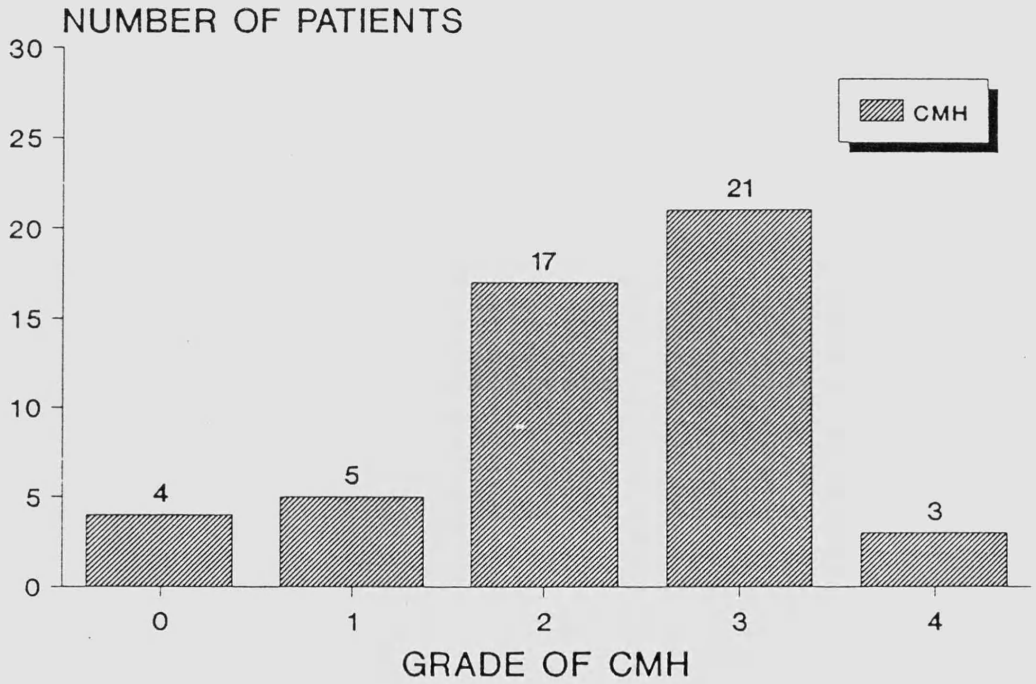


Figure 122.

Circular muscle hypertrophy (CMH), Histogram showing the distribution of disease.

The effect of stripping

In the pre-stripping specimens, the endothelium was intact. Following the passage of a Hall valvulotome only 10% of the cases studied retained a normal endothelium content. In the vast majority of cases there was 50-100% loss of endothelium, (Figure 123).

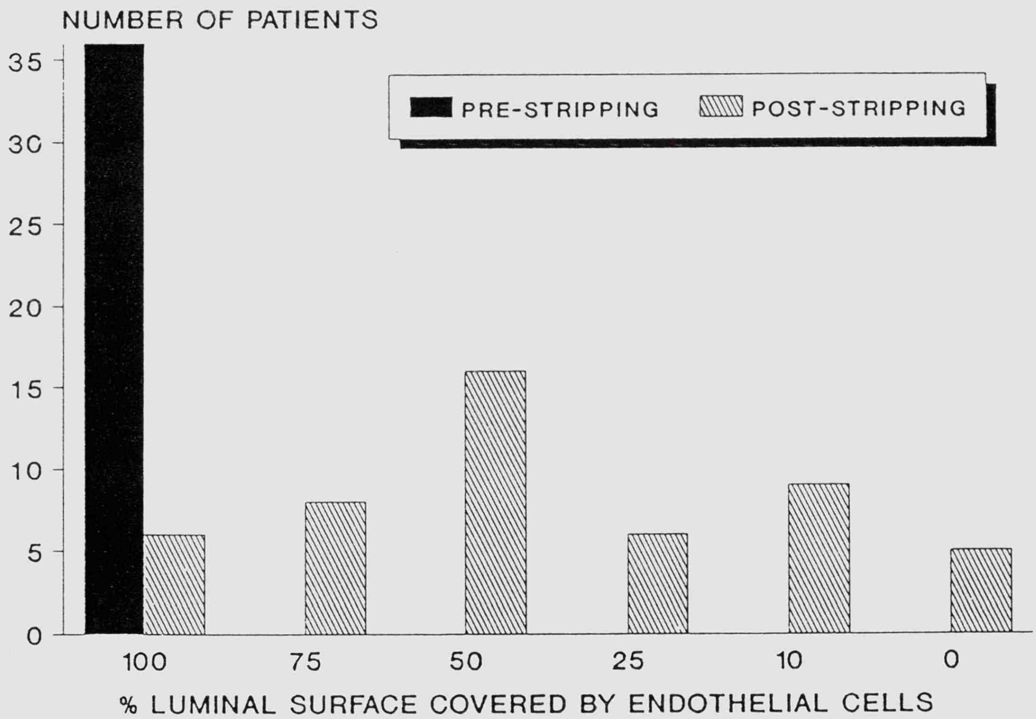


Figure 123.

Histogram showing the effect of valve stripping on endothelial cell coverage.

Electron microscopy

Results

Scanning Electron Microscopy (SEM)

Pre-stripping

In the pre-stripping specimen, the endothelial surface had a smooth regular appearance (Figure 124). At higher power the flat endothelial cells appeared to cover the entire luminal surface. Surface projections consistent with microvilli were noted at higher magnifications (Figure 125). On the luminal surface several globular structures were seen adhering to the luminal surface. These were thought to be lipid droplets (Figure 126).

Figure 124. SEM of the luminal surface prior to the passage of the Hall valvulotome.

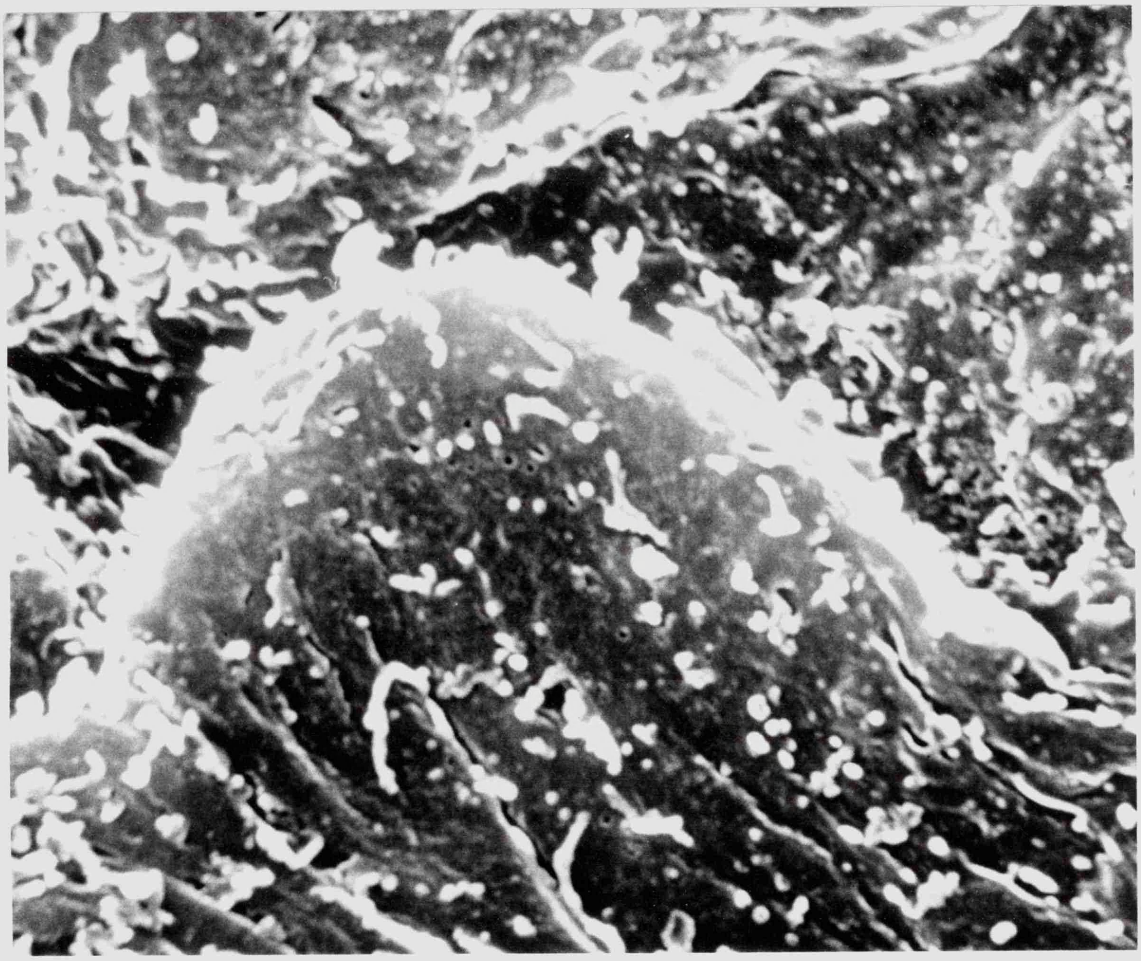


Figure 125.

SEM showing microvilli on the surface of endothelial cells, Magnification x 22,000.

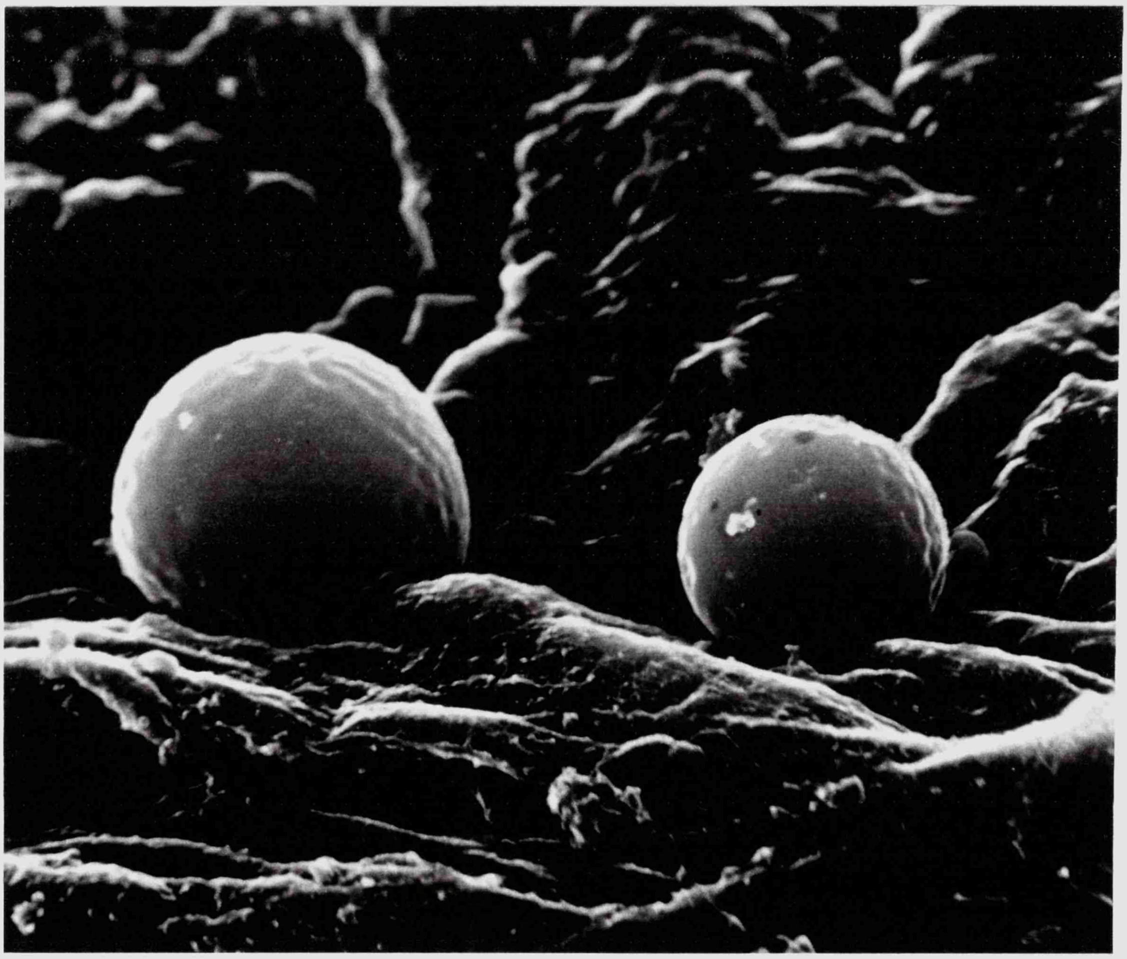


Figure 126.

SEM showing lipid droplets on the endothelial surface, magnification x 4,000.

Post-Stripping

Following the passage of the Hall valvulotome, there was marked endothelial damage with exposure of the underlying collagen fibres and smooth muscle cells (Figures 127 and 128).

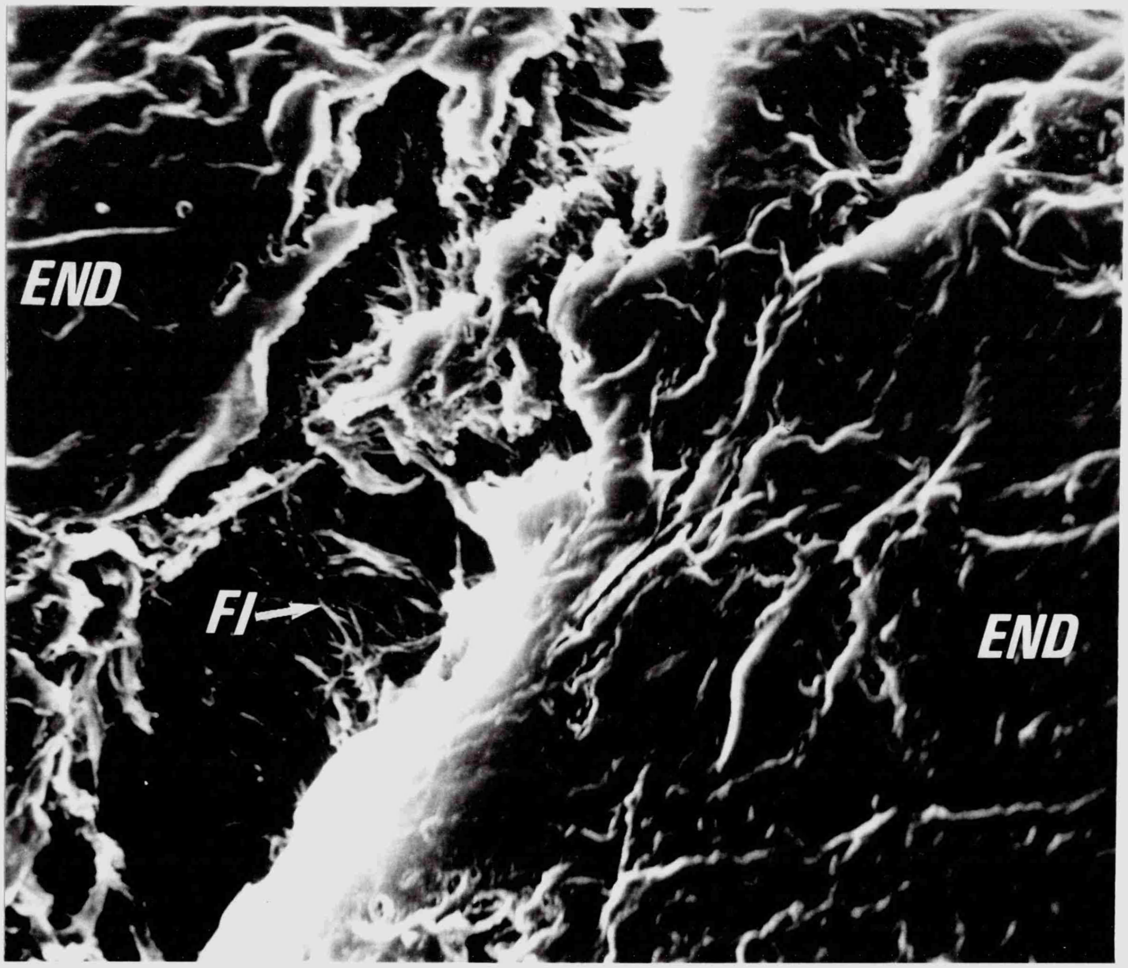
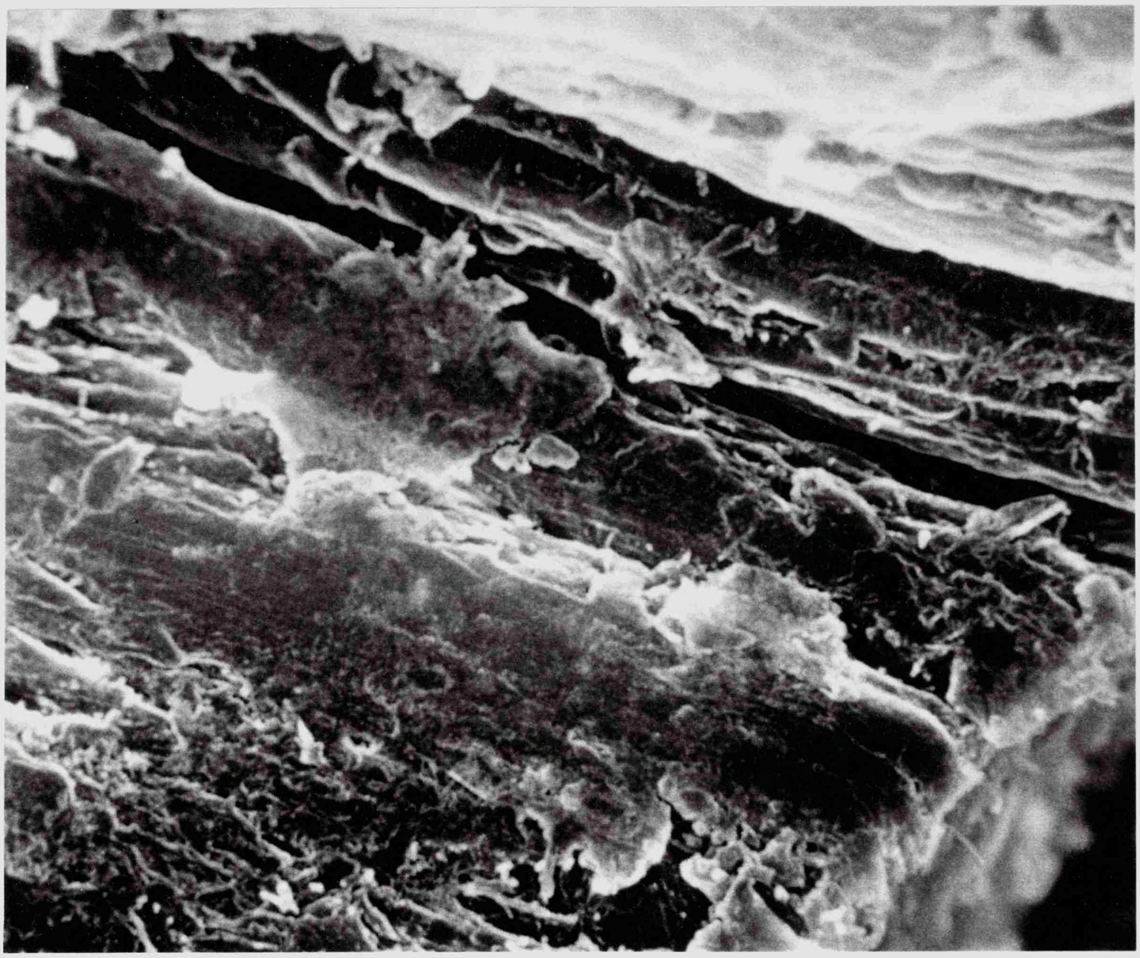


Figure 127.

SEM showing disruption of the normal smooth regular endothelial surface. Magnification x 1000.

Figure 128.

SEM following the passage of a Hall valvulotome. Disruption of the endothelial layer can be seen with exposure of the underlying collagen fibres. Magnification x 10,000.



Transmission Electron Microscopy (TEM).

Pre-stripping

The normal arrangement of endothelial cells, basal lamina (BL) and the underlying smooth muscle cells (SMC) and collagen was clearly demonstrated (Figure 129).

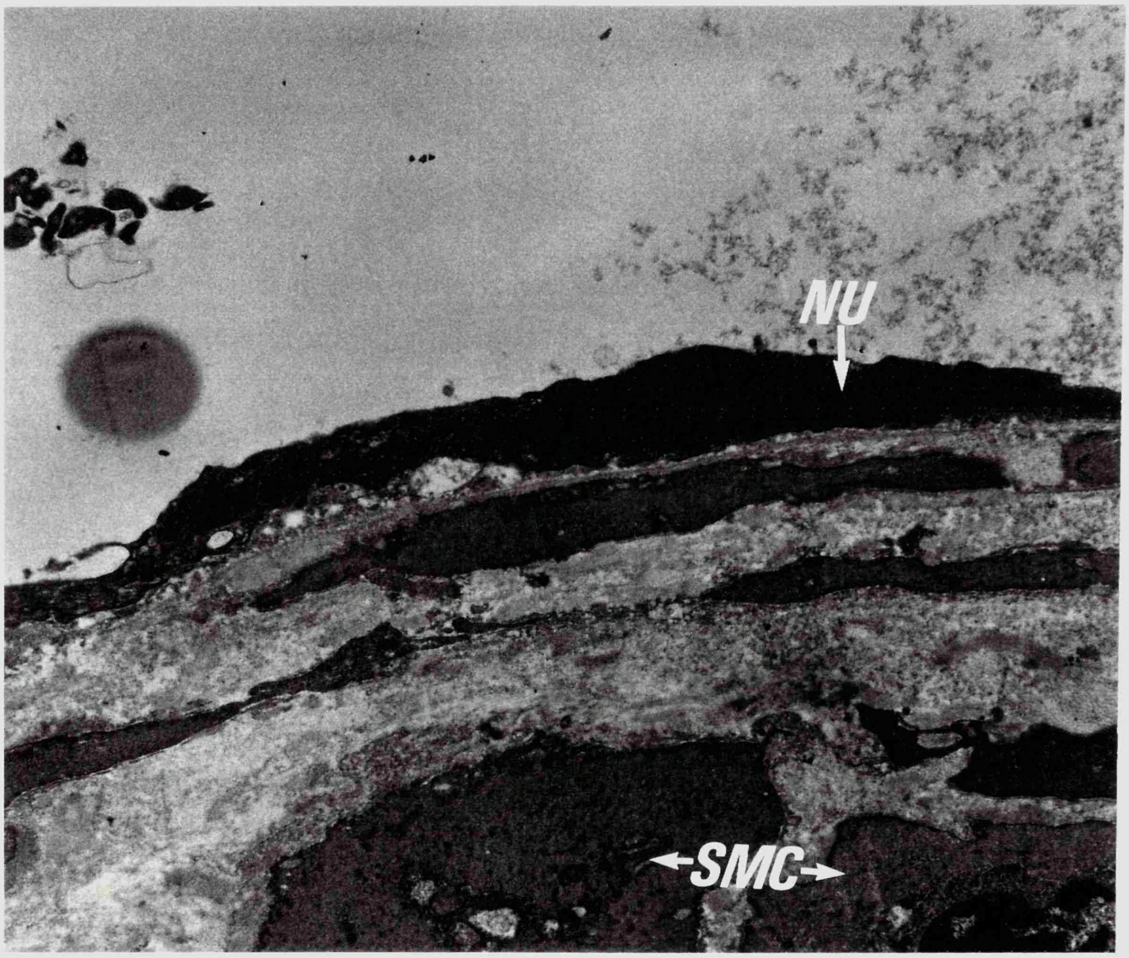


Figure 129.

TEM of the endothelium from a saphenous vein prior to stripping. Very fine microvilli (Mv) are present on the endothelial surface. (Nucleus of endothelial cell (NU), Smooth muscle cell (SMC)).

Phagocytic activity was evident, particular on the luminal surface. Vacuoles, inclusion bodies and lipid droplets were noted in the cytoplasm of the phagocytic cells (Figure 130). The shape and position of (A) is suggestive of the final stages of absorption of extracellular lipid.

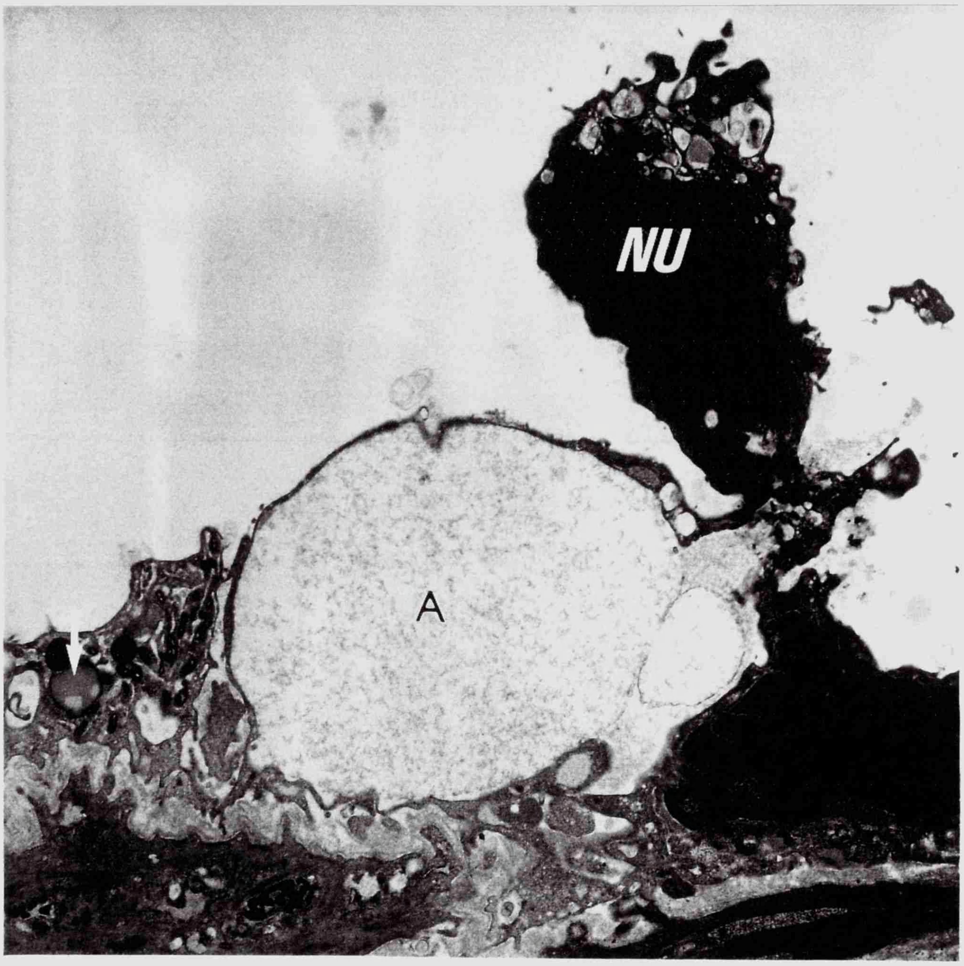


Figure 130.

TEM of a phagocytic cell in association with the endothelial surface (prior to stripping). Vacuoles, inclusion bodies and lipid droplets are evident (arrowed) in the cells cytoplasm. Profile A by size (8 μm), shape and position is suggestive of the final stages of absorption of extracellular lipid droplet. Magnification x 7,000.

Numerous smooth muscle cells in varying degrees of activity were noted. These were often surrounded by large amounts of collagen and elastic tissue. In addition globular structure (Li) similar to those seen on the luminal surface were noted in smooth muscle cells, (Figure 131).

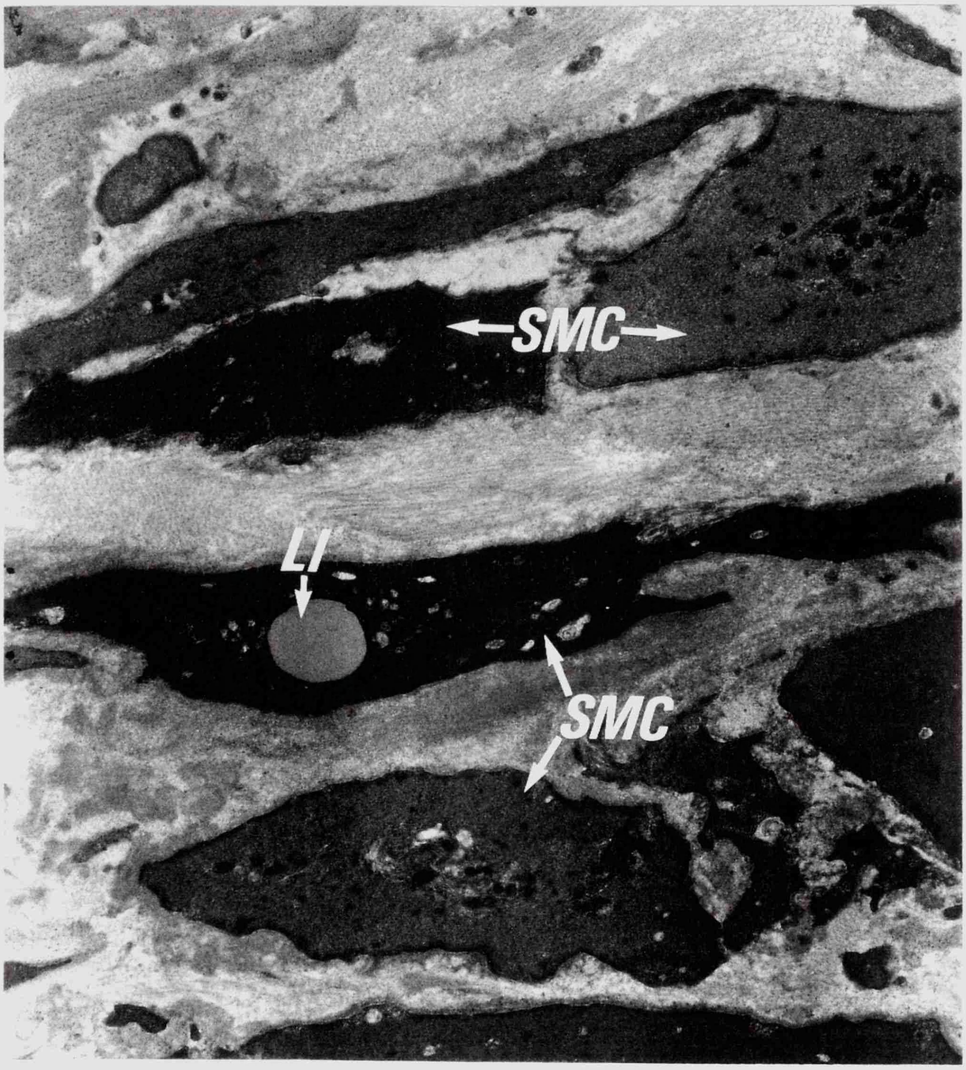


Figure 131.

TEM of smooth muscle cells (SMC) in the media region with a lipid (Li) inclusion body. Magnification x 10,000.

Post-Stripping.

Varying degrees of intimal and medial damage were noted following the passage of the Hall valvulotome. Endothelial cell damage was prominent, leaving a rather tenuous basal lamina (BL) to maintain the tissue-vascular boundary (Figure 132).

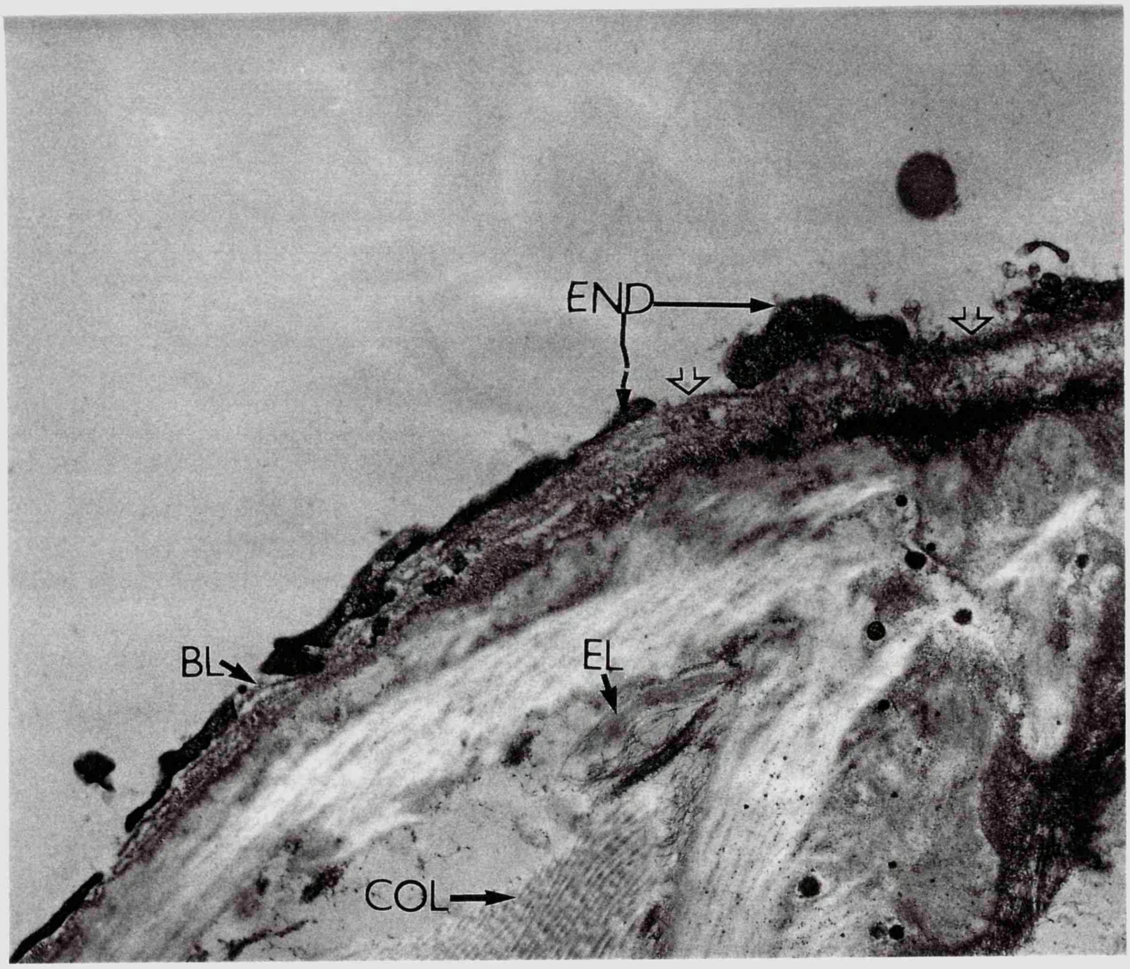


Figure 132.

TEM of a damaged endothelium following the passage of a Hall valvulotome. Intracellular gaps (arrowed) are present with regions of exposed basal lamina (BL). Collagen (COL), elastin (EL), endothelial cell process (END).

Where the BL was lost smooth muscle cells from the underlying intima appeared to have migrated towards the luminal surface, in an attempt to re-establish the tissue-vascular interface (TVI) (Figures 133 and 134).

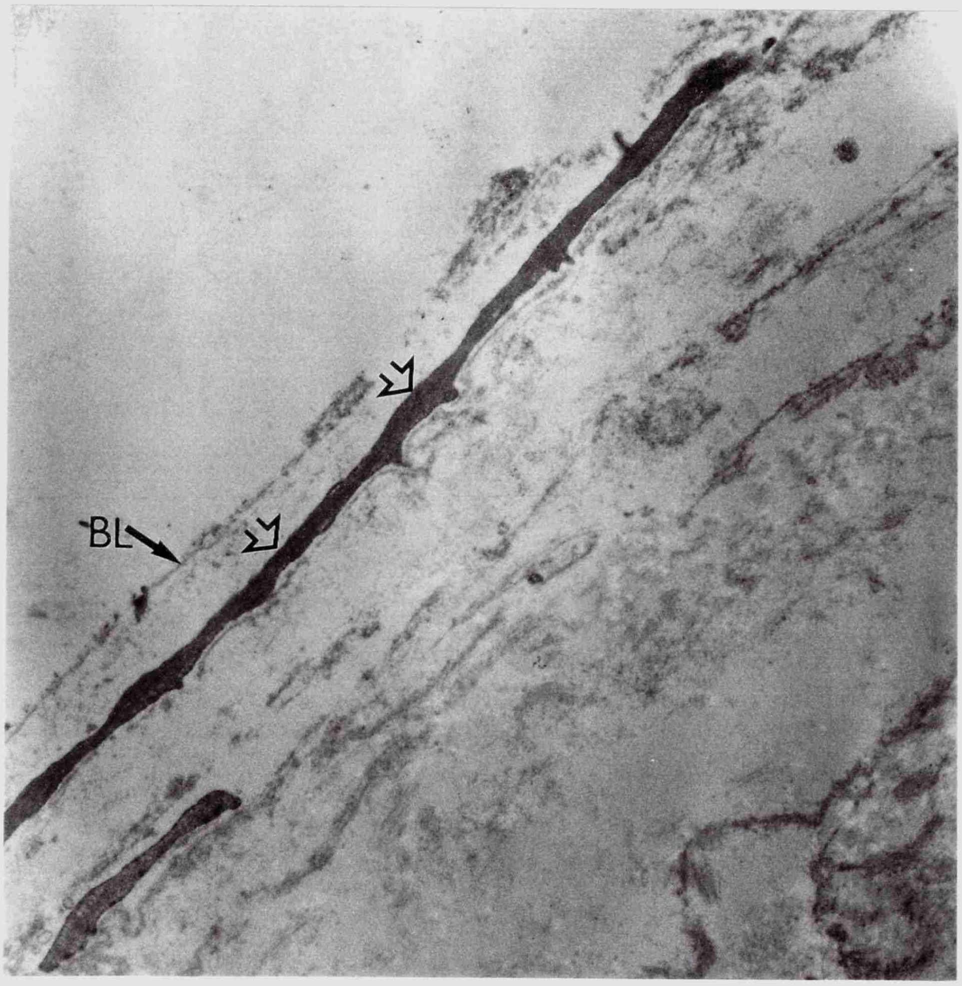


Figure 133.

TEM of the vascular surface after the passage of a Hall valvulotome. Complete loss of the tissue-vascular boundary is evident. Remnants of the basal lamina (BL) can be seen. There is marked longitudinal extension and smooth muscle cell flattening suggesting an attempt to re-establish a tissue-vascular surface.

Figure 134.

TEM of the vascular surface following the passage of the Hall valvulotome. There is loss of the basal lamina and the normal tissue-vascular interface. A physical reorganisation of the smooth muscle cells is evident towards the vascular surface. Magnification x 14,500.

In the absence of any smooth muscle activity, the filamentous material (FM) restored the TVI (Figure 135).

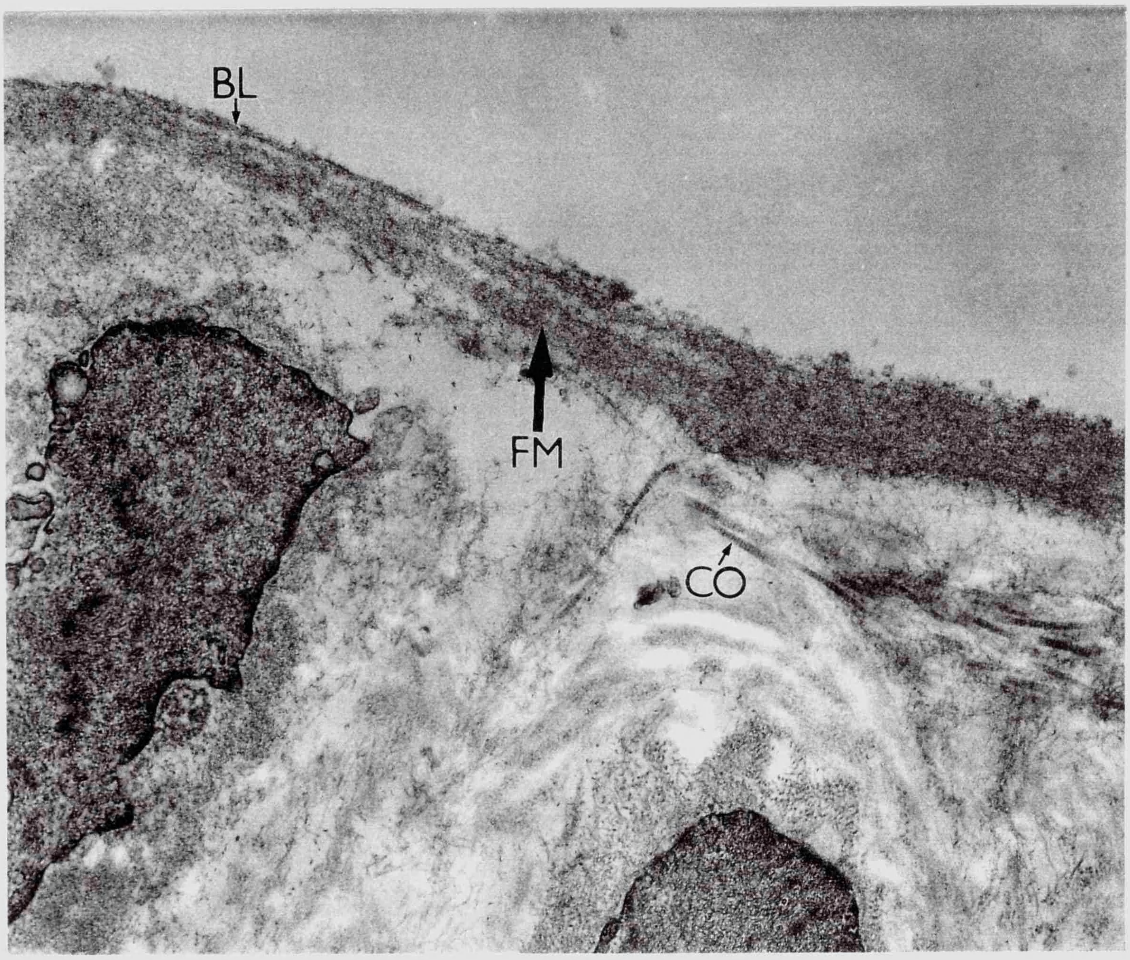


Figure 135.

TEM of the vascular surface following the passage of a Hall valvulotome. There is complete loss of endothelial cells. A thickened band of filamentous material (FM) is seen in association with the basal lamina (BL) attempting to maintain the tissue-vascular interface. Magnification x 31,000.

Discussion

Early and late graft failure have been attributed to (i) endothelial cell damage at the time of vein harvesting and (ii) the development of intimal hyperplasia. Numerous animal studies have investigated the effect of distension, irrigation solutions, temperature and pharmacological agents on endothelial and smooth muscle cell survival in vein grafts.

Szilagyi et al in 1973 in a long term arteriographic study of 377 autogenous vein grafts reported several morphological abnormalities following implantation including; (i) intimal thickening, (ii) atherosclerosis, (iii) fibrotic valves and stenoses, (iv) traumatic stenoses, (v) suture stenoses and (vi) aneurysmal dilatation.

Two important histological features were recognised following implantation, (i) smooth muscle cell loss with collagen replacement and (ii) intimal thickening which consisted of subendothelial smooth muscle cell proliferation and successive deposits and layering of fibrin. By two years 80% of the veins studied had evidence of atherosclerosis with fibrotic plaque formation and lipid infiltration. Szilagyi concluded that these intimal changes were the result of altered haemodynamics.

Dissatisfaction with the results of the reversed femoro-popliteal vein grafts led Rob, Connolly and Hall to pioneer the in situ vein technique in the early sixties. The subsequent modifications by Karmody and Leather produced excellent long term graft patency results at 18 months. Several theoretical advantages were proposed to explain the apparent differences between the two techniques. These included; (i) reduced warm ischaemic time, (ii) preservation of an intact endothelial surface, (iii) improved proximal and distal anastomotic fit, and

(iv) a more compliant vessel (Leather, Powers and Karmody 1979).

Nevertheless recent evidence both from animal and clinical studies have raised doubts about some of these theories (Bush, Graber, Jakubowski et al 1984, Furuyama, Kusaba, Moriyanma et al 1980, Beard, and Fairgreave 1986a and Beard, Lee, Aldoori et al 1986b).

Cheanvechai et al (1975) in a study of 1,179 patients reported that 27% of long saphenous veins studied had intimal plaques composed of acellular collagen and hypertrophy of the tunica media. Thiene et al (1980) in a similar study reported that only 6.6% of long saphenous vein segments were disease free at the time of implantation. The vast majority showed evidence of intimal fibrosis and muscle hypertrophy. Waller and Roberts (1985) also detailed intimal fibrosis and its effect on luminal narrowing, but they failed to distend the vein segments.

In this study, the aim was to assess the long saphenous vein prior to implantation in patients undergoing femoro-distal bypass for critical ischaemia.

Intimal fibrosis, elastosis and hypertrophy of the muscle layers were seen in all cases. The intimal lesions were composed of fibrous tissue, elastic tissue and longitudinally arranged smooth muscle cells. The latter were apparently similar to those seen in arteries. No lipid laden cells were seen on light microscopy but spherical globules consistent with lipid have been observed on the luminal surface of the vein and within smooth muscle cells on TEM and SEM. Arterial smooth muscle cells are known to migrate from the media to the intima where they produce dermatan sulphate, chondroitin sulphate, hyulronic acid and elastin in response to various mitogenic factors including platelet derived growth factor (PDGF) and low lipid density lipoproteins (LDL). A similar situation probably exists with smooth muscle cells in veins.

Normal endothelium forms a physical barrier between the vessel lumen and the thrombogenic subendothelial collagen (Hütter and Gabbiani 1982). Surface proteins on both endothelium and platelets probably account for the absence of platelet adherence to normal endothelial cells. Several factors have been implicated in endothelial damage; (i) hypertension (Meairs, Weihe, Mittmann et al 1984), (ii) hypercholesterolaemia (Faggiotto and Ross 1984), (iii) shear forces (Joris, Zands and Majno 1982), (iv) anoxia (Morrison, Orci, Berwick 1977), (v) specific antibodies and (vi) sensitised lymphocytes (Ryan 1976). All of which lead to increased permeability and thrombogenicity. The resultant exposure of type I and III collagen fibres leads to rapid platelet deposition with release of thromboxane A_2, ADP and PDGF. Two theories have been postulated to account for the activation of the coagulation system and fibrin formation.

(A) Damaged endothelial cells may release thromboplastins and thus activate the extrinsic pathway.

(B) Proteolytic enzymes released from damaged endothelial cells may activate factor XII and thus initiate the intrinsic pathway (Nemerson and Bach 1982).

The focally demarcated intimal lesions seen in this study suggest that there has been previous microthrombus formation with incorporation of the organised thrombus. A similar finding has been reported in umbilical veins as a cause of intimal fibrosis in placental vessels (De Sa 1973).

During the study it became apparent that the passage of the Hall valvulotome resulted in marked endothelial cell loss. This was confirmed on both light and electron microscopy. The attempt to preserve the barrier between lumen and the subendothelial structures by elongated SMC deserves further study.

The extensive damage caused by these instruments clearly represents an avoidable factor in early graft thrombosis and the possible late development of vein strictures. The use of various pharmacological agents to prevent platelet adherence has important implications in the per-operative management of these cases.

Following the completion of this study, an intensive IA DSA surveillance and non-invasive graft surveillance graft programme was instituted. Over half of the patients assessed had significant stenoses, the majority being at or near the distal anastomosis. This may reflect the site of maximal damage during the passage of the valvulotome.

Both longitudinal and circular muscle layers were thicker than the classical histological descriptions would imply. This was due to a combination of both muscle hypertrophy and fibrosis. Marked changes were noted in relationship to tributaries, valves and may represent areas of excessive shear forces or increased venous pressure, The association between focal intimal plaques and muscle hypertrophy remains unsure.

In the past, the presence of intimal hyperplasia and muscle hypertrophy have been termed "arterialization". The fact that these changes are present prior to implantation implies that the term "arterialization" is incorrect and that vein quality may be a very important factor in graft survival.

Summary.

Early and late graft failure has been attributed to endothelial cell damage at the time of vein harvesting and the development of intimal hyperplasia. The in situ vein technique has several theoretical advantages but the clinical results have not confirmed this. Fifty consecutive patients undergoing non-reversed femoro-distal vein bypasses were studied. There were 33 men and 17 women with a median age of 71 range 31-80 years. Segments of the long saphenous vein (usually below knee) were taken in excess of that required for surgery, one before mobilisation and one after valve stripping with a Hall valvulotome.

A semi-quantitative histological grading system was used to quantify the degree of pathological change. Marked abnormalities were noted in all the long saphenous veins.

Endothelial cell coverage of the luminal surface was quantified before and after valve stripping with a Hall valvulotome. Between 0 - 100 % of endothelial cells were lost and replaced by a layer of fibrin.

In marked contrast to other studies these results suggest that intimal hyperplasia is already present in the veins before implantation into the arterial circulation and the presence of muscle hypertrophy and fibrosis suggests pre-existing vein damage. The use of the Hall valvulotome is associated with endothelial cell loss and exposure of the underlying smooth muscle cells. All the features are potential causes of early and late graft failure.

CHAPTER 7.

RESULTS; LONG TERM FOLLOW UP.

Patients.

Eighty one non-reversed vein grafts were performed for critical ischaemia, 36 for rest pain and 45 for gangrene. There were 51 men and 30 women with a median age of 71, range 47-87 years. Thirty nine grafts were to the distal popliteal artery, 15 to the tibioperoneal trunk and 27 to a single calf vessel. There were 57 non diabetics and 24 diabetics (15 diet controlled and 9 insulin dependant). The primary patency rate at one month was 76%. Seven grafts required revision, 3 interposition vein grafts, 3 jump grafts and one revision of a distal anastomosis. This gave a secondary patency rate of 85%. The early hospital mortality (< 30 days) was 0%. The cumulative patency rates at 1 and 2 years were 73% and 60% respectively, limb salvage 77% and 70% and patients survival 86% and 79% respectively (Figure 136).

Statistical Analysis.

All grafts were analysed on a SSPS statistical package. The minimum follow up was 3 months with a maximum of 45 months. Graft patency, limb salvage and patient survival were calculated at 3 monthly intervals. Graft patency was determined by duplex scanning. The Lee-Desu test was used to analyse the difference between various groups eg PGR score.

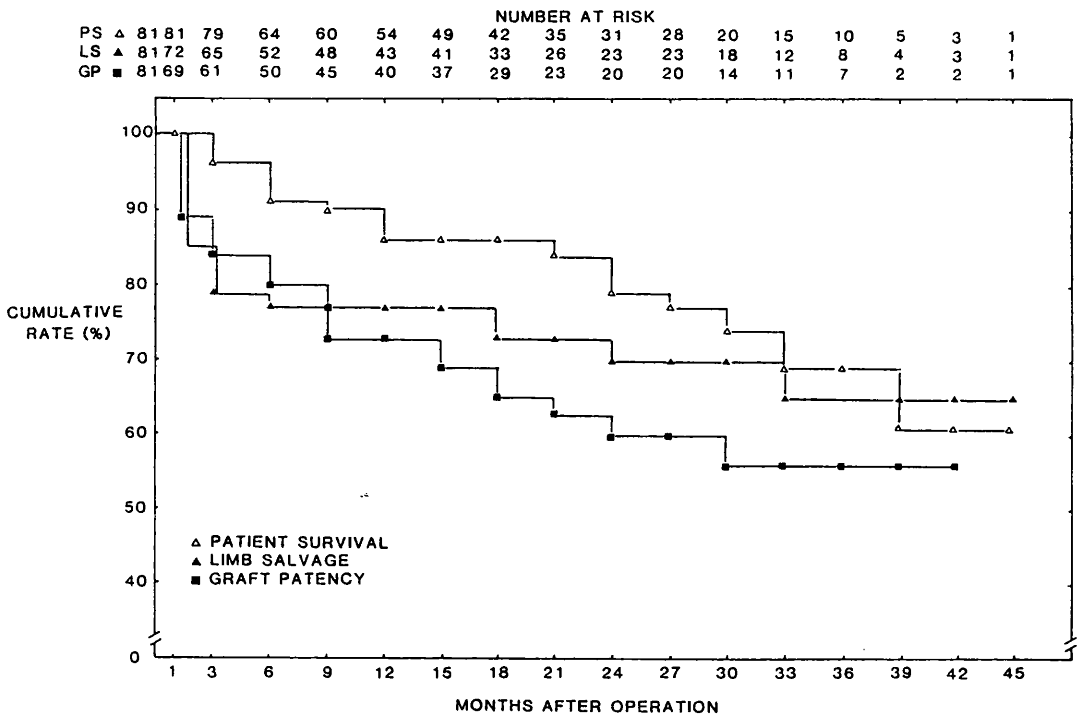


Figure 136.

Cumulative graft patency, limb salvage and patient survival rates.

<u>*Status of patient.*</u>

There was no significant difference in cumulative graft patency between the grafts for rest pain and gangrene. A similar finding was noted in the non-diabetics versus diabetics grafts, (Lee-Desu $p < 0.8$ respectively), (Figures 137 and 138).

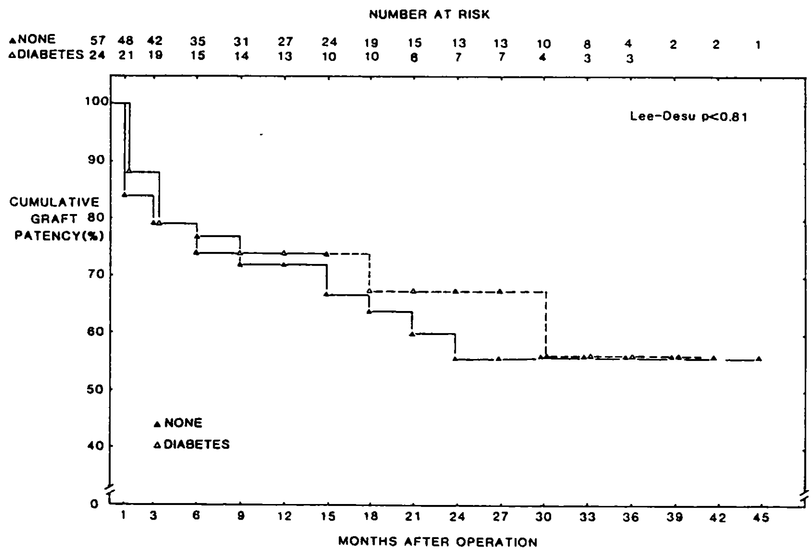


Figure 137.

Cumulative graft patency for diabetics versus nondiabetics.

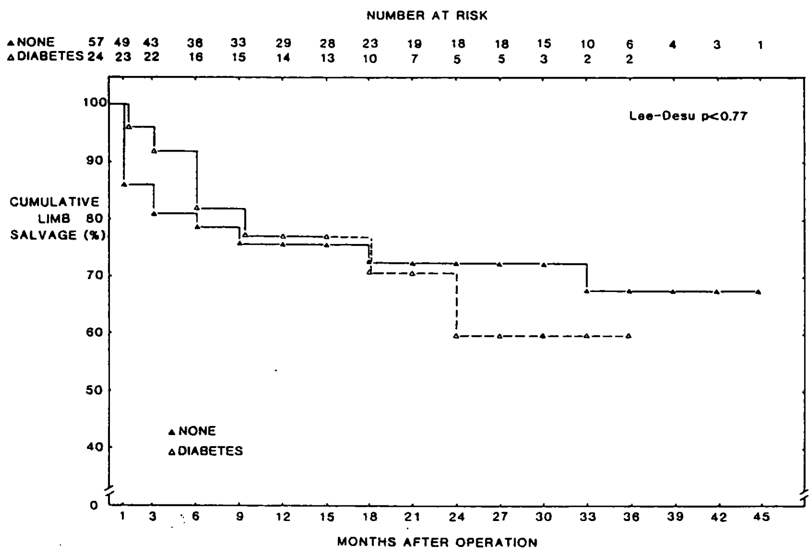


Figure 138.

Cumulative limb salvage rates for the diabetic status of the patient.

Level of Distal Anastomosis.

There was a significant difference in cumulative graft patency rates between grafts anastomosed to (i) distal popliteal artery (DP), (ii) tibioperoneal trunk and a single calf vessel, $p < 0.006$). The one year cumulative graft patency rates for distal popliteal (DP), tibioperoneal (TPT) and calf vessel grafts were 87%, 80% and 47% respectively, (Figure 139).

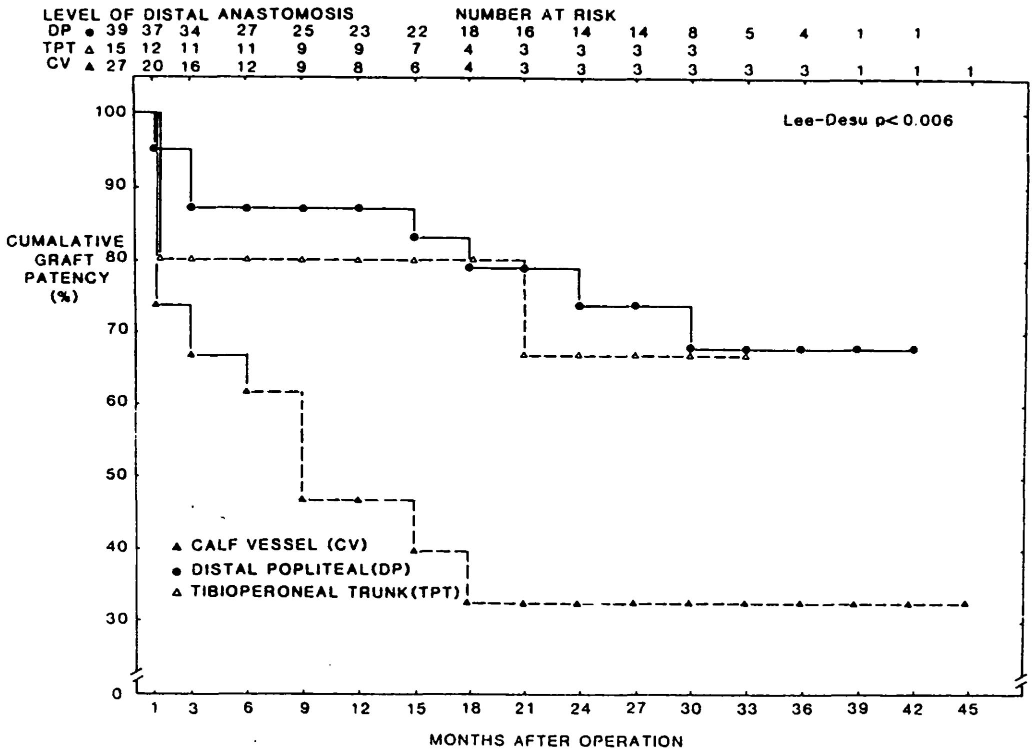


Figure 139.

Cumulative graft patency for the level of the distal anastomosis.

Level of distal anastomosis.

There was a significant difference in the limb salvage rate between grafts anastomosed to (i) distal popliteal, (ii) tibioperoneal trunk and (iii) calf vessel, Lee-Desu $p < 0.003$ (Figure 140) . The 1 year cumulative limb salvage rate for the DP, TPT and SCV grafts was 92%, 73% and 54% respectively.

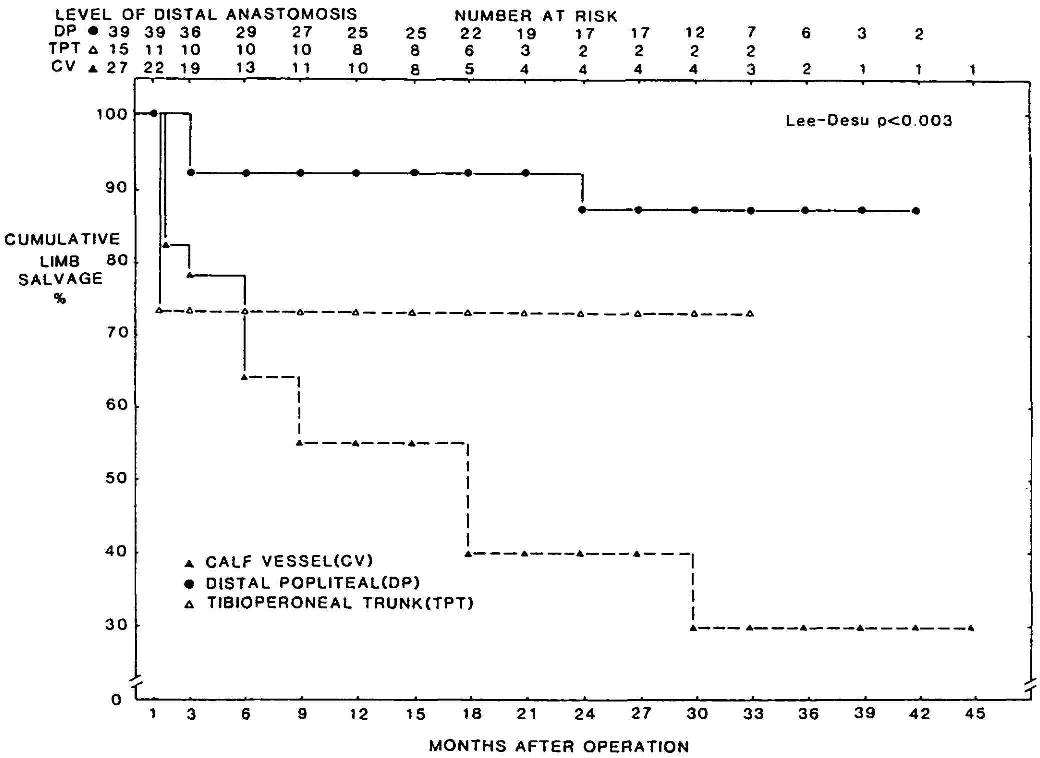


Figure 140.

Cumulative limb salvage rate for level of the distal anastomosis.

Arteriogram score

Two groups were analysed. Grafts with an arteriogram score of > 2 versus those with a score of ≤ 2. There was a significant difference between the two groups ($p < 0.027$), (Figure 141). The two year cumulative graft patency was 74% and 51% respectively.

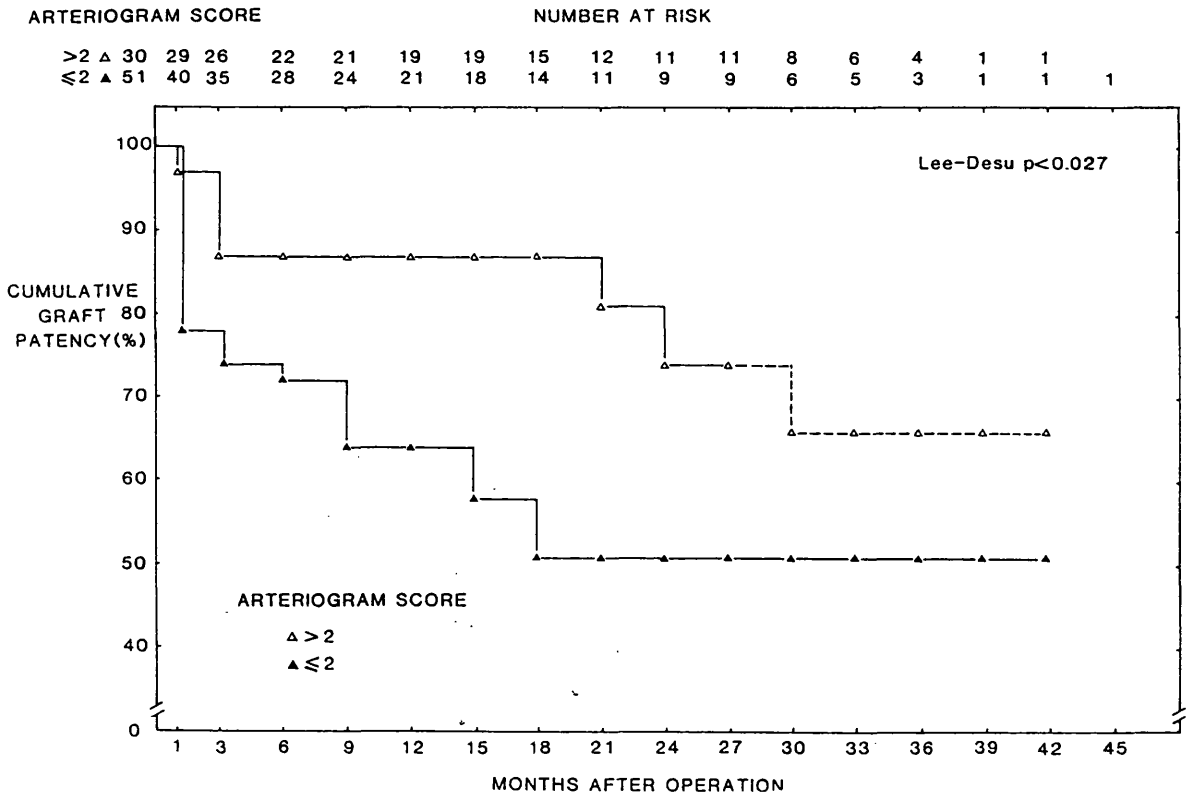


Figure 141.

Arteriogram score; cumulative graft patency rates.

Arteriogram score.

There was no significant difference between the two groups. The 1 year cumulative limb salvage rate for grafts with an arteriogram score of ≤ 2 and 2 was 86% and 71 % respectively, (Figure 142).

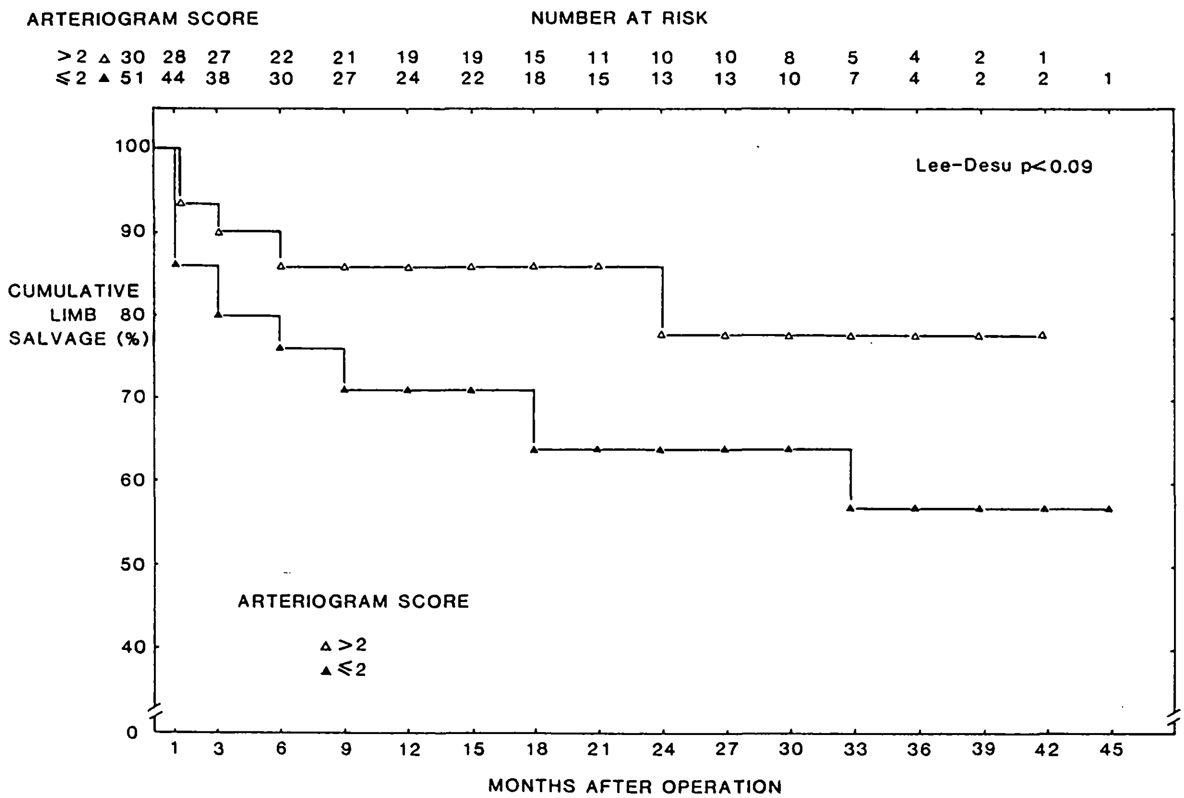


Figure 142.

Arteriogram score; cumulative limb salvage rate.

PGR score.

Two groups were analysed, grafts with a PGR score of ≥ 2 versus < 2. There was a significant difference between the two groups $p < 0.002$. The two year cumulative graft patency rates were 65% and 14% respectively (Figure 143).

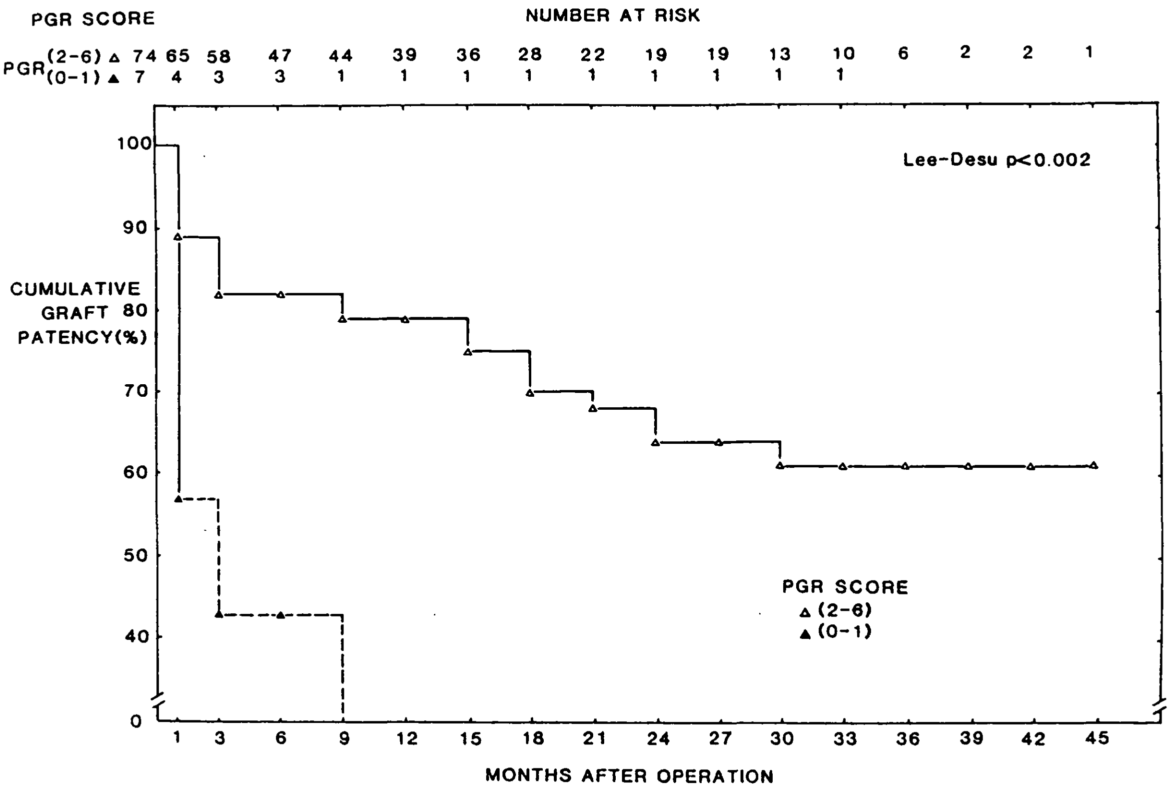


Figure 143.

PGR score; cumulative graft patency rates.

PGR score.

There was a significant difference between the two groups, $p < 0.001$. Grafts with a PGR score of two or more had a 1 year limb salvage rate of 82% compared to 29% for those grafts with a low PGR score ie (0-1), (Figure 144).

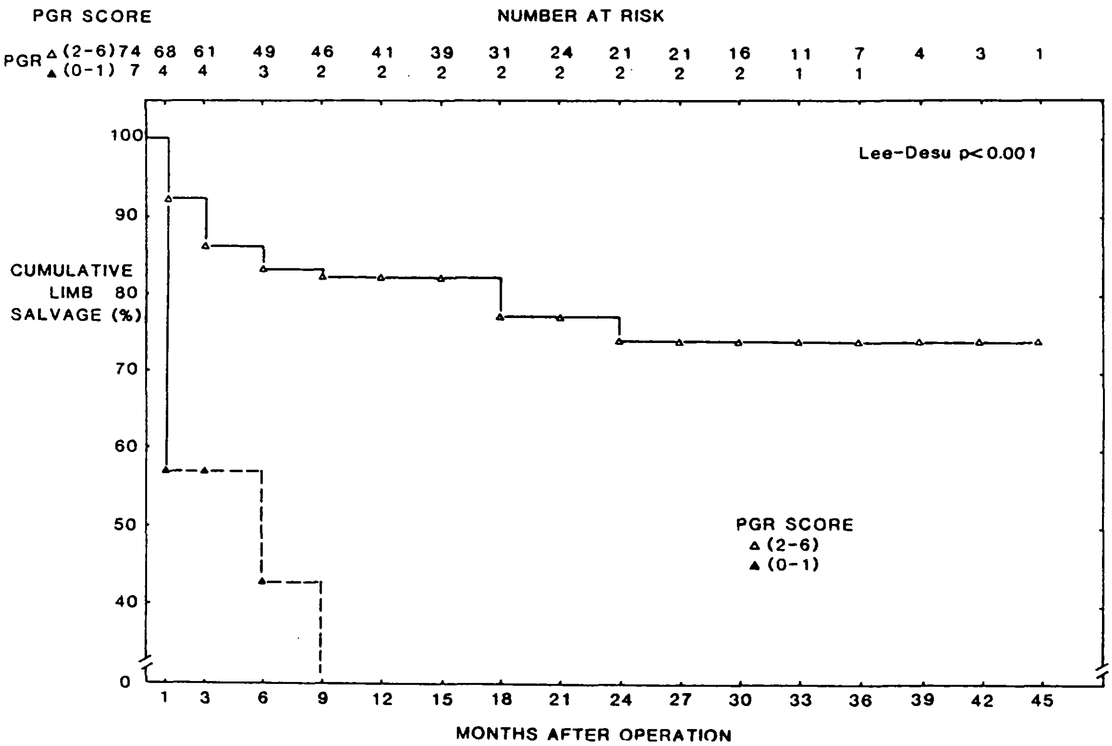


Figure 144.

PGR score; cumulative limb salvage rate.

Vein Size.

Vein size (external diameter) was measured at the end of the operation after the administration of papaverine hydrochloride. Grafts were divided into two groups (i) 0-4 mm and (ii) > 4mm. There was no significant difference in the graft patency rates between the two groups (Figure 145). The one year cumulative graft patency rates for grafts with a vein size of 0-4 mm and > 4mm were 66% and 92% respectiveley.

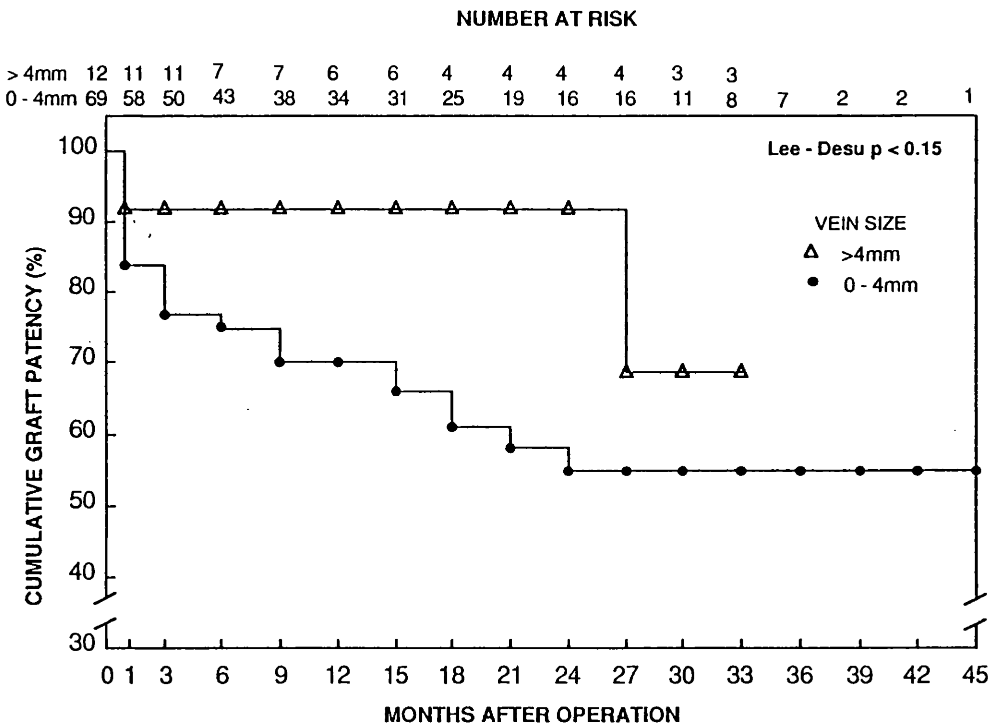


Figure 145.

Vein size; cumulative graft patency rates.

Vein size.

There was no significant difference in the cumulative limb salvage rates between grafts with a diameter of 0-4 mm versus > 4 mm, p < 0.81, (Figure 146).The one year cumulative limb salvage rate for grafts with a vein size of 0-4 mm and > 4mm were 76% and 83% respectiveley.

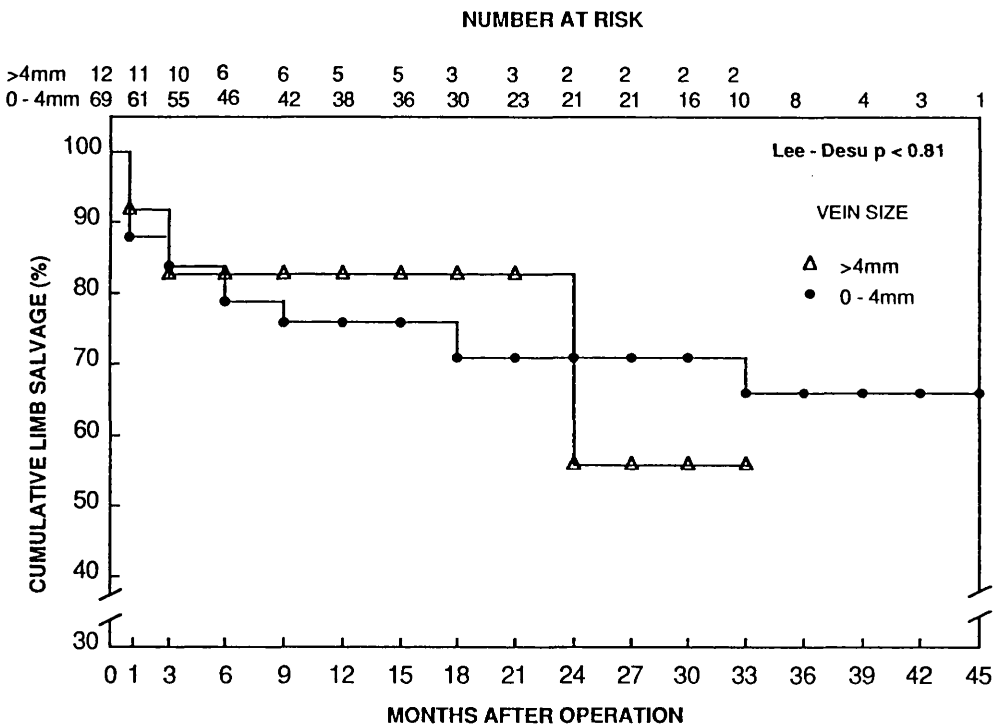


Figure 146.

Vein size; cumulative limb salvage rates.

Peripheral Resistance (PR)

Grafts were divided into two groups, (i) PR < 1 PRU's and (ii) PR > 1.0 PRU's. Grafts with a peripheral resistance of < 1 PRU's had a significantly better cumulative graft patency rate ($p < 0.001$). The one year cumulative patency rates for grafts with a PR of < 1PRU and > 1 PRU were 81% and 44% respectively (Figure 147).

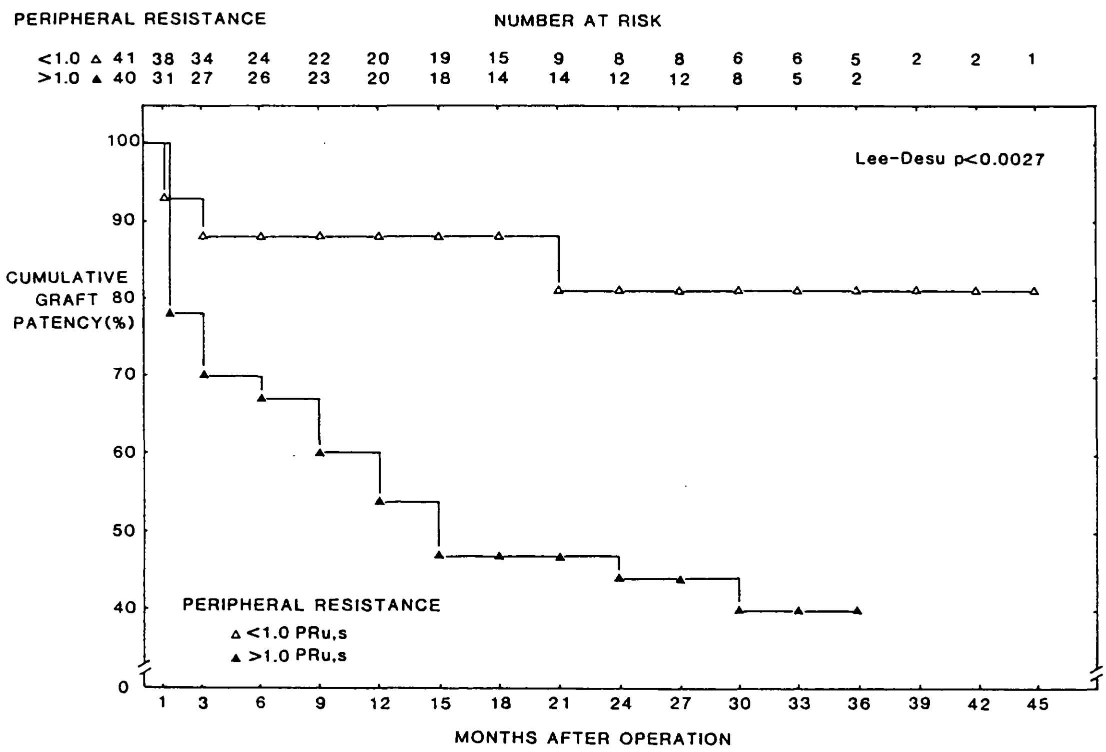


Figure 147.

Peripheral resistance: cumulative graft patency rates.

Peripheral resistance.

There was a significant difference between the two groups, $p < 0.019$. The 1 year limb salvage rate for grafts with a PR < 1 PRU and > 1 PRU was 87% and 67% respectively, (Figure 148).

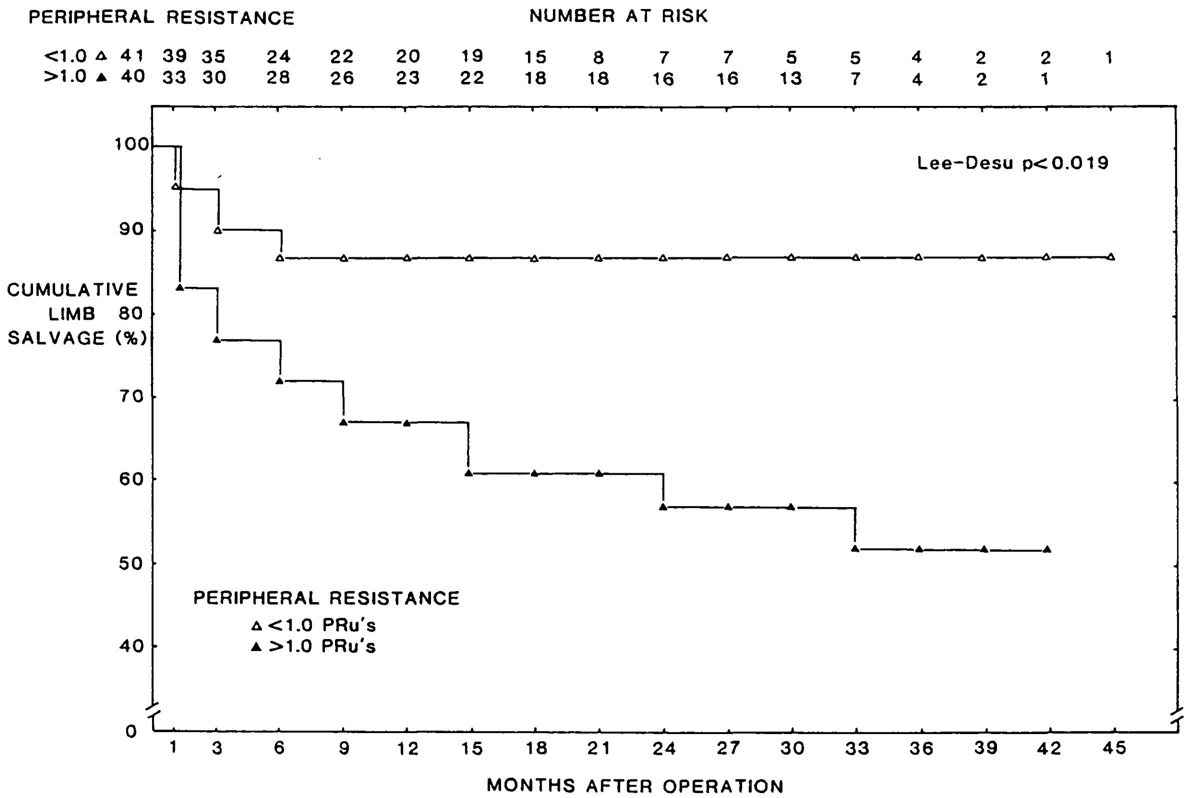


Figure 148.

Peripheral resistance; cumulative limb salvage rate.

Graft resistance pre-papaverine (GR1).

Following completion of the graft, the peripheral resistance was measured at rest. Two groups of grafts were analysed, (i) PR < 1 PRU's and (ii) PR > 1 PRU's. No significant difference was noted between the two groups (Figure 149). This probably reflects the degree of spasm that occurs during these prolonged procedures.

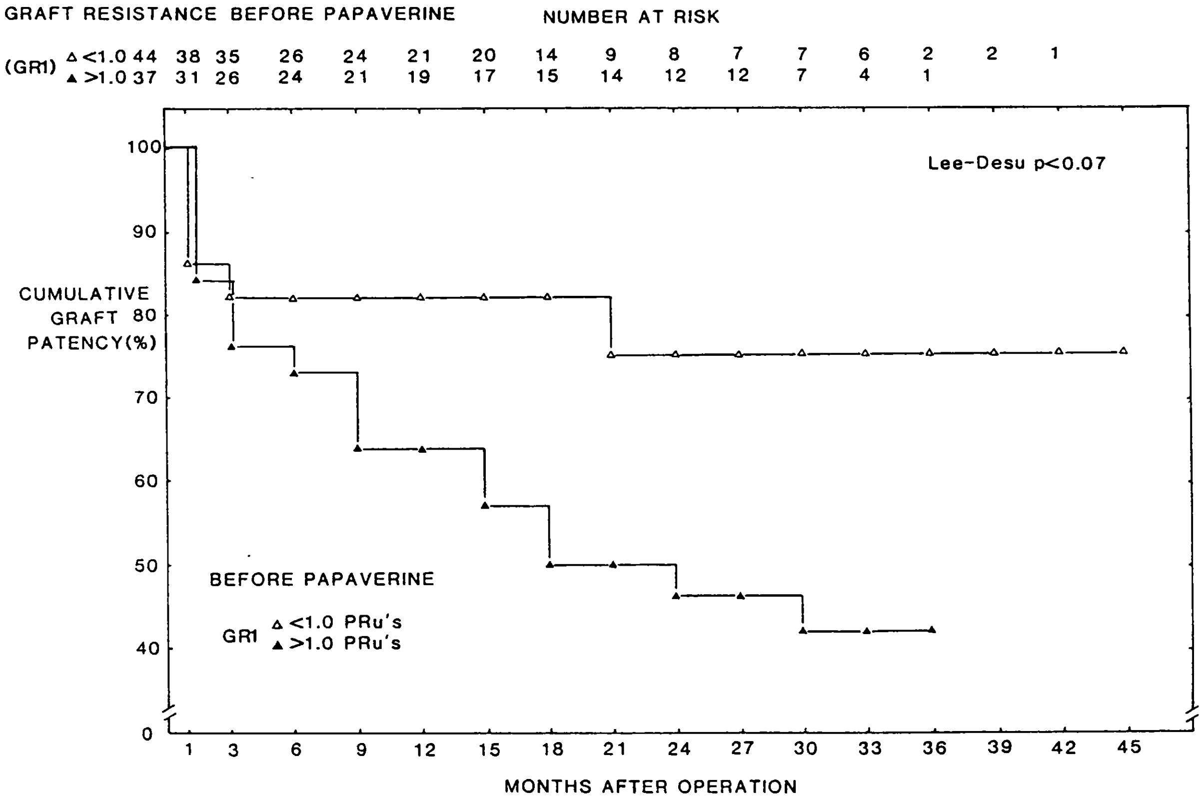


Figure 149.

Graft resistance before papaverine (GR1); cumulative graft patency rates.

Graft resistance before papaverine (GR1).

There was no significant difference in limb salvage between the two groups, $p < 0.23$.The one year cumulative limb salvage rates for grafts with a GR1 of < 1PRU and > 1 PRU was 81% and 72% respectively, (Figure 150).

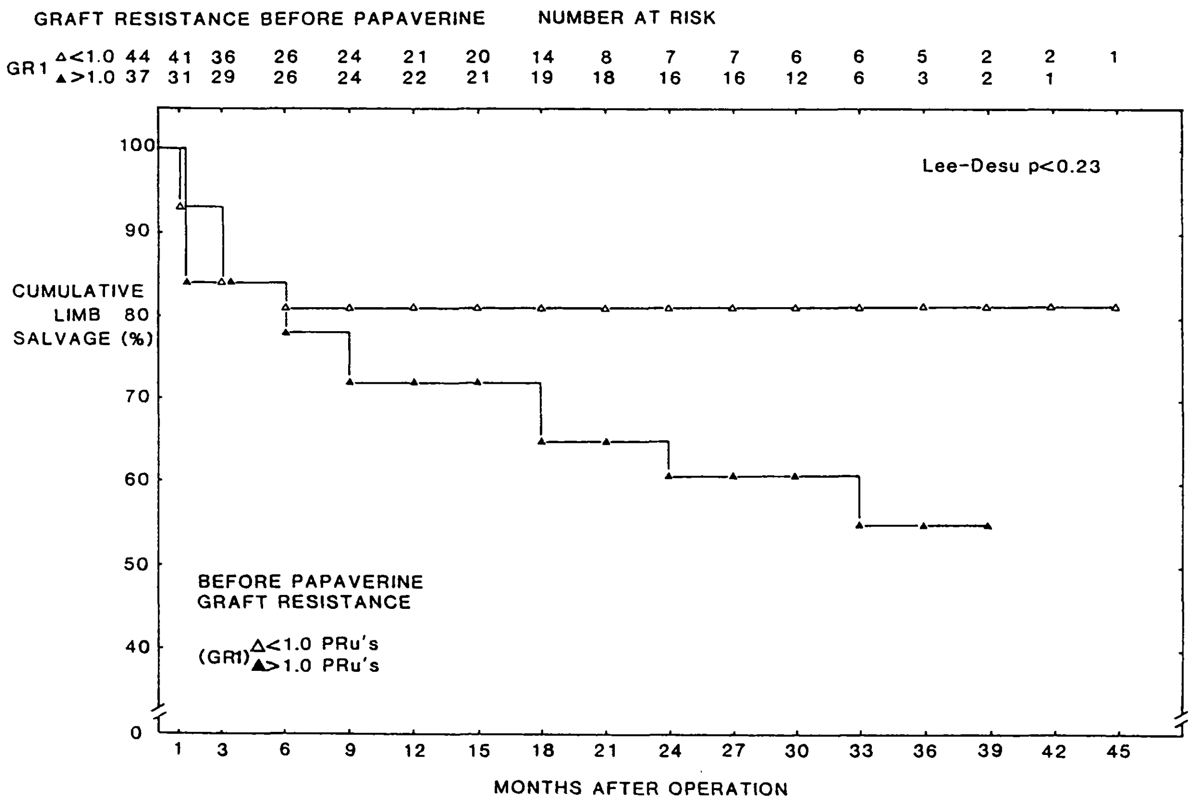


Figure 150.

Graft resistance before papaverine (GR1); cumulative limb salvage rates.

Graft resistance post papaverine (GR2).

The peripheral resistance was again measured after the administration of 15 mg of papaverine hydrochloride. There was a significant difference between the two groups; (i) PR < 1 PRU's and (ii) PR > 1 PRU's, $p < 0.0001$). The two year cumulative graft patency rates were 69% and 14% respectively (Figure 151).

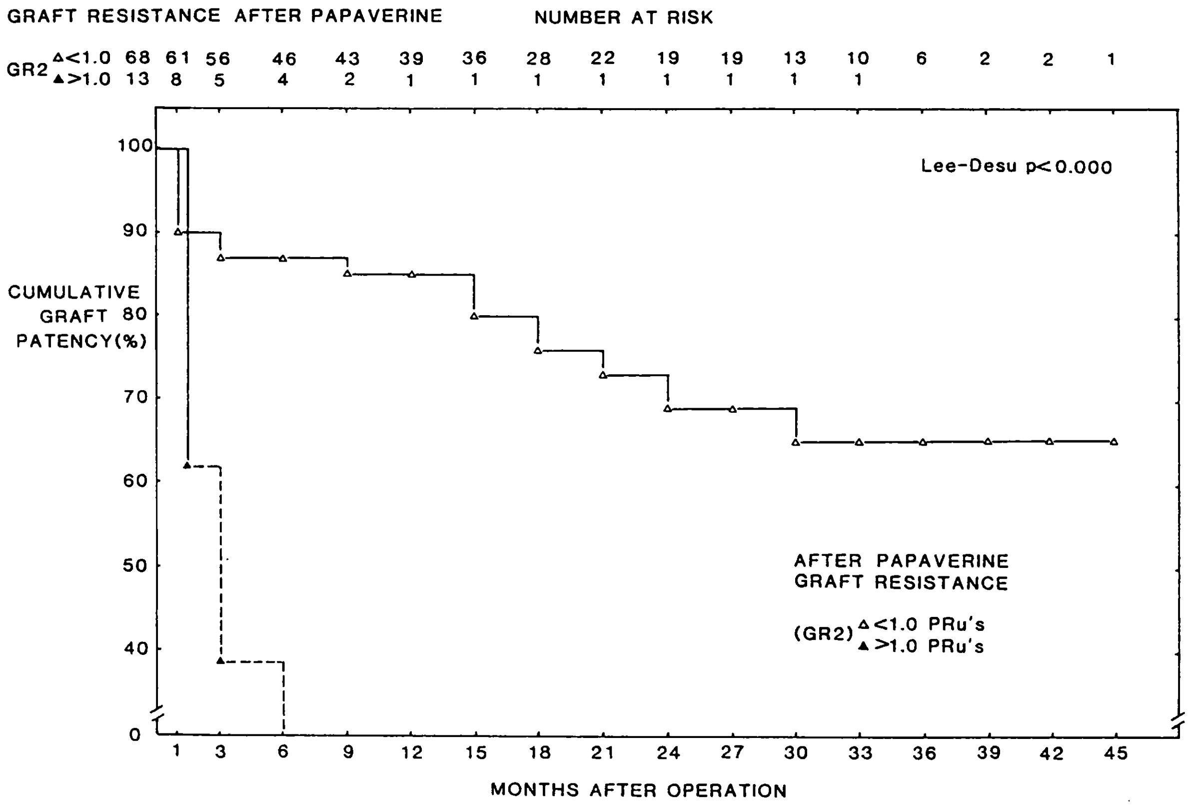


Figure 151.

Graft resistance post papaverine (GR2); cumulative graft patency rates.

<u>*Graft resistance after papaverine (GR2).*</u>

There was a significant difference between the two groups; GR2 < 1PRU versus GR2 > 1PRU, $p < 0.005$. The one year cumulative limb salvage rate was 83% and 46% respectively, (Figure 152).

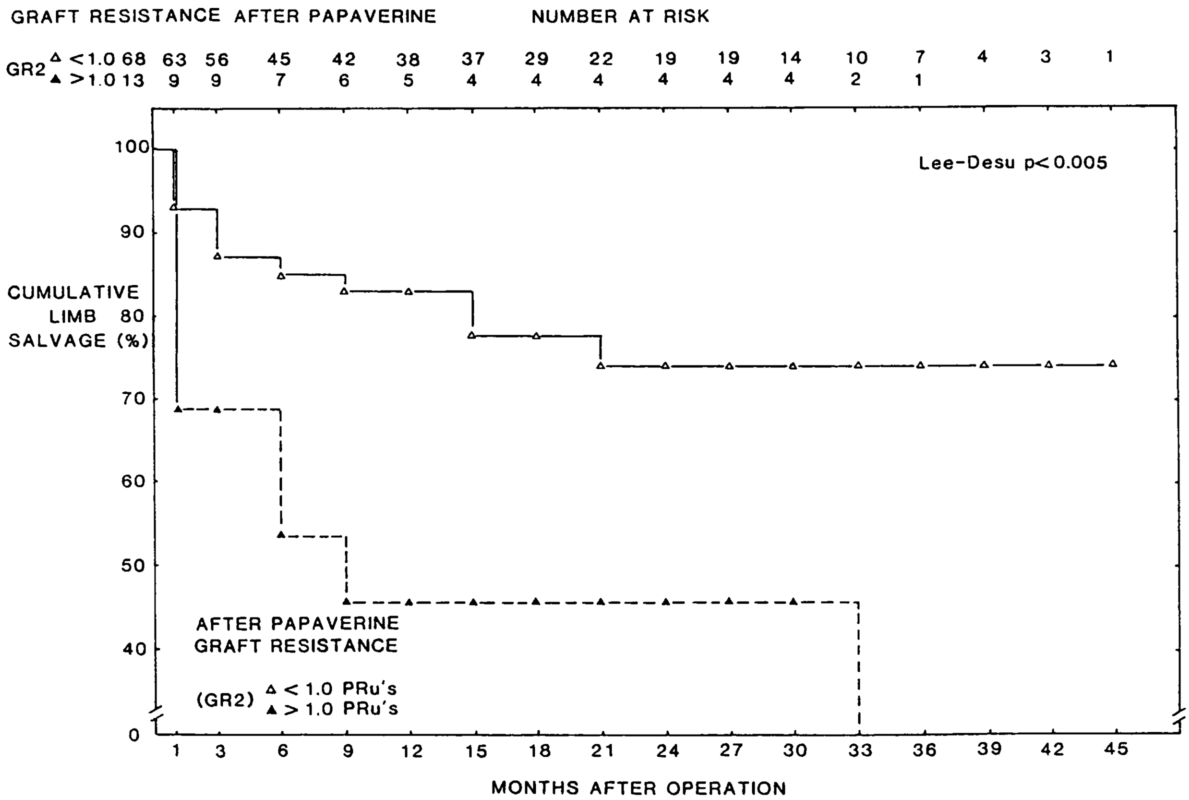


Figure 152.

Graft resistance after papaverine (GR2); cumulative limb salvage rates.

<u>*Criteria for success.*</u>

The combination of a graft resistance after papaverine (GR2) < 1PRU and a retrograde flow of < 33% of the total graft flow has been shown to be a good predictor of short term success. There was a significant difference between those grafts with a GR2 < 1PRU & RF < 33% and a GR2 > 2 and or a RF > 33%, p < 0.0009. The one year cumulative graft patency rates were 87% and 32% respectively, (Figure 153).

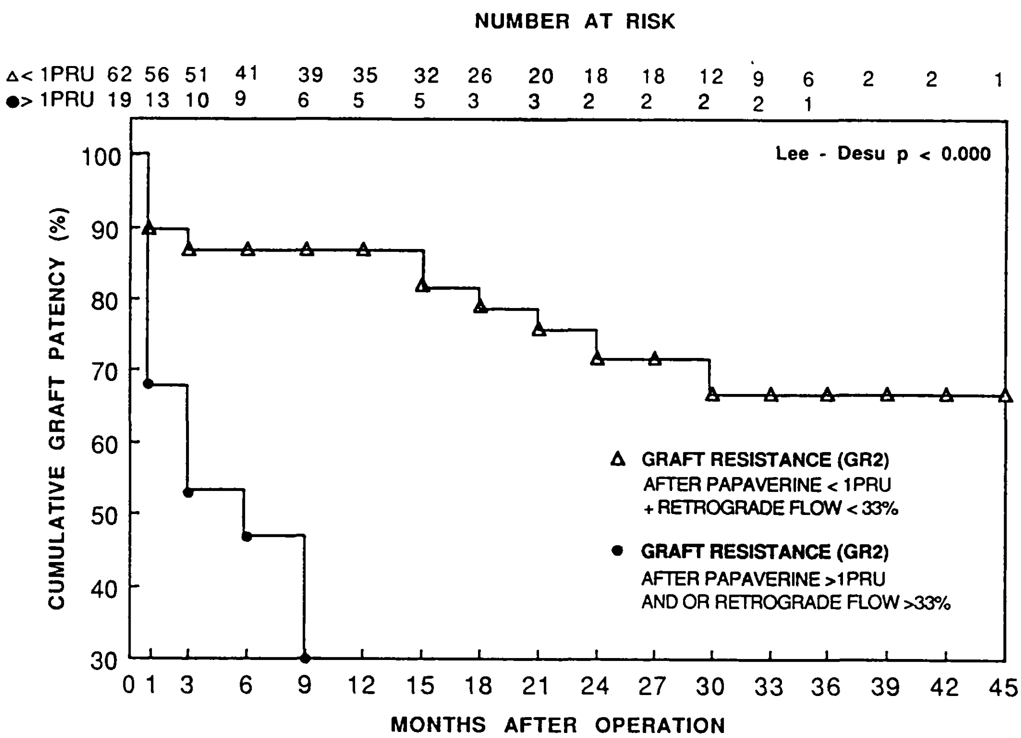


Figure 153.

Graft resistance post papaverine (GR2) and retrograde flow (RF); cumulative graft patency rates.

<u>*Criteria for success.*</u>

There was a significant difference in the limb salvage rates between the two groups (i) GR2 < 1PRU & RF <33% and (ii) GR2 > 1 PRU & or RF > 33%, $p < 0.0009$. The one year cumulative limb salvage rates for the two groups were 87% and 47% respectively, (Figure 154).

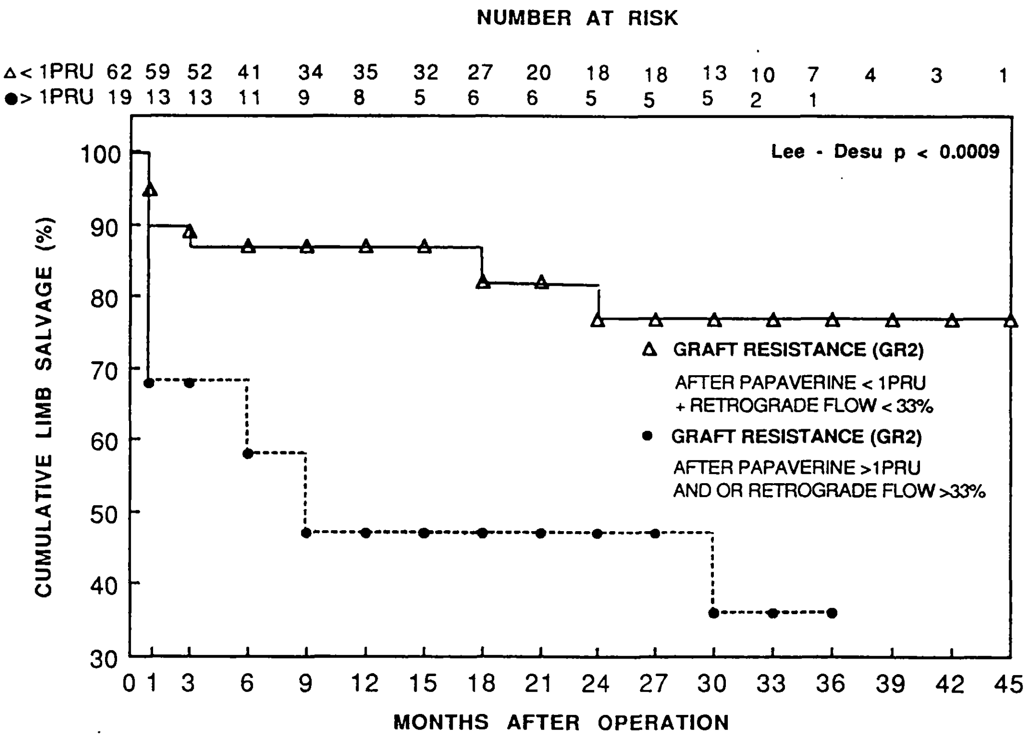


Figure 154.

Criteria for success; cumulative limb salvage rate.

Discussion

A viable limb at one year is a reasonable short term aim when treating patients with critical ischaemia. It is important therefore to assess the results of any new diagnostic test over a similar time period. The overall results of this study of 81 patients with critical ischaemia is comparable with most other reported series.
Peripheral vascular disease is a common complication of diabetes and historically, diabetics have been considered a high risk group (Reichle, Rankin, Tyson et al 1979). In this study, diabetes was not a major factor in graft occlusion or amputation in patients undergoing femoro-distal bypass for critical ischaemia. The one year graft patency and limb salvage rates are similar to that reported in the literature (Kacoyanis, Whittemore, Couch et al 1981 and Beard 1987). More recently, Shah et al (1988) in a series of 681 in situ tibial vein bypasses, reported limb salvage rates in diabetics and non-diabetics of 96% and 99% respectively.
Grafts to the popliteal artery are technically easier and are known to have a higher patency rate. This may be a function of the length of the graft, a lower peripheral resistance and the avoidance of the knee joint. The higher graft failure rate in single calf vessel grafts has been attributed to a poor outflow and a considerable technical learning curve. As a result, several authors have advocated grafting to an isolated popliteal segment rather than isolated calf vessels.
Darke et al (1989) reported no difference in graft patency or limb salvage between two groups of patients, randomised to either an isolated popliteal segment or a distal calf vessel. In this study, the cumulative graft patency and limb salvage rates for grafts to the distal popliteal and tibioperoneal trunk are similar to that reported in the literature. By contrast, the results from single calf vessel grafts were not as good. Only 54% of the patients had a viable limb at the

end of the first year. The reasons for this remain uncertain, but these longer grafts may be more prone to the development of strictures within the body of the graft or at the site of the distal anastomosis. The introduction of an interventional graft follow up programme may be able to address the problem of failure within the distal grafts and this has now been implemented.

Although conventional arteriography is able to discriminate between success and failure at one month, there are still patients suitable for reconstruction who would be turned down on the basis of the arteriogram alone. The long term results confirm that arteriography is a poor predictor of success. Although intra-operative arteriography may improve the visualisation of these more distal vessels, it may not identify those vessels in continuity with the pedal arch and remains a uniplanar examination, with all its inherent errors. The introduction of IA-DSA may improve the visualisation of the distal popliteal artery and proximal calf vessels and may prove more useful in the future. In an attempt to improve the value of arteriographic runoff, the arteriogram score was divided into three groups (0-1),(2-3) and (4-6). The graft patency rates at one year were 60%, 72% and 91% respectively. These results reiterate the message that patients with no evidence of run off on the arteriogram should not be denied the chance of a reconstruction.

In the past, PGR has been shown to correlate well with both post-reconstruction arteriography and measured peripheral resistance, but identifies more patent calf vessels than pre-operative arteriography. A PGR score of ≥ 2 has been shown to correlate well with early outcome. The long term data confirms the value of PGR in selecting patients for femoro-distal bypass. Grafts with a PGR score of < 2 had one year graft patency an limb salvage rates of 14% and 29% respectively. The high occlusion rate within the first month probably represent inappropriate selection.

During the study it became apparent that grafts with a PGR score made up of 1+1 (2) fared worse than those with a single good vessel (2+0). Although the numbers were too small for realistic analysis, there was a significant trend between the two groups, (1+1), (2+0), with one year graft patency rates of 20% and 69% respectively. If the PGR score is further subdivided into three groups (0-1), (2-3) and (4-6), there is a significant difference in both graft patency and limb salvage rates. With one year graft patency rates of 14%, 72% and 90% and limb salvage rates of 29%, 81% and 83% respectively. These results support the hypothesis that patients can be selected for femoro-distal bypass on the basis of the PGR score. In those patients with a pre-operative PGR score of <2 or a score composed of 1+1, a primary amputation should be considered.

Vein size and quality have been implicated in graft failure. Buxton et al (1980) reported that internal diameter and wall thickness significantly influence graft patency. By contrast, Corson et al (1984) in a series of 83 femoro-distal in situ vein grafts, reported no difference in the graft patency, with veins < 3.5mm versus > 3.5mm. In this study, the grafts were divided into two groups, 0-4mm and >4 mm. No difference was noted between the groups in terms of graft patency or limb salvage. Although there was a trend in favour of large veins.

There is a paucity of long term haemodynamic data in the literature. The majority of studies have evaluated the results over a short period of time. The most notable exception is the Montefoire group in New York, who have published extensively on the long term value of peripheral resistance measurements in femoro-distal grafting.

Ascer et al (1984) have reported no significant difference in terms of peripheral resistance in grafts anastomosed to the popliteal artery. By contrast, peripheral resistance measured on completion of femoro-distal grafts appears to be an important predictor of long term graft function. Grafts with a PR of between 0.6 - 1.0 PRU's had a one year graft patency rate of 48%, and none of the grafts with a PR of > 1 PRU's were patent at one year.

In a further study on the value of short vein grafts, Ascer et al (1988) reported that short vein grafts fared better in high resistance outflow tracts. They concluded that PR was an important predictor of graft failure but should not be the sole criteria used to select patients for amputation.

In this study, PR measured at the time of calf vessel exploration appeared to be a good predictor of graft patency. In those patients with a high outflow resistance there was a significant failure within the first year. On completion of the graft, the graft resistance before papaverine (GR1) was a poor predictor of graft success. This may well be due to the combined effects of arterial and venous spasm that occur during these prolonged procedures. By contrast, the graft resistance after papaverine (GR2) was a powerful discriminant of outcome, with only one graft with a GR2 > 1 PRU's, surviving beyond one year In a discriminant analysis of 47 femoro-distal grafts, Beard et al (1989), reported that the combination of a PR on completion of the graft and after papaverine of < 1 PRU's and a retrograde flow of < 33% was the best discriminant of a successful outcome. This study confirms the value of these measurements in predicting long term success.

In conclusion, the impact of PGR and PR measurements on femoro-distal grafts is significant in both pre-operative selection and per-operative management. These results support the use of PGR in the selection of patients for femoro-distal bypass. The use of per-operative haemodynamic monitoring, in particular the combination of GR2 < 1 PRU and a RF < 33% will accurately identify those patients with a successful graft at one year. In those patients with a PGR score of < 2 and a PR of between 1-2 PRU's, there may be a place for adjuvant therapy, including dAVF and prostanoid infusions. In those patients with a PGR score of ≤ 1 and or a PRU > 2 PRU, a primary amputation should be considered as the surgical treatment of choice.

Summary

In the presence of critical ischaemia, arteriography may fail to demonstrate patent calf vessels which are suitable for distal reconstruction. Preoperative assessment of calf vessels using Pulse Generated Runoff (PGR) provides functional information about the quality of the vessel and continuity with the pedal arch. In combination with the operative measurement of peripheral resistance before and after grafting, PGR enables early graft success to be predicted at one month.

Eighty one non-reversed femoro-distal vein grafts were performed for critical ischaemia, median age 71 years (range 41 -87). The cumulative secondary patency rates at 1 and 2 years were 73% and 60%, limb salvage 77% and 70% and patient survival 85% and 79% respectively. Grafts with a PGR score of > 2 had 1 and 2 year patency rates of 79% and 64% respectively, this being significantly better than grafts with a score of < 2 of 14% (Lee-Desu $p < 0.002$). The 2 year patency rates for grafts with arteriogram scores of < 2 and > 2 were 51% and 74% respectively ($p < 0.003$). Grafts with resistances of < 1, 1-2, > 2 PRU's after the administration of papaverine had patency rates of 85%, 20% and 14% at one year ($p < 0.001$).

These results support the view that selection for femoro-distal bypass should be based upon haemodynamic parameters and not on arteriographic data alone.

CHAPTER 8.

DISCUSSION AND FUTURE DEVELOPMENTS.

Over the last 50 years there has been a dramatic increase in the elderly population and the number of patients presenting with critical ischaemia. In the current social and economic climate, it has become increasingly important to assess the results of various surgical interventions in terms of the quality of life. Two recent studies have confirmed the clinical impression that successful reconstruction produces a better quality of life than amputation (Shearman, Ashley, Gwyn et al 1990 and Allen, Fergus and Chant 1990). In addition there is good economic evidence to support those advocates of femoro-distal reconstruction in patients with critical ischaemia. Allen et al (1990) calculated the cost per gained year for an amputee at £30,000 compared to £1,000 for a pain free mobile patient. This contrast with £1,000 for a hip replacement and £4,000 for a renal transplant.

In the not so recent past, patients were often denied access to investigation and the chance of distal reconstruction. Conventional transfemoral arteriography has improved the evaluation of patients for reconstruction, but is limited by the problems of contrast delivery to the distal vessels. The recent advances in digital subtraction arteriography, interventional radiology and physiological assessment of inflow disease have refined the selection of patients for vascular reconstruction but still may miss patent distal vessels suitable for reconstruction.

In this study the arteriographic runoff scores derived from conventional arteriograms correlated poorly with the measured peripheral resistance and outcome which is in accordance with others. The development of IA-DSA with its improved sensitivity has been reported to improve distal calf vessel visualization. In this study, the arteriogram scores derived from the IA-DSA correlated better with PR compared to the arteriogram scores derived from conventional arteriography. In particular there was a good correlation between the arteriogram scores derived from IA DSA and PR in patients undergoing distal popliteal reconstructions compared to single calf vessel grafts. Interestingly the more complex scoring system (C) did not confer any additional benefit in predicting the peripheral resistance at the time of surgery. Clearly some additional method was required to assess calf vessel patency.

Simple Doppler examination has been used for some time in the assessment of distal calf vessels. Although more sensitive in terms of detecting patent calf vessels than arteriography, the interpretation of these signals is often difficult, particularly in patients with severe ischaemia. Pulse Generated Runoff (PGR) is a new non-invasive method of determining calf vessel patency. This has been shown to correlate well with arteriographic runoff and peripheral resistance studies. In its present form PGR gives little information about the popliteal artery but gives excellent information about the distal calf vessels. This is reflected in the excellent correlation between the PGR score and peripheral resistance in the single calf vessel grafts. Moving the cuff to the above knee position may well improve proximal calf vessel assessment and this could form the basis of a further study.

In an attempt to improve the correlation between the PGR score and PR, multiple linear regression analysis was used to derive a series of equations which would describe the relationship between the various components of the distal runoff and the PR. In all three equations the ARCH component appeared to be a major factor in the overall determination of PR. In particular, grafts to a single calf vessel with no arch component had a predicted PR value of greater than 1, which in our experience is not compatible with long term success. This highlights the importance of a patent arch in the outcome following surgery and reinforces the importance of a full assessment of the distal calf vessels prior to a decision about reconstruction.

The presence of an adequate long saphenous vein is an important factor in the planning and outcome of femoro-distal grafting. The absence of an adequate LSV may alert the clinician to the possibility of using another source of autogenous vein, such as arm or short saphenous vein. This has important implications in the planning for surgery and the provision of equipment in hospitals. Duplex scanners can now be found in many district general hospitals, where they are often used for the assessment of carotid disease or in other disciplines. The vast majority of physicists, ultrasonographers and radiologists who are at ease with a duplex scanner will pick up the technique of long saphenous vein scanning relatively quickly. The long saphenous vein is best identified at the saphenofemoral junction, from which it can be traced into the thigh and beyond. It may, however, be quite difficult to image the vein, particularly in the large fat thigh and may be hard to trace around the knee. In this study PGR was used to apply a signal to the superficial veins, which enabled the observer to confirm that the LSV was patent. Duplex scanning provided an accurate assessment of the size, patency and course of the LSV. Pre-operative venous mapping proved to be invaluable prior to femoro-distal bypass surgery. During the period of this study the number of serious wound infections fell dramatically compared to an earlier period without duplex vein scanning highlighting the importance of not undermining the skin flaps. An attempt was made to quantify vessel wall thickness and compliance but this proved to be unreliable with the available technology. Further studies could be done to investigate compliance, wall thickness and other physical properties of the LSV which may be important factors in the outcome of non-reversed femoro-distal bypass.

The value of per-operative haemodynamic monitoring is well established in the literature. The lack of enthusiasm to use some form of haemodynamic monitoring during femoro-distal bypass can be in part attributed to the trials and tribulations experienced with EM flowmeters. An inexpensive and easy to use Doppler flowmeter previously developed in this department was used in this study. It had the facility to measure PR at the time of calf vessel exploration and to measure graft flow and resistance on completion of the graft.

In this study PR at the time of calf vessel exploration was unable to differentiate between success and failure at one month. In contrast to the previous study there were a greater number of single calf vessel reconstructions and these results clearly reflect uncertainty as to the acceptable PR levels for distal calf vessel as apposed to distal popliteal reconstructions. Despite these reservations, PR measurements were helpful in determining the level of reconstruction and confirming the pre-operative PGR findings as to the most suitable vessel for distal grafting. The addition of intra-arterial papaverine hydrochloride to the distal circulation should have improved the distinction between success and failure but these measurements proved to be inconsistent and were abandoned in the early part of this study.

Completion graft resistance (GR1) and flow (GF1) were unable to differentiate between success and failure at one month, the combination of venous and arterial spasm during these prolonged procedures may have accounted for these results. Graft resistance of < 1 PRU's after papaverine however was found to be a good discriminant between success and failure at one month. This figure is similar to that reported by Ascer, Veith, Morin et al (1984) and Parvin (1987). It is clear from this study that at the level of the distal popliteal artery a GR2 of < 1PRU is compatible with long term success. If the value is > 2, then it would seem sensible to explore a more distal vessel with a view to performing a more distal bypass graft. If the peripheral resistance remains > 2 PRU in a single calf vessel, than a primary amputation should be considered as all these patients grafts failed at six months. This approach may well avoid the problems of a failed femoro-distal bypass, a higher amputation level and increased morbidity and mortality.

The criteria for a successful graft GR2 < 1 PRU and a RF < 33% were validated in a prospective study with a sensitivity of 97% and specificity of 63%. In total 90% of the successful grafts were correctly predicted at the time of surgery. There were unfortunately a few patients with haemodynamic parameters consistent with success but who failed as a result of a technical error. Distal intimal flaps and missed valve leaflets were the two common causes where the initial peripheral resistance was normal. In a teaching environment with junior surgeons performing some of these distal anastomoses technical errors are inevitable, but with the availability of intra-operative duplex and vascular endoscopy these errors may be reduced in the future.

Peripheral resistance measurements may have an additional role to play in the evaluation of new modification to femoro-distal bypass eg dAVF or pharmacological manipulation. For example it would be inappropriate to assess the role of dAVF in patients with a graft resistance of < 1 PRU after papaverine where the probability of a successful outcome is high. A more appropriate group would be patients with a PR > 1 PRU's in a single calf vessel.

The quality of the long saphenous vein has been implicated as a potential cause of graft failure. This study confirms the histological findings of intimal hyperplasia in the long saphenous vein before implantation into the coronary circulation by Cheanvechai, Effler, Hooper et al 1975. More importantly it raises doubt over the use of the Hall valvulotome in small veins. The resultant endothelial damage and exposure of underlying collagen and smooth muscle cells is a potential source of early graft failure. The response to injury mounted by macrophages and smooth muscle cells may account for the development of graft strictures and neointimal hyperplasia. Small veins tend to do less well than larger veins and the critical size and method of valve destruction need to be further investigated. The availability of vascular endoscopes and the techniques of valve localization and valvulotomy will hopefully reduce the endothelial trauma produced by the "blind" passage of the Hall valve stripper. In addition it will enable side branches to be identified and ligated through small transverse skin incisions.

There is little data in the literature on the pre and per-operative prediction of long term outcome. This study confirms the value of both PGR and peripheral resistance in the assessment of patients for femoro-distal bypass. Grafts with a PGR score of 0,1, and 1+1 have a poor prognosis as do those with an occluded pedal arch. We would recommend that these patients are considered for primary amputation rather than an attempted femoro-distal bypass. Graft resistance after papaverine is the best per-operative predictor of outcome. In those patients with PR between 1-2 PRU, additional surgical measures eg dAVF, jump grafts and or pharmacological manipulation may have a role in prolonging graft function.

Despite these apparently good predictors of success, there is an appreciable graft attrition rate during the first year. It has become increasingly apparent that graft surveillance programmes can now identify "at risk" grafts. Controversy still remains about the best form of treatment, balloon angioplasty versus surgical revision for graft strictures, but high secondary patency rates can be achieved by such a surveillance programme.

The introduction of IA-DSA has improved the visualization of calf vessel runoff and the prediction of peripheral resistance. A non-invasive peripheral resistance value can now be derived using PGR which will accurately predict the measured peripheral resistance. These predictive factors plus operative measurement allow accurate prediction of graft function and therefore selection of patients for reconstruction or amputation. The long saphenous vein has been shown to be a potential source of graft failure.

The technique of Pulse Generated Runoff (PGR) has now been changed by placing the cuff above and below the knee. This enables the observer to determine the patency of the popliteal artery, tibioperoneal trunk and single calf vessels. Complex waveform analysis of PGR signals may improve the prediction of a successful outcome. The combination of a PVR and a PGR signal may be used to derive a non-invasive impedance prior to surgery. The recent development of colour duplex scanners open up a new field of non-invasive assessment, in particular the assessment of the long saphenous vein. An attempt will be made to improve the pre-operative assessment of the quality of the vein. This will include M-mode imaging in combination with an echo-tracking system to recorded wall movement during the PGR distension of the vein. Compliance could be examined using transit time studies using PGR.

Despite the use of per-operative haemodynamic measurements there remains a group of patients who will fail within the first 24 hours. It would seem logical to extend the monitoring period not only to the recovery room but to the ward. The use of implantable Doppler probes or surface flat Doppler probe would allow a signal to be obtained. This could be fed into the computer fitted with a transputer board. This could be programmed to recognise failing grafts and suitable alarms systems activated. The role of dAVF and prostanoids needs further evaluation in those patients with an incomplete or occluded pedal arch and in those with a peripheral resistances between 1 and 2 PRU's.

Theobold Smith once said that "research is fundamentally a state of mind involving continual reexamination of the doctrines and axioms which current thought and actions are based". It is therefore, critical of existing practices and like any other piece of research this Thesis raises many more questions than answers. This approach to patients with lower limb ischaemia will hopefully improve early graft and limb salvage rates. We must not however lose site of the primary objective in this condition which is that of improving the quality of life. This was so poignantly expressed by George Bernard Shaw in the Doctor's Dilemma. " In surgery all operations are recorded as successful if the patient can be got out of hospital or nursing home alive, though the subsequent history of the case may be such as would make an honest surgeon vow never to recommend or perform the operation again".

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