THE INVESTIGATION AND MANAGEMENT OF

FACTORS AFFECTING EARLY FEMORODISTAL

VEIN GRAFT PATENCY

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PREFACE

Dedicated to Nicky for her persistence and encouragement.

The work contained within this thesis was carried out while I was based in the Vascular Studies Unit at the Leicester Royal Infirmary, during which time I was supported by a grant from the Leicestershire District Health Authority. I was primarily responsible for all of the work described except for the following:

Construction of the peripheral resistance machine

(Dept of Medical Engineering, Leicester Royal Infirmary)

Construction of the continuous monitoring system

(Miss A Thrush and Prof D Evans)

Processing of the continuous monitoring data

(Miss A Thrush)

Technical backup in theatre was provided principally by Tim Hartshorne with assistance from Steve Bentley, Abigail Thrush and Ann Reid.

Statistical analysis was carried out with Arcus Pro-II (Arcus 1991), except for the Life Table analysis in Chapter 4 which was performed by Dr P Burton using the BMDP package on the University of Leicester mainframe.

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SYNOPSIS

This thesis investigates the principal factors responsible for early failure of femorodistal vein grafts. Chapter 1 provides an overview of severe lower limb ischaemia which is their principal indication. Chapter 2 outlines the role of surgery in the management of the severely ischaemic limb, concentrating on the development of distal bypass using autogenous vein. Chapter 3 considers the multiple causes of vein graft failure, concentrating on the early period and includes an account of currently employed methods designed to reduce the problem.

Chapter 4 is a retrospective review of the results of 130 in situ vein grafts performed at Leicester Royal Infirmary in the 8 year period prior to the commencement of this study. The primary early failure rate was 30%, with two thirds of patients undergoing amputation.

Chapter 5 outlines the methods used in a series of 42 patients undergoing distal vein bypass. Preoperative assessment included arteriography and 3 methods using Doppler ultrasound. Doppler signal augmentation by dependancy and by Pressure Generated Runoff (PGR) were compared. Intraoperative methods included on-table arteriography, prebypass resistance measurement, completion flow and resistance measurement, and completion arteriography. A new system of continuous monitoring using Doppler ultrasound was employed to study the early postoperative period.

There were 10 early failures, 9 of which resulted in amputation. None of the preoperative investigations was able to discriminate between successful and failed cases, although dependant Doppler and PGR provided additional qualitative information regarding distal runoff. Prebypass resistance was the best single investigation for predicting outcome prior to reconstruction. Measurement of graft resistance provided the best means of bypass assessment, although maximum benefit was achieved when combined with arteriography. The continuous monitoring system proved to be a reliable means of following early graft haemodynamics and was able to predict outcome in 93% of cases.

It was the best of times, it was the worst of times
it was the age of wisdom, it was the age of foolishness,
it was the epoch of belief, it was the epoch of incredulity,
it was the season of Light, it was the season of Darkness,
it was the spring of hope, it was the winter of despair,
we had everything before us, we had nothing before us,
we were all going direct to Heaven, we were all going direct the other way

from, A Tale of Two Cities
Charles Dickens

CHAPTER 1

SEVERE CHRONIC LOWER LIMB ISCHAEMIA

An overview

INTRODUCTION

Atherosclerosis is a common condition in Western society in which stenotic lesions and complete occlusions occur to varying degrees throughout the vascular tree, with resultant ischaemic effects. Peripheral vascular disease (PVD) is the clinical manifestation of atherosclerosis affecting the arterial supply to the lower limbs. The commonest presentation is mild intermittent claudication, which is generally managed by conservative measures such as exercise and cessation of smoking, with minimal disturbance to the patients' lifestyle (Housley 1988). In a proportion of cases, however, circulation to the limb is so compromised that the patient experiences ischaemic pain in the foot at rest. This may occur in isolation or in association with tissue necrosis, in the form of ischaemic ulcers or gangrene affecting the toes and forefoot (Figs 1.1, 1.2). This severity of ischaemia clearly represents a threat to viability of the limb.

In its most severe forms PVD represents a considerable challenge in terms of patient management. When reviewing the options in an individual case the potential benefits of any procedure aimed at reversing ischaemia must be carefully weighed against not only the risks that the proposed intervention may contain, but also the possible outcome achievable by conservative measures. In order to clarify the issues involved this chapter aims to provide an overview of severe chronic lower limb ischaemia.

Fig 1.1 A critically ischaemic foot in a patient with rest pain and ankle systolic pressure of 40 mmHg. There is no tissue necrosis but there is typical discolouration of the toes and paradoxical rubor of the forefoot.
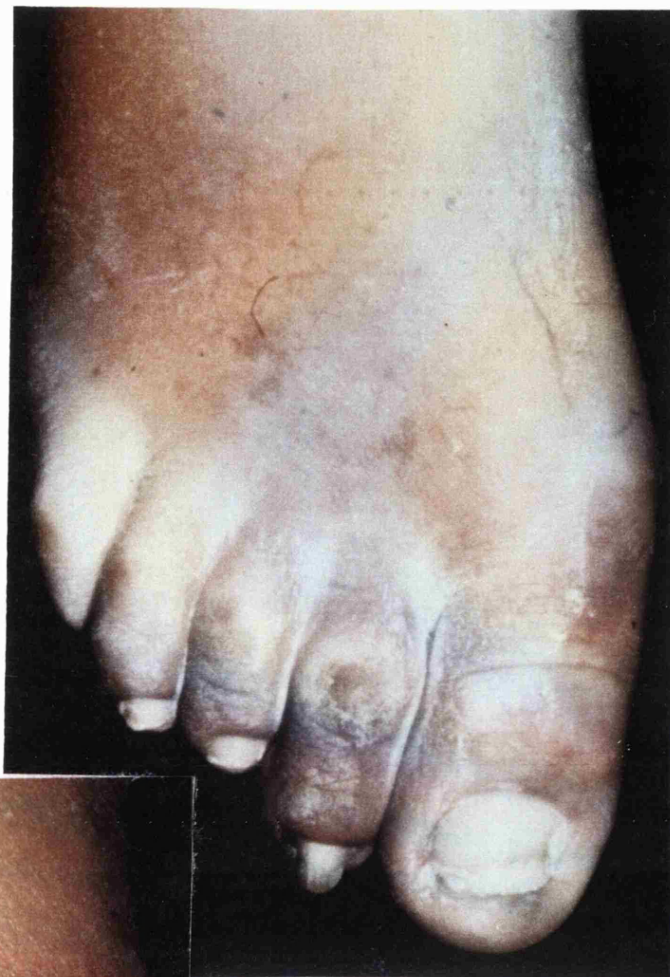
Fig 1.2 Critically ischaemic foot with established dry gangrene of toes and forefoot.

Definition

In order to assess the results of intervention for severe PVD it is important to carefully define the degree of ischaemia in the population under study before any meaningful comparisons can be made between different centres. In general it is true that the outcome is better in younger patients and those with less severe disease, and studies including a large proportion of patients in these categories will inevitably produce more favourable results. In this respect the outcome after infrainguinal vein bypass is significantly influenced by the proportion of claudicants included *eg* Darling *et al* (1967) reported a 1 yr graft patency of 87% where 68% were claudicants, compared with DeWeese and Rob (1977) who reported a 63% 1 yr patency where the proportion of claudicants was 41%.

In the past, classification has been primarily based on clinical assessment. Fontaine *et al* (1951) divided PVD into four stages (Table 1.1), and this grading has been widely adopted in Europe, whereas in Britain and the US, although patients have been grouped according to clinical findings, the Fontaine classification itself has not been used. It can be seen therefore, that the most severely affected patients fall into Fontaine groups III and IV, but in Britain and the US such patients have been grouped under the term "limb salvage", which was introduced to describe patients in whom it was considered that intervention of some form was required to save the limb.

Stage I	Asymptomatic stenosis/occlusion
Stage II	Intermittent claudication, no symptoms at rest
Stage III	Ischaemic rest pain
Stage IV	Ischaemic ulcers and/or gangrene

Table 1.1 Fontaine classification of peripheral vascular disease

Limb salvage and "critical ischaemia"

There is no doubt that in the severest cases of lower limb ischaemia use of the term limb salvage is appropriate. It is also apparent, however, that many series reporting the results of intervention for "limb salvage" include a proportion of patients in whom amputation would not have been the inevitable outcome had treatment been withheld, and that to claim the limb has been saved by intervention is an overstatement. Bloor (1960) found that less than half (47%) of 304 limbs presenting with either rest pain or tissue necrosis came to amputation, indicating the poor sensitivity of clinical assessment alone. The tendency to include patients with lesser ischaemia has led to optimistic reports concerning the outcome of treatment for end stage ischaemia, accounting for much of the discrepancy automatically encountered when attempting to compare results from different centres and also for the common finding that graft occlusion is not inevitably followed by amputation.

In order to achieve greater standardisation in reporting, a Working Party for the International Vascular Symposium (Bell *et al* 1982) was set up to establish simple clinical and objective criteria to define a new term, "critical ischaemia". The aim was to ensure that this new term was strictly limited to those patients in whom the previous concept of limb salvage remained valid. The recommendation was that critical ischaemia be defined as:

1. Pain in the foot at rest which is persistent, severe and prevents the patient from sleeping, and requires repeated analgesia for at least 4 weeks.

2. Ultrasonic, systolic ankle blood pressure lower than 40 mmHg.

3. Ultrasonic, systolic ankle blood pressure lower than 60 mmHg in the presence of superficial tissue necrosis of the foot, or digital gangrene involving the base of the phalanx.

4. Diabetics should be excluded from an ideal clinical study.

In the United States the Ad Hoc Committee on Reporting Standards agreed with this definition (Rutherford *et al* 1986). More recently the European Working Party on Critical Limb Ischaemia, in its Concensus Document (1989), raised the

ankle pressure limit to 50 mmHg with the cut-off value applying both to those with rest pain and those with tissue necrosis. In order to negate the unreliability of measurements in diabetics, it was recommended that absent pedal pulses were sufficient for definition in this group. It was also recommended that further evidence of ischaemia should be sought by one or more additional methods such as measurement of toe systolic pressures, transcutaneous oxygen pressure, or capillary microscopy.

The validity of the original definition was examined by the Joint Vascular Research Group (JVRG) in a multi-centre prospective study of all patients presenting with severe lower limb ischaemia over an 8 month period, including diabetics (Wolfe 1986). It was found that once tissue necrosis developed, the ankle pressure was of no prognostic significance. In the presence of rest pain alone, however, the ankle pressure was important. Those with ankle pressures < 40 mmHg had a similar outcome to the group with tissue necrosis, whereas those with pressures > 40 mmHg fared significantly better. It was also found that the inclusion of diabetics in the analysis did not alter the overall findings. On the basis of these findings it was concluded that the criteria for critical ischaemia could be modified to,

1. rest pain + ankle pressure < 40 mmHg, or

2. rest pain with ulceration + / - gangrene

with the recommendation that diabetics could be included, but should be analysed as a separate group.

If the definition from the European Concensus Document (ECD) is adhered to strictly then patients with severe ischaemia will be seen to fall into three groups,

1. rest pain alone + ankle pressure > 50 mmHg,

2. rest pain with tissue necrosis + ankle pressure > 50 mmHg, and

3. critical ischaemia.

In order to achieve greater uniformity between the two it is probably reasonable to raise the ankle pressure limit in the JVRG definition to 50 mmHg. By dividing Fontaine group III (rest pain) into IIIA for those with ankle pressure > 50

mmHg and IIIB with ankle pressure <50 mmHg, an internationally acceptable and easily implemented definition is then provided, with two groups,

1. rest pain + ankle pressure >50 mmHg (Fontaine IIIA), and

2. critical ischaemia (Fontaine IIIB and IV).

In practice this latter classification is the one being used most frequently since so that patients with tissue necrosis are not separated according to ankle pressure measurements. It is therefore important to state which method is being used, and provided the guidelines are followed it should be easier to compare the results of treatment in different centres. It is true to say that until recently the majority of reports in the literature concerning the management of severe PVD have included patients with the entire range of PVD, albeit the majority having either rest pain or true critical ischaemia. It is important, therefore, to analyse these studies carefully, with particular regard to the defining criteria outlined above, in order to gain a true picture of the outcome for critical ischaemia alone.

Incidence

The true incidence of critical ischaemia is not accurately known since no large epidemiological studies have used the objective criteria outlined above. It is possible, however, to arrive at an estimate by extrapolating data from population and clinical studies, with particular regard to amputation statistics. Long term follow up data from the Basle and Framingham studies indicate that only a small proportion of claudicants, 1.6% and 1.8% respectively, eventually progress to amputation (Widmer *et al* 1985, Kannel and McGee 1985). In those referred to a specialist centre this figure rises to nearer 5%, but less than half are ever referred and of those that are there is an inevitable weighting toward those with more severe disease (Dormandy and Thomas 1988).

The actual number of amputations performed, however, remains high. In 1986, in England and Wales, almost 5,000 patients were referred to limb fitting

centres following amputation for vascular insufficiency, of whom a quarter were diabetic (Coddington 1988). When one considers the large number of patients not actually referred, either because they die shortly after surgery, or because the surgeon considers that they are unlikely to mobilise, the actual number of amputations performed annually is likely to be closer to 10,000 (Dormandy and Thomas 1988). Based on this information, and taking into account the number of patients benefitting from revascularisation procedures, Norgren (1990) has estimated that the incidence of critical ischaemia in Western Europe may be as high as 500-1000 per million population per year.

Outcome

The generalised nature of atherosclerosis means that patients with PVD have an increased incidence of coronary artery and cerebrovascular disease compared with age matched controls. Even milder forms of PVD are associated with a twofold increase in 5 year mortality when compared with the general population (Peabody *et al* 1974). Prognosis after the development of critical ischaemia is even worse since up to 75% of patients will have associated ischaemic heart disease or pre-existing stroke (Dormandy and Thomas 1988), from which we can conclude that this is a high risk group whichever treatment option is selected. Wolfe (1988) reported a 1 year mortality of 18% in a series of patients presenting with rest pain or worse, although this fell to 9% in those who underwent surgical reconstruction. Of the survivors 26% overall had a major amputation in the first year, including 14% of those in whom revascularisation was performed. Longer term studies reveal a 5 year mortality of 50% in non-diabetics and 60-70% in diabetics presenting with critical limb ischaemia (Dormandy and Thomas 1988, Norgren 1990). The overwhelming majority of these deaths are a result of ischaemic heart disease and occur irrespective of the mode of management, be it reconstruction or amputation.

A direct comparison of mortality following reconstruction or amputation is

not possible since no controlled studies have been carried out, nor are they likely to be. Simplistic comparison of the literature favours the former, but this bias is almost certainly a consequence of patient selection, with higher risk patients not being considered for bypass. It is probably more realistic to conclude that successful reconstruction may prevent amputation of a critically ischaemic limb but is unlikely to improve survival and is aimed more at improving the quality of the individuals' remaining years (Jamieson 1988).

PATIENT ASSESSMENT

Before considering some form of intervention it is important that the patient is carefully assessed in order to;

    1. enable accurate classification of the severity of ischaemia, and

    2. determine the most appropriate management plan.

In the ideal situation all patients presenting with severe ischaemia should be assessed by a specialist, generally a vascular surgeon, who is familiar with the range of options available. If it is decided that conservative measures are most appropriate then this is a decision which should be made positively rather than stemming from a poor knowledge of alternative approaches (Ruckley 1990).

Patient assessment consists in the main of a combination of clinical examination, Doppler studies, and arteriography. In addition to these, a number of other methods have been developed to quantify ischaemia and each has its advocates.

Clinical assessment

A detailed history and examination is of utmost importance. It is possible by clinical assessment alone to identify the small group with either advanced ischaemia or severe concurrent disease in whom further investigations are not warranted, treatment being either conservative measures or primary amputation (Ruckley 1990). In the remainder one is able to guage to a large extent the severity of risk factors such as ischaemic heart disease and diabetes, and to determine whether these are being adequately managed.

It is important to elicit the duration of symptoms and to accurately document the extent of any ischaemic ulceration or gangrene which may be present. Examination of the peripheral pulses acts as a preliminary guide to the level of occlusion.

Clinical assessment, therefore, acts as a preliminary selection process, separating out those patients who are likely to benefit from active management.

Doppler studies

Measurement of ankle pressures with Doppler ultrasound is an established part of the assessment of patients with peripheral vascular disease (Corson *et al* 1978). In the presence of severe disease pressure measurement is mandatory in order to accurately classify patients, since it is an integral feature of the definition of critical ischaemia (Bell *et al* 1982).

Standard Doppler assessment is performed with the patient supine (Fig 1.3) but in the presence of severe disease the signals may be markedly damped and it is possible to improve the sensitivity of the test by placing the limb in a dependant position (Campbell *et al* 1986). In addition to determining individual calf vessel patency at ankle level, it is also possible to assess pedal arch status by insonating the first web space. If flow is detected in the foot, application of the compression test described by Roedersheimer *et al* (1981) can be applied (Fig 1.4), in which the calf

vessels are compressed in turn at ankle level in order to determine which is the principal contributor to runoff, and to assess whether the arch is complete (either two or three inflow vessels) or incomplete (single vessel inflow).

Fig 1.3   Measurement of ankle pressures with Doppler ultrasound.

Fig 1.4   Assessing pedal arch status using the compression test of Roedersheimer.

Angiography

Visualisation of the arterial tree in the affected limb is generally considered to be an essential part of the evaluation where treatment is indicated. Conventional arteriography using the Seldinger technique via the contralateral groin is the more usual method, enabling demonstration of vessels from aorta to foot in the affected limb. An advantage of this approach is that it allows the iliac segment to be evaluated, since steps should be taken to correct significant proximal lesions prior to considering distal reconstruction (Brewster *et al* 1982). Uniplanar arteriography may miss eccentric atheromatous plaques, however, and particularly when there is a clinical impression of a weak femoral pulse, full evaluation of the proximal segment may have to be supplemented by additional measures such as biplanar views (Sethia *et al* 1975, Baird 1988), pull-through pressure measurements (Udoff *et al* 1979) or a papaverine test (Quin *et al* 1975), all of which can unmask "hidden" lesions.
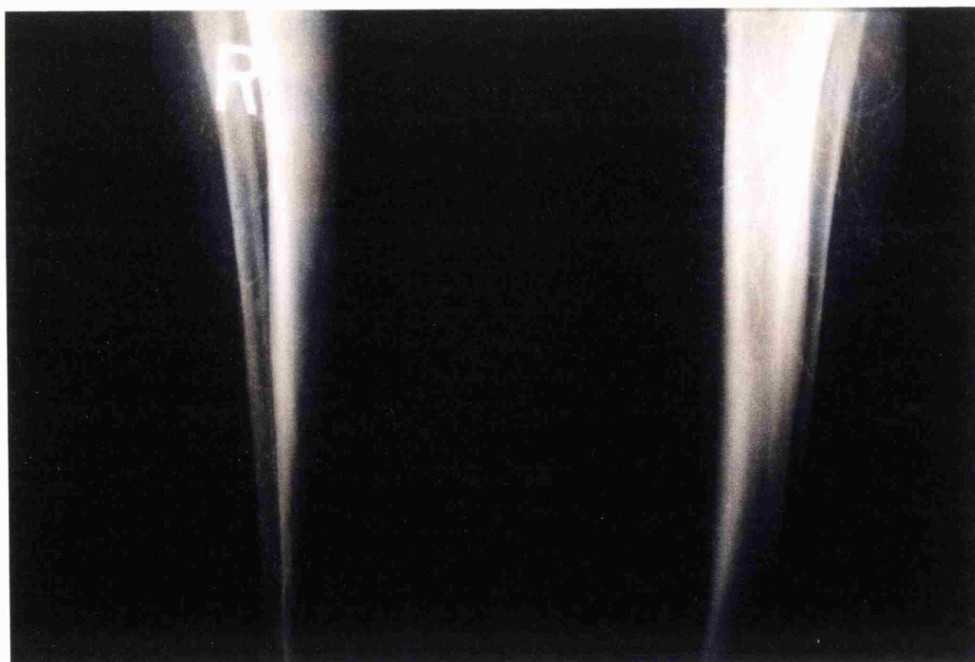
Fig 1.5   Arteriographic findings in a patient with severe bilateral ischaemia. Wispy collaterals are seen in the lower legs, but no satisfactory runoff vessels are demonstrated (see Fig 3.6).

A persistent criticism of arteriography is that in the presence of extensive disease it is often difficult to adequately visualise distal calf vessels and the pedal circulation (Campbell *et al* 1986), and selection for surgery on arteriographic findings alone would result in a large reduction in the numbers considered suitable candidates (Fig 1.5). Better visualisation of the distal circulation can be achieved with intra-arterial digital subtraction angiography (DSA), and as this modality becomes more widespread more patients will be identified as suitable for distal reconstruction (Turnipseed *et al* 1982, Kaufman *et al* 1984).

Other methods

A large amount of research has been concentrated on alternative non-invasive techniques aimed at refining the assessment of patients with critical ischaemia, with particular emphasis placed on the ability to predict outcome.

Transcutaneous measurement of oxygen tension ($TCpO_2$) has been studied widely in patients with PVD (Clyne *et al* 1982, Dowd *et al* 1983). The theoretical advantage of this method is that it is a metabolic rather than a haemodynamic test, and as such is held to be a useful means of categorising disease severity. Howd *et al* (1988) found that $TCpO_2$ measurements with the limb dependant were a more reliable indicator of outcome than simple Doppler assessment in patients with critical ischaemia. An oxygen tension of less than 35 mmHg was considered to represent an irreversible level of tissue perfusion and an indication for primary amputation. Hauser *et al* (1984) considered transcutaneous oximetry to be the non-invasive investigation of choice in diabetics, where Doppler pressure measurement can be notoriously unreliable. In practice however, $TCpO_2$ measurements are rather time consuming and laborious to perform, making this an unattractive method for regular use, although the technique has been used more widely as a means of predicting amputation levels in patients with PVD (Burgess *et al* 1982, Ratliff *et al* 1984).

Laser Doppler flowmetry is a newer technique which has been applied to the assessment of patients with PVD (Allen and Goldman 1987A). In a separate study Allen and Goldman (1987B) found this method to be comparable to $TCpO_2$ assessment in ischaemic limbs, with the considerable advantage of being much easier to perform. Similarly to $TCpO_2$ however, laser Doppler has been used more widely as a means of predicting amputation stump healing rather than forming part of the baseline assessment of the ischaemic limb (Holloway and Burgess 1983). Indeed there is some evidence to suggest that in diabetic amputees laser Doppler is superior to $TCpO_2$ (Fairs *et al* 1987, Deane *et al* 1988).

A further technique used to assess the ischaemic limb is vital capillary microscopy in which flow in nutritional skin capillaries is observed under the microscope (Fagrell 1973). Capillary flow can be graded in such a fashion that it is possible to predict the development of tissue necrosis with a high level of accuracy (Fagrell and Lundberg 1984).

In spite of favourable reports, however, none of these methods have gained widespread acceptance as part of the routine investigation of patients with severe lower limb ischaemia and their use is restricted to a few interested centres.

NON-SURICAL MANAGEMENT OF CRITICAL ISCHAEMIA

The mainstay of treatment for critical ischaemia continues to be surgical reconstruction, and since the occlusive process usually extends into the distal popliteal and proximal calf arteries, this generally takes the form of a femorodistal bypass. The results of successful surgery are very rewarding but the patient population is elderly and they represent a high risk group. As a result the role of less invasive means of revascularisation continues to be explored and their role is worth considering.

Percutaneous transluminal angioplasty (PTA)

Dilating stenoses and occlusions with a balloon catheter is now a widely established technique in the management of PVD (Gruntzig and Kumpe 1979), although in general it is used in patients whose symptoms are not severe enough to warrant surgery (Michaels 1990). While good results are reported following successful treatment of proximal lesions in patients with claudication (Gallino et al 1984), the outcome in the presence of severe ischaemia is not as good. The commonest disease pattern seen in this situation, with long occlusions of the femoral and popliteal arteries mean that it is frequently not possible to recanalise the vessel and there is a high early re-occlusion rate in initially successful cases (Mosley et al 1985). The technique does, however, have distinct advantages over surgery, in that it does not require a general anaesthetic and only entails a short hospital stay, and it is for these reasons that its role in the management of severe ischaemia is continually being developed.

In a retrospective study comparing PTA with surgery in limb threatening ischaemia, Blair et al (1989) found that although the 2 yr patency after PTA was significantly lower than that for femoropopliteal bypass, limb salvage in the two groups was comparable. The study was uncontrolled, however, and can be criticised on the grounds that PTA was only used in cases in which initial success was considered likely. Of 54 limbs treated by PTA, only 19 (35%) were salvaged by a single treatment, 7 required further PTA and 16 required subsequent surgery. Rush et al (1983) reported a 76% limb salvage rate in poor risk patients by adopting an aggressive approach, often entailing multiple and repeat dilatations. Initial angiographic success was seen in 90%, but only 63% had haemodynamic improvement as evidenced by improved ankle pressures. It is of interest to note that amputation was only required in 34% of those in whom there was no haemodynamic improvement, indicating that not all of the patients had true critical ischaemia. Cooper and Welsh (1991) studied a prospective series of 110 patients with critical ischaemia and found that only 24 had lesions suitable for angioplasty, and only 12

(11%) of these experienced clinical improvement following treatment.

In general the initial results of PTA in patients with limb threatening ischaemia are up to 20% worse than in claudicants, with limb salvage rates of around 80% after 6 months (Krings and Peters 1990), although these figures are almost certainly produced in selected patients rather than all-comers such as the group reported by Cooper and Welsh.

The indications for PTA are continually being widened, however, and improvements in catheter technology mean that PTA of distal below knee vessels is now possible (Tamura *et al* 1982, Schwarten and Cutliff 1988). In addition, the development of adjunctive technology, in the form of lasers (Sanborn *et al* 1988) and mechanical devices (Kensey *et al* 1987) may enable more patients with extensive disease to be treated by percutaneous methods. At present it would appear that PTA may be considered as a first line treatment, especially in patients considered to be a poor operative risk, but that a high failure rate should be anticipated.

Intra-arterial thrombolysis

The final event producing a critically ischaemic limb is often thrombosis of a severely stenosed femoral or popliteal artery. This process provides the rationale for the use of thrombolytic agents to clear the occluding thrombus, enabling the underlying stenosis to be treated by balloon angioplasty. Most experience has been gained using a regime of low dose streptokinase infused directly into the occlusion (Dotter *et al* 1974, Hess *et al* 1982, Walker and Giddings 1985).

In a large series, Hess *et al* (1987) achieved successful recanalisation and 2 week patency in 45% of 151 patients with rest pain and 43% of 152 patients with tissue necrosis. The majority of the occlusions were of short duration, but successful recanalisation was still achieved in 37% of lesions which had been present for longer than 6 months. This degree of experience and level of success is rather unusual, however, with most series containing small numbers of carefully selected patients.

The most common indication is in patients presenting acutely with limb threatening ischaemia, which is felt to be due to either acute thrombosis or late presentation of an embolus. Provided the limb is still viable thrombolysis is advocated, particularly if arteriography confirms the presence of thrombosis extending into the below-knee arteries, with poor run off (Earnshaw *et al* 1987). The alternative in this situation is surgical reconstruction but there has been no controlled study to compare the two, and opinion on the method of choice is likely to remain polarised.

Thrombolysis has also been used in the management of occluded vascular grafts, both prosthetic and vein (Hargrove *et al* 1982, Kakkasseril *et al* 1985) and in general is often used in a more acute setting, in patients who do not strictly satisfy the criteria for critical ischaemia, and it is not therefore possible to compare the results with those of surgery in patients with true critical ischaemia.

Despite its theoretical potential, there has been some reluctance to adopt thrombolysis as a therapeutic alternative in critical ischaemia (Hirshberg *et al* 1989), and this is likely to be due to problems with radiological facilities and drug administration since the intra-arterial infusion requires careful monitoring, and repeat x-rays are required to assess progress, making it very labour intensive (Browse *et al* 1991). In addition to these factors it should be borne in mind that in spite of the low doses now used, systemic fibrinolysis is responsible for stroke in 1% and major haemorrhage in 5%, both of which can be fatal (Berridge *et al* 1989).

As more experience with the techniques is gained thrombolysis may become more widely used in patients with critical ischaemia, allowing a realistic comparison with the results of surgery.

Lumbar sympathectomy

Prior to the development of bypass surgery and percutaneous catheter techniques, lumbar sympathectomy was widely used in the management of patients with rest pain and early trophic changes (DeBakey *et al* 1950, Szilagyi *et al* 1967)). It was originally

believed that ablating sympathetic arterial tone in the limb would improve perfusion and allow trophic areas to heal, but the available evidence suggests that this is not the case. Most studies lack control groups with which to compare outcome, the importance of which was emphasised by Rivers *et al* (1986) who reported clinical improvement in 11 out of 14 patients with severe ischaemia managed by conservative measures alone.

Sympathectomy can be achieved either chemically by paravertebral injection of phenol under x-ray control, or surgically by excising the chain via a retroperitoneal approach. Moore and Walton (1981) found no appreciable difference between the two methods in terms of effectiveness. In a randomised double-blind study, phenol sympathectomy failed to improve either ankle pressures or foot blood flow when compared with a placebo injection (Cross and Cotton 1985). There was, however, a significant improvement in rest pain, the explanation for this being that the phenol also destroys afferent pain fibres which run with the sympathetic chain.

Sympathectomy has now been displaced from its previously prominent role, and is generally reserved for elderly, poor risk patients in whom reconstruction is not thought feasible. Its role in these patients is to control rest pain, any trophic lesions being managed by conservative means (Campbell 1988).

Primary pharmacotherapy

A wide variety of agents, including oxpentifylline, inositol and naftidrofuryl have been advocated for use in patients with PVD. In general, however, their use has been studied in patients with intermittent claudication and even here their role remains controversial (Drug and Therapeutics Bulletin 1990). Very few studies have examined the efficacy of vasoactive drugs in patients with critical ischaemia, and the current concensus is that they have no place in the management of this group (Boobis and Bell 1982).

Potentially more encouraging are the results of experimental work examining

the role of prostanoids such as PGE_1, PGI_2, and the PGI_2 analogue iloprost. These agents have antiplatelet and anti-leucocyte activity which are theoretically able to reverse some of the microcirculatory processes considered to of importance in the pathophysiology of critical ischaemia (deGaetano *et al* 1990). This work has been extended to clinical studies but initially favourable reports with PGE_2 (Carlson and Eriksson 1973) have not been substantiated by more carefully controlled studies (Schuler *et al* 1984). One important fact which has emerged is the significant placebo response reported in most controlled studies, which emphasises the need for caution when reviewing uncontrolled data.

A major problem with prostanoids is the need for parenteral administration. PGE_2 needs to be infused intra-arterially since it undergoes metabolism in the lung whereas PGI_2 and iloprost are more stable and can be administered intravenously. This has led to the latter agents being used more widely in clinical studies, although evidence of efficacy is not convincing. Belch *et al* (1983) reported improvement in rest pain following continuous infusion of PGI_2 for 96 hrs, compared with placebo, whereas Cronenwett *et al* (1986) did not find any benefit following infusion for 72 hrs. Indeed Negus *et al* (1987) failed to show any difference in response following infusion with either PGI_2 or naftidrofuryl, an agent which most would dismiss as being of no value in this situation.

In summary the case for prostanoids as primary therapy in critical ischaemia remains unproven, although their role continues to be explored (deGaetano *et al* 1990).

SUMMARY

Critical lower limb ischaemia presents a considerable challenge in terms of assessment and appropriate management. The recent efforts to create an acceptable definition, culminating in the European Consensus Document, should serve to increase the uniformity of clinical reporting so that a true picture of what happens to these patients eventually emerges. There is no doubt that the majority of patients can be offered some form of intervention to relieve their symptoms, the art is to know how best to treat the individual case. The mainstay of assessment continues to be clinical examination coupled with Doppler studies and some form of arteriography, and appropriate surgical reconstruction remains the gold standard by which to compare treatment. Alternative methods continue to be developed, however, and the results of these will undoubtedly improve with time. In patients considered unfit for surgery the first line therapy is probably percutaneous angioplasty combined with some form of pharmacotherapy.

The next chapter considers the various surgical options available for the management of severe lower limb ischaemia, emphasising the role of femorodistal bypass using autologous saphenous vein.

CHAPTER 2

SURGICAL MANAGEMENT OF

SEVERE LOWER LIMB ISCHAEMIA

INTRODUCTION

It is probably the case that some form of surgical reconstruction is technically feasible in most patients presenting with critical ischaemia (Hickey *et al* 1991), and while alternative therapeutic methods continue to be developed, surgery remains the preferred option. This premise assumes, however, that all patients with critical ischaemia are assessed in a centre with the facilities and resources necessary to carry out full investigation and to perform the appropriate surgery, which is unfortunately not the case (Greenhalgh 1988). In recent years, however, the situation has improved somewhat and current awareness of the potential for successful reconstruction has resulted in an increase in the number of bypasses performed for critical ischaemia (Leather *et al* 1988).

When weighing up the options in an individual case there are two important questions to answer,

1. Is primary reconstruction indicated or not ? and, if so

2. What is the procedure of choice ?

THE PLACE OF PRIMARY RECONSTRUCTION

The first point to consider is whether or not the patient is actually fit for a surgical procedure. The incidence of concurrent disease in patients with critical ischaemia, particularly diabetes and varying degrees of heart failure, mean that careful assessment of the patients overall health and optimisation of drug therapy are of great importance in the preoperative work up. It is important to appreciate that when it occurs in association with severe concurrent illness, critical ischaemia often represents a pre-terminal event, and robust attempts at revascularisation are not indicated. In these circumstances the primary aim is simply to ensure patient comfort (Harris and Moody 1990).

The question of anaesthetic risk is particularly relevant for patients requiring proximal reconstruction via either a transabdominal or retroperitoneal approach, where postoperative recovery is likely to be prolonged and more stressful when compared with infrainguinal procedures. In cases of aorto-iliac disease where fitness is in doubt an extra-anatomical procedure such as an axillobifemoral graft should be considered (Corbett *et al* 1984). With appropriate medical management, however, the majority of cases will be fit enough to undergo a surgical procedure, the choice lying between some form of reconstruction and primary amputation.

Reconstruction v. amputation

There is undoubtedly a small group of patients in whom the degree of ischaemia at presentation is too advanced for reconstruction to be worthwhile and the correct option in these cases is to perform a primary amputation. This decision is largely based on the clinical findings of extensive tissue loss, often in the presence of ascending infection, and the important decision is to determine the most suitable level for amputation. Other groups in whom primary amputation is appropriate include those with contracture deformities of the affected limb and patients already

confined to a wheelchair *eg* as a result of a previous stroke, since revascularisation will not improve mobility (Jamieson 1988, Harris and Moody 1990). In real life, however, the picture is rarely so clear cut, with the final judgement based on a qualitative assessment of the individual circumstances.

The real debate between reconstruction and primary amputation concerns those patients in whom successful revascularisation would result in a usefully functioning limb. To vascular surgeons with an interest in critical ischaemia the preferred option is to consider reconstruction wherever possible, and indeed this policy is supported by Recommendation 25 of the European Consensus Document (1989) which states that "Primary amputation should only be undertaken if the possibility of revascularisation procedures has been excluded". In spite of this guidance there is no doubt that patients presenting with critical ischaemia outside specialist centres continue to be offered amputation as the only available course.

It is not possible to compare directly the results after reconstruction with those following amputation with regard to issues such as cost and patient benefit since this would require a randomised prospective trial of the two methods which will probably never be carried out. It is necessary, therefore, to make inferences from published studies of the two approaches, the potential advantages and disadvantages of which are summarised in Table 2.1. The argument in favour of reconstruction appears fairly convincing and primary amputation seems to have little to recommend it, except in the situations already described. In practice of course things are not so clear cut and an important point to consider is the consequence of a failed bypass since there is evidence to suggest that in 50-70% of cases this will result in amputation at a higher level than would have been originally required (Szilagyi *et al* 1979, Kazmers *et al* 1980), although this view has been challenged recently (Tsang *et al* 1991). In order to gain a better perspective it is worth reviewing more closely the available data regarding amputation.

	REVASCULARISATION	**AMPUTATION**
FOR	Restores mobility Cost effective Shorter hospital stay	Shorter operation time
AGAINST	Time consuming surgery Risk of early failure	Prolonged rehabilitation High mortality High incidence of wound breakdown Psychosocial impact Poor subsequent mobility

Table 2.1 The relative advantages and disadvantages of revascularisation and primary amputation.

Primary amputation for critical ischaemia

In England, Wales and Northern Ireland 5780 patients were referred to limb fitting centres following lower limb amputation in 1986 (DHSS 1986). Of this total 64% were a result of PVD and a further 20% were due to vascular complications of diabetes. It has been estimated that these figures may represent as little as half the true number if one takes into account patients not referred for limb fitting for various reasons *eg* those dying shortly after amputation, and patients with other disabilities which preclude rehabilitation (Dormandy and Thomas 1988). Using such methods Harris and Moody (1990) arrived at an estimate of the incidence of amputation for critical ischaemia as 10-15 per 100 000 population per annum in Britain. DHSS statistics for the last 30 years show that limb fitting referrals rose steadily between 1959 and 1980 but have levelled out over the last decade (Coddington 1988). It is clear, therefore, that despite increased interest in surgical reconstruction for critical ischaemia the number of amputations remains high.

Rehabilitation

One fact which cannot be disputed is the generally poor outlook for patients undergoing amputation for vascular disease. While some centres write encouraging reports of the good results obtainable with an enthusiastic team approach towards rehabilitation (Malone *et al* 1981, Ham 1988), the future for most is bleak. At best one can only expect around 70% of below-knee amputees (Kihn *et al* 1972, Jamieson and Ruckley 1983) and 20-30% of above-knee amputees (Kihn *et al* 1972, Gregg 1985) to ever achieve full mobility. The rest face the prospect of wheelchair rehabiliation, which often presents considerable problems to these predominantly elderly patients and their families. The better mobility achieved by below knee amputees is mostly a result of the mechanical advantage conferred by preservation of the natural joint (Waters *et al* 1976) and it would therefore seem desirable that as many amputations as possible should be performed at this level. Current opinion suggests that it should be possible to achieve a below-knee (BK) to above-knee (AK) ratio of 2.5 or greater which would be of obvious benefit to patients (Cumming *et al* 1987). In practice, however, the overall ratio is slightly less than unity (DHSS 1986), although centres with a special interest indicate that this situation could be considerably improved.

The main factor responsible for the less than ideal number of BK amputations being performed is their poor track record in terms of delayed healing and the need for revisional surgery. In general one can expect a primary healing rate of 70% with a further 15% healing by secondary intention, the worst outlook being reserved for the remaining 15% who ultimately require conversion to an AK amputation (Dormandy and Thomas 1988). The two principal techniques used for BK amputations are the long posterior flap and the skewflap. In a recent randomised study Ruckley *et al* (1991) found that healing rates whichever method was used, but cosidered that the skewflap produced a superior stump, enabling earlier limb fitting. The skewflap may also be feasible when the proximal extent of ischaemia precludes consideration of a long posterior flap (Harrison *et al* 1987).

The use of methods which provide an objective measure of skin perfusion at the proposed amputation level should improve primary healing rates, since this is a crucial factor in stump wound healing (Malone *et al* 1987). Among the most reliable and clinically applicable of these are transcutaneous oximetry (Ratliff *et al* 1984), radioisotope clearance (Moore *et al* 1981), and laser Doppler fluximetry (Fairs *et al* 1987), and it is reasonable to expect that centres with a special interest in critical ischaemia should now be employing one of these techniques to select amputation levels (Holstein and Hansen 1988).

Mortality after amputation

A further disadvantage of AK amputation is the higher hospital mortality of around 20% compared with 8% for BK amputation (Kihn *et al* 1972, Gregg 1985). Most of this difference is likely to be due to the fact that AK amputation is used more often in poor risk patients who are unlikely to mobilise and in whom primary healing is a chief requisite, and should not be attributed to the level of operation alone (Dormandy and Thomas 1988). The hospital mortality following primary reconstruction is generally lower but it is probably true that in most published series patients undergoing amputation have more severe ischaemia and represent a poorer operative risk group (Jamieson 1988).

Cost effectiveness

Increasing financial restraint within the NHS has resulted in an ever increasing emphasis on resource efficiency, one feature of which is the role of cost analysis of proposed treatment options. The important factors to consider in patients with critical ischaemia are operation time, duration of hospital stay, the need for revisional surgery, and rehabilitation requirements. Two separate studies from the US concluded that when all these factors were taken into account, the costs of

primary amputation and surgical reconstruction were equivalent (Mackey *et al* 1986, Raviola *et al* 1988). In the UK similar cost analysis work from the St Mary's group came to the conclusion that primary amputation is a more expensive option (Cheshire *et al* 1991). These studies clearly lend powerful support to those in favour of surgical reconstruction.

RECONSTRUCTION FOR CRITICAL ISCHAEMIA

Where reconstruction is the preferred option the approach in individual cases is governed by the level of obstruction which may be proximal, distal, or multisegmental. The proportion falling into each of these categories varies between centres but a good overall view was provided by a large multicentre study carried out by the Joint Vascular Research Group (Wolfe 1986). A total of 428 ischaemic limbs with either rest pain or tissue loss were entered into the study and of these 259 (61%) were deemed suitable for primary reconstruction and 73 (19%) underwent primary amputation. Of the revascularisation procedures 37% were aortoiliac, 50% were infrainguinal, and in 13% both proximal and distal segments were reconstructed.

Assessing outcome

The outcome following surgery is commonly assessed nowadays by Life Table analysis, a method originally developed for follow up of patients with cancer (Peto *et al* 1977), and although this approach has some limitations when applied to vascular surgery it is generally accepted to be the best available method (Underwood *et al* 1984). Results are commonly expressed in terms of graft patency, limb salvage (converse of amputation rate), and patient survival, each represented as a stepwise "curve". Assessment is carried out at defined intervals, usually after the first and

third months and then 3 monthly thereafter, with the number entering each interval displayed on the graph since meaningful conclusions cannot be drawn when the sample size falls below a calculated level.

For the purposes of clinical reporting it is accepted that clinical criteria alone are not sufficient for determining graft patency and that some form of objective assessment is required. In addition it is also necessary to record whether or not surgery has resulted in clinical improvement, and again objective confirmation is required. The need for more standardised reporting of results has been tackled in comprehensive fashion in the US by the Society for Vascular Surgery with clear guidelines being established (Rutherford *et al* 1986). It was recommended that continued patency should be based on either direct imaging with some form of angiography or Duplex ultrasound, or maintenance of the established improvement in the Doppler ankle brachial pressure index (ABPI), which should be at least 0.1 above the preoperative ABPI. It is also important to clarify whether or not patency is primary (uninterrupted) or secondary (patency restored after occlusion, or continued after revision of some part of the graft).

Clinical improvement should be indicated by resolution of, or upward improvement in, symptoms plus an increase in the preoperative ABPI. There are two clinical situations in particular in which the need for such guidelines is apparent. First is the graft which remains patent without clinical improvement, the so called haemodynamic failure, where amputation may still be required despite a technically "successful" procedure. Second is the situation in which a graft performed for critical ischaemia occludes but the limb remains viable. This accounts for the fact that the limb salvage rate is invariably greater than the cumulative patency rate in Life Tables. This phenomenon has two conflicting explanations, the first being that the operative indication was not true critical ischaemia, and secondly that credit should be given to a graft which stays patent long enough for healing of critical lesions and development of a collateral circulation (Rutherford *et al* 1986). The truth is probably somewhere in the middle, but now that critical ischaemia has been clearly

defined incorrect classification should no longer be a problem.

PROXIMAL RECONSTRUCTION

Although aorto-iliac disease in isolation does not often result in critical ischaemia, in the study cited earlier (Wolfe 1986) half of the patients undergoing surgery for rest pain or worse required some form of proximal reconstruction, either alone or in combination with a distal procedure. This finding can be viewed as encouraging since the results of bypass in this situation are excellent. The type of procedure performed depends upon the disease pattern and fitness of the patient.

Aorto-iliac reconstruction

In the presence of bilateral disease an aortic bifurcation graft is the preferred option, with the distal anastamoses at the bifurcation of the common femoral artery. Patency rates in excess of 95% should be expected, although there is an operative mortality of up to 5% (Bell 1990). The aorta may be approached either trans- or retroperitoneally, the latter being less traumatic and providing equally good results (Johnson et al 1986). If the patient is considered to be unfit for such a major procedure the alternative is an axillo-bifemoral graft which has a significantly lower 1 year patency of around 70% (Corbett et al 1984).

Iliac reconstruction

For unilateral disease a number of options are available, the main debate being between an ipsilateral bypass or an extra-anatomic cross over graft. There is little to choose between these approaches in terms of operative mortality and long term patency (Piotrowski et al 1986, Fahal et al 1989). Cross over grafts were originally

used in poor risk patients but the excellent results have led to wider usage. The initial description was of a femoro-femoral bypass which could even be carried out under local anaesthesia, but it is more common now to use the external iliac as the donor artery, leaving the contralateral groin free for future radiological access (Baker and Barrie 1988).

Multisegment reconstruction

Critical ischaemia is frequently the result of occlusive disease occurring at two levels but it is not always necessary to reconstruct both levels. Although this area remains contentious the conventional view is that proximal disease should be corrected first, as outlined above, and the situation reviewed (Brewster *et al* 1982). More recently, however, Harris *et al* (1985) found that the 5 year patency of aortofemoral bypass in the presence of a femoropopliteal occlusion was significantly better in those undergoing simultaneous distal reconstruction. There is unfortunately no test available at present which can reliably predict whether distal reconstruction is also necessary, and it is left to clinical judgement to decide whether simultaneous procedures should be performed at the first sitting.

INFRAINGUINAL RECONSTRUCTION

The term distal refers to disease below the inguinal ligament and this category can be divided further according to whether the distal anastamosis is above (femoropopliteal) or below (femorodistal) the knee joint. It is generally acknowledged that the outcome, both short and long term, following infrainguinal bypass is inferior to that following bypass for more proximal disease and this becomes an important consideration when evaluating the judiciousness of surgical intervention.

ABOVE KNEE FEMOROPOPLITEAL BYPASS

Occlusion of the superficial femoral artery with reconstitution of the popliteal artery above the knee is an extremely common finding in patients with PVD but, as an isolated lesion, rarely results in critical ischaemia. Where such a lesion does exist in a critically ischaemic limb it is usually in association with either proximal or distal disease as part of the multisegment pattern already described. This makes it difficult to get a clear picture of the results of femoropopliteal bypass for critical ischaemia. It is commonly the case that patients with minimal distal disease are grouped together with bypasses performed for more severe ischaemia. Conversely, above knee grafts performed for severe ischaemia are often grouped together with more distal grafts. Either way, the patency figures must be carefully scrutinised in order to decide whether a given report is able to provide the relevant data.

One controversial area in which an above knee bypass may be performed is that of an isolated popliteal segment (IPS), in which there is occlusion of the superficial femoral artery with reconstitution of the popliteal artery, but no discernible runoff beyond. Acceptable graft patency and limb salvage has been reported in such cases (Corson *et al* 1982), a finding confirmed in a randomised study carried out by the JVRG in the UK, in which patients with an IPS on preoperative arteriography were randomised to either femoropopliteal or femorodistal bypass. There was no difference in 12 month patency between the two groups, and it was concluded that where possible a graft to the above knee popliteal artery was the preferred option in these cases (Darke *et al* 1989).

Graft material

For above knee grafts the main choice lies between autogenous long saphenous vein and a prosthetic graft. The first successful femoropopliteal bypass was performed by Kunlin in 1949 using reversed saphenous vein, and this was for a long time the first choice conduit, providing acceptable long term patency of around 70% at 5 years,

when performed for severe ischaemia (Szilagyi *et al* 1973, Grimley *et al* 1979, Budd *et al* 1990). In a large review of the literature Michaels (1989) concluded that autogenous vein remains the material of choice for all infrainguinal reconstruction.

In a proportion of patients, however, the vein is either of poor quality or has been previously removed (varicose vein surgery, coronary artery bypass grafting) and prosthetic materials are used. A number of different prosthetic grafts are available but the two which have been used most extensively are polytetraflouroethylene (PTFE) and human umbilical vein (HUV). Although many vascular surgeons would contend that autogenous vein is superior to prosthetic materials in terms of patency, there is now evidence to suggest that this is not necessarily the case. Yeager *et al* (1982) found that there was no significant difference between PTFE and vein, and these findings were confirmed by Veith *et al* (1986) in a randomised study. More recently a large multicentre trial in the UK found no difference in patency between autogenous vein and prosthetic materials (PTFE and HUV) (McCollum *et al* 1991). A large retrospective review of femoropopliteal bypasses performed in Leicester (Budd *et al* 1990) also came to the conclusion that there was no significant difference in patency between vein, PTFE or HUV for above knee grafts.

The durable patency provided by prosthetic materials in the above knee situation has led to some centres, including our own, pursuing a policy of preferentially using them for above knee grafts, preserving the saphenous vein for subsequent use below the knee if the first graft fails (Rosen *et al* 1986). This rationale has been challenged (Michaels 1989) but will probably become more widespread as the trend towards distal reconstruction grows. One distinct advantage offered by prosthetic grafts over autogenous vein is a reduced operating time with fewer technical complications. Both PTFE and HUV have their proponents, but the findings from the large UK femoropopliteal bypass trial, in which the two were compared in randomised fashion, indicate that neither is superior in terms of patency (McCollum *et al* 1991). The choice is therefore determined by the surgeons own preference. One potential disadvantage of HUV is its tendency to form

aneurysms after prolonged implantation (Dardik *et al* 1984A).

FEMORODISTAL BYPASS

The majority of patients with critical ischaemia requiring distal reconstruction have occlusive disease extending into the distal popliteal artery and often into the proximal tibial vessels, and therefore require a bypass with a distal anastamosis below the knee. In this situation there is little doubt that autogenous vein provides better results than prosthetic materials, especially for bypasses distal to the popliteal trifurcation (Veith *et al* 1986, Rutherford *et al* 1988, Budd *et al* 1990).

Prosthetic grafts

If there is no vein available then a prosthetic graft can be considered as an alternative to amputation. The Second European Concensus Document on Critical Ischaemia (1992) makes the recommendation that reconstruction is worth attempting if there is a 25% chance of limb salvage at 1 year, based on local experience. This qualifier is important and emphasises the importance of the individual surgeons experience with the material and technique used.

Dardik pioneered the use of HUV in the early 1980's, and reported a one year patency of 57% for tibial and peroneal grafts (Dardik *et al* 1982B), although these results have not been matched by others. Using the same material, Harris *et al* (1984) only achieved a 35% one year patency for grafts to the below knee popliteal artery.

More experience has been gained using PTFE in this situation, again with varying degrees of success. Reported one year patency rates range from 50-84% for below knee popliteal grafts, and from 31-60% for infrapopliteal grafts (Yeager *et al* 1982, Veith *et al* 1986, Raferty *et al* 1987). Eickhoff *et al* (1987) compared PTFE and HUV in a randomised study of patients undergoing below knee popliteal bypass.

Fig 2.1   Arteriogram demonstrating a Miller collar interposed between
            a PTFE graft and the below knee popliteal artery.

Patients with HUV grafts had significantly better patency after 1 and 4 years with cumulative rates of 74% and 42% compared with 53% and 22% for PTFE, although these findings have been criticised on the grounds that antithrombotic therapy was not standardised in the two groups (Franks 1991).

The importance of local experience is emphasised when the results of prosthetic distal bypass in Leicester are compared with these studies. The combined

1 year patency rates for PTFE and HUV were 46% for below knee popliteal grafts and only 16% for tibial grafts (Budd *et al* 1990). The majority of the tibial grafts were fashioned with HUV in the face of very poor runoff following Dardik's favourable reports of its use in this situation (Dardik *et al* 1980), and confirm the existence of inter-centre variation. Tyrrell *et al* (1989) reported more encouraging results with PTFE grafts to distal calf arteries, in which a vein collar (Miller *et al* 1984) was interposed between the graft and recipient artery. Fourteen out of 30 grafts remained patent after mean follow up of 14 months. In the light of these results it is clear that the decision to attempt bypass in such circumstances should only be taken after frank discussion with the patient.

Autogenous vein grafts

In spite of the admirable results achievable in some centres with prosthetic materials, autogenous saphenous vein is still acknowledged as the graft material of choice for bypasses to the below knee popliteal artery and beyond. The vein can either be used reversed or left in situ, with the valves rendered incompetent by some means. Following its introduction by Kunlin the reversed vein technique became the method of choice for infrainguinal revascularisation, with large numbers of grafts performed throughout the world. In general, however, its use was restricted to the popliteal artery, and only limited experience was gained in more distal situations (Evans and Bernard 1970). The main limitations of the technique related to vein and artery mismatch at the anastamoses, and the fact that the length of the bypass frequently necessitated use of a narrow distal vein segment, which resulted in a high degree of early graft thrombosis. These difficulties were magnified by the presentation of increasing numbers of patients in whom tibial bypass appeared to be the only means of limb revascularisation, and prompted development of an alternative; the in situ vein technique.

Development of the in situ method

The main problem with leaving the saphenous vein in its bed was devising some means of successfully rendering the valves incompetent. The original proponents of this new method were Cartier in Montreal, who first described it in 1959, and Hall in Oslo, in 1960 (Samuels 1987). Cartier devised a stripper with a special head which could be passed up the vein and as it was withdrawn a cutting edge incised the valves leaving them incompetent. The stripper, or valvulotome, was passed after the most proximal valve had been excised under direct vision and the vein anastamosed to the femoral artery. In this way the graft was distended with arterial blood down to the next competent valve allowing easier engagement of the valve leaflets by the stripper and minimising damage to the vein endothelium. Once satisfactory arterial flow was achieved from the free lower end the distal anastamosis was performed. This method, with minor variations, is the one most widely used currently (Galland *et al* 1981). One major difference with Cartier's technique, however, is that he does not routinely ligate the vein branches whereas many would consider this an important aspect (Gannon *et al* 1986, Beard *et al* 1989).

Hall originally excised the valve leaflets through separate venotomies but although this approach resulted in excellent patency, 94% at 2 years (Hall 1962) , the method was tedious and failed to gain popularity. Indeed, Hall himself finally abandoned excision in favour of a personally designed valvulotome, and reported similarly good results (Skagseth and Hall 1973).

In spite of its introduction over 30 years ago the in situ technique has only gained in popularity over the last 10-15 years. This was largely due to the technical problems inherent in rendering the valves incompetent and reports of poor early patency (Barner *et al* 1969). The operation did not disappear altogether, however, and regained popularity in the late 1970's, largely due to the work of Leather and Karmody in Albany, New York (Leather *et al* 1981). They developed a long single shafted scissor which was passed down the vein to incise the valve leaflets, since this was sufficient to produce incompetence. The technique was modified in 1979 by

introduction of a small-calibre hooked valvulotome which was used for the narrow distal vein. They have produced excellent results with this method and reported a 90% one year patency, falling to 76% after 5 years, having performed over 1000 cases in a 12 year period (Leather *et al* 1988).

In situ v. reversed vein

Since its popularisation the in situ technique has become the dominant method in centres performing distal grafts for critical ischaemia, with a number of reports attesting to the excellent patency rates achievable (Bush *et al* 1983, Corson *et al* 1984, Buchbinder *et al* 1988, Leather *et al* 1988).

The in situ technique has a number of theoretical advantages over reversed vein bypass which are used to account for the superior patency rates reported. The principal factors quoted are,

1. Better size match between the artery and vein, particularly at the distal end, resulting in technically easier anastamoses.

2. Allows the use of narrower veins.

3. Produces a conduit with a better haemodynamic profile.

4. Minimal vein handling resulting in preservation of endothelial lining.

5. Eliminates the risk of vein twisting.

The most significant of these are the first two, which mean that used in situ it is easier to perform grafts to more distal levels than with reversed vein, and that it is possible to use veins down to a minimum diameter of 2-2.5mm (Leather *et al* 1981, Corson *et al* 1984) which leads to higher utilisation rates, since reversed veins need a minimum diameter of 3.5-4 mm (Denton *et al* 1983, Leather *et al* 1988). There is, however, evidence to suggest that small veins are associated with poorer results. Moody *et al* (1992) have recently reported the long term results of a controlled trial comparing in situ and reversed vein grafts. Veins with a diameter below 4 mm were associated with significantly worse patency rates, 63% at 1 year and 36% at 5 years,

compared with 94% at 1 year and 76% at 5 years for larger veins. Small in situ grafts fared as badly as small reversed grafts. The deleterious effect of poor quality vein, of which diameter is perhaps the most significant factor, on subsequent graft patency was first emphasised by Szilagyi some 13 years earlier (Szilagyi *et al* 1979).

Aside from the practical advantages, however, the evidence available from clinical studies does not support the role of other factors. Two separate studies found that the more natural taper of in situ grafts does not in fact confer any haemodynamic advantage (Beard *et al* 1986, Gannon *et al* 1986). The in situ technique has been shown to result in greater endothelial preservation in animal studies (Cambria *et al* 1985), and also to result in increased production of prostacyclin (Bush *et al* 1984), when compared with reversed veins. In contrast, however, Sayers *et al* (1991) reported that after passage of a 2.5mm valvulotome there was total loss of endothelial cells and variable smooth muscle necrosis from distal vein segments. Another factor which has been studied is graft compliance, since it has been suggested that preservation of the vasa vasorum with the in situ technique allows the vein to maintain more of its natural elasticity, conferring some protection from arterial haemodynamics. Cambria *et al* (1985) found in situ and reversed grafts to be similarly compliant whereas Harris *et al* (1987) reported that in situ grafts had a lower compliance, although both types of graft were significantly less compliant than native arteries. Beard *et al* (1986) did not find any difference in compliance between in situ grafts whether left minimally disturbed or completely mobilised.

Thus, while there may continue to be debate as to the different effects of vein preparation between the two methods, in practice they appear to be have little bearing on graft patency. In a randomised prospective study Harris *et al* (1987) found no difference in patency between the two methods in grafts to the popliteal artery (above and below knee). This was supported by a Veterans Administration study (1988) which reported 2 year patencies of 77% and 75% for in situ and reversed vein grafts respectively, to the below knee popliteal, and although the in

situ method resulted in superior patency for infrapopliteal grafts, 76% after 2 years compared with 67%, this did not reach statistical significance. In addition Taylor *et al* (1987) have added further fuel to the debate by reporting patency rates of 90% at 1 year and 85% after 5 years, for reversed vein grafts to infrapopliteal vessels. They cite the role of improvements in preoperative and intraoperative management as more important than any innate deficiency with the technique itself.

It would seem, therefore, that when the two methods are compared directly, there is probably little to choose between them in terms of patency even at the tibial level. Nevertheless, there is a strong body of opinion favouring the in situ technique, particularly for more distal grafts, and perhaps the most important factor behind this is the beneficial effect of accumulated experience with a single method, as exemplified by the Albany group.

How distal?

One of the basic principles of revascularisation is that the distal anastamosis should be placed beyond any atheromatous disease, to a vessel in continuity with the distal runoff. This frequently entails bypass to a single vessel in the lower calf, something which has become commonplace in recent years, principally as a result of widespread adoption of the in situ technique.

Perhaps the most interesting aspect relating to these more distal grafts has been the changing fortune of the peroneal artery. Dible (1966) studied the distribution of atherosclerosis in limbs amputated as a result of PVD, and found that the peroneal artery was more likely to be disease free than either the anterior or posterior tibial arteries. In early series of tibial bypasses, however, the peroneal artery was largely ignored (Imparato *et al* 1974), and Szilagyi *et al* (1979) recommended that use of the distal peroneal artery should be abandoned. This advice was not entirely heeded, however, and Dardik *et al* (1979) reported a 1 year patency of 55% for peroneal bypasses compared with a 63% 1 year patency for tibial

grafts. Kacoyanis *et al* (1981) found that all three calf vessels fared similarly, with 1 year patencies of around 65%. In current practice the peroneal artery is recognised as eminently suitable for grafting, with Leather *et al* (1988) reporting that it was the most widely used calf vessel in their large series.

The natural progression following the success achieved with distal calf bypass, has been to examine the role of grafting to pedal vessels in appropriate cases. Experience of such cases is limited, but there are reports of successful bypass to the dorsalis pedis and plantar arteries (Andros *et al* 1988, Ascer *et al* 1988). These grafts are performed almost exclusively in diabetics, often in the presence of considerable pedal sepsis (Andros *et al* 1989).

Technical variations

The standard in situ femorodistal graft consists of the vein lying minimally disturbed in its bed with a proximal anastamosis to the common femoral artery and a distal anastamosis below the knee. There are, however, situations in which this method is not practicable. One limitation is the need for an intact long saphenous vein that is of good quality, a situation which does not exist in 25-33% of cases in whom distal bypass is being considered (Taylor *et al* 1987, Hickey *et al* 1991). For these reasons there are a number of alternative approaches which have been used successfully, with the general principle that autologous vein should be used wherever possible.

Non-reversed vein - in order to eliminate tension, particularly at the proximal anastamosis, the vein can be fully mobilised through a long incision, and although it is not reversed it is not strictly in situ either. This approach also allows all of the branches to be identified and ligated. This technique was used by Beard *et al* (1989), who reported a 77% 1 year patency in a series of 85 patients undergoing femorodistal bypass.

Short grafts - provided there is only minimal disease in the superficial femoral artery the proximal anastamosis may be sited as distally as the above knee popliteal artery, thus allowing use of the best portion of vein (Veith *et al* 1981, Taylor *et al* 1987). These grafts have been shown to achieve similar patency to full length bypasses (Veith 1981), and the concept has even been extended to the use of tibial vessels as the site of proximal anastamosis (Veith 1985). The "short graft" can be fashioned as part of a sequential graft, in which a prosthetic femoropopliteal graft is performed in order to bypass an occlusion, and the vein graft taken from just below this to a more distal site (Rosenfeld *et al* 1981).

Fig 2.2   Arteriogram of a short vein graft with the proximal anastamosis in the mid superficial femoral artery.

Multiple outflow tracts - these have been proposed as a means of maximising runoff where there is more than one patent calf vessel. Branches of the saphenous vein in the lower leg may be used to construct an anastamosis to an additional vessel as part of a bifurcated in situ graft. McCollum (1988) found that this approach was possible in 50% of patients undergoing in situ bypass.

Alternative veins - in situations where the ipsilateral saphenous vein is unavailable the poor results obtained using prosthetic materials for distal grafts have resulted in surgeons harvesting vein from alternative sites, including the contralateral limb and the arm (Campbell *et al* 1979, Shandall *et al* 1987, Taylor *et al* 1987). Vein harvested in such a manner can be used either reversed or in situ, and the results achieved support the concept of a "totally autologous vein" approach (Hickey *et al* 1991).

DISCUSSION

This chapter illustrates the large part which surgery has to play in the management of critical lower limb ischaemia. Appropriate patient selection coupled with technical competence can result in excellent limb salvage which is cost effective. As the message from specialist centres gradually filters out, increasing numbers of patients are likely to be considered for reconstruction. Patients undergoing amputation for critical ischaemia generally have severe distal disease but it is now clear that in most of these some form of distal reconstruction using autologous vein is feasible. Vein grafts are not without their problems, however, and the aim should be to maintain patency at least throughout the first year (Bell 1985), to enable healing of ischaemic lesions. The next chapter considers in detail factors responsible for femorodistal vein graft failure, and looks at the currently available methods of prevention, detection and management.

CHAPTER 3

FEMORODISTAL VEIN GRAFT FAILURE

Causes, detection and management

INTRODUCTION

Femorodistal bypass has been one of the growth areas in vascular surgery over the last 10-15 years, and increasing numbers are being performed each year. The resurgence of the in situ vein technique outlined in the previous chapter is probably the major factor behind this development, with the favourable patency rates reported in the literature persuading surgeons to attempt reconstruction in situations where amputation may have been the automatic choice. There is still, however, resistance to a more widespread acceptance of this type of surgery outside centres with a special interest and there are number of reasons for this.

As with all new operations, femorodistal bypass has a learning curve during which there will be an inevitable number of failures, and good results require that the procedure is performed regularly. The operations are time consuming with even an uncomplicated bypass taking in excess of 3 hours, and this represents a considerable drain on resources. More importantly, however, even in experienced hands graft failure continues to be a problem, and although patency rates in excess of 90% are possible (Leather *et al* 1988, Hickey *et al* 1991), the more usual experience may not be so encouraging (LiCalzi *et al* 1982).

A number of different factors, both patient orientated and technically related, are known to be responsible for femorodistal bypass failure, and it is the responsibility of enthusiasts to devise the means whereby these can be reliably

identified and circumvented before this surgery is embraced by a wider audience. In the majority of cases failure equates with graft thrombosis, but in a small minority the conduit actually remains patent yet there is no clinical improvement, and obviously this also represents a clinical failure. In cases of thrombosis the penultimate event is a reduction in graft blood flow below a critical level, or thrombotic threshold (Sauvage *et al* 1979), beyond which the coagulant/ anticoagulant balance is tipped in favour of the former, and the column of blood within the graft thromboses. In the few grafts which remain patent without clinical improvement, blood flow exceeds the thrombotic threshold, but the runoff situation is such that the critically ischaemic area remains under perfused.

Vein graft failure is generally considered in three categories, depending on the time from insertion to occlusion (Whittemore *et al* 1981),

1) Early :- within 30 days,

2) Intermediate :- from 30 days to one year, and

3) Late :- beyond one year.

This chronological division provides a convenient framework within which to consider more specifically the various factors ultimately resulting in the failure of femorodistal vein grafts. Since this thesis is concerned primarily with early graft failure, however, this category will be considered in more detail.

(I)   CAUSES OF VEIN GRAFT FAILURE

EARLY FAILURE

Failure of a femorodistal vein graft in the perioperative period is especially severe since there is no time for healing of ischaemic lesions to occur, and if subsequent attempts to restore patency are unsuccessful, amputation will be required if the operative indication was critical ischaemia. Successful bypass is dependent upon

selecting those patients in whom distal bypass is appropriate and then performing a technically correct procedure. Early failure is generally attributed to an error in one or both of these categories (Whittemore *et al* 1981, Harris 1987). The proportion of grafts which fail perioperatively is variable, and it is often not clear whether primary or secondary patency is being reported. Bush *et al* (1983) reported a 100% 30 day patency but closer inspection reveals that 5 out of 30 grafts required some form of intervention in order to maintain patency, giving a primary patency of 83%. It is important that this distinction is made clear, since secondary procedures represent a considerable burden in terms of further operating time, often taking place out of normal working hours. Surgeons planning to perform distal grafts should be aware that revisional surgery in the early postoperative period will be inevitable in a proportion of patients. Licalzi *et al* (1982) reported that this proportion is of the order of 25%, and more recent series report early failure rates of between 11% and 20% (Bandyk *et al* 1987, Hickey *et al* 1991, Gannon *et al* 1986B, Beard *et al* 1989)

It is clear, therefore that early graft failure is a continuing problem. Having established that a patient is fit for distal reconstruction the factors which have been shown to have an important influence on early patency fall into the two categories already alluded to,

1. **Patient determined** - probably the most significant factor of all is the anatomical distribution of occlusive disease, with an adequate distal runoff being of paramount importance. Also necessary are a satisfactory vein, avoidance of hypercoagulability, and the maintenance of good cardiac function to prevent hypoperfusion.

2. **Technical factors** - there are a number of technical pitfalls to be avoided during femorodistal bypass, whether the vein is being used reversed or in situ, and even experienced surgeons will admit to occasional difficulty when the distal anastamosis is to a small calibre vessel at ankle level.

PATIENT DETERMINED FACTORS

Proximal disease

Significant inflow disease, usually an iliac occlusion, is generally dealt with prior to considering femorodistal bypass, as part of a staged approach (Brewster *et al* 1982). It is occasionally the case, however, that an iliac stenosis occurs in association with distal occlusive disease. In these circumstances the proximal disease is unlikely to have a major influence on graft patency, although correction by angioplasty is desirable in order to maximise inflow (Harris 1987). The proximal segment is most commonly assessed by preoperative arteriography, with the true significance of any stenosis being accurately determined by pressure measurements. These can be performed in one of two ways, either by measuring the gradient across the lesion using a pull-through technique (Udoff *et al* 1979), or by carrying out a papaverine test in which pressure in the common femoral artery is recorded before and after the injection of 20 mg of papaverine, and compared with simultaneous radial artery pressure measurement (Quin *et al* 1975). Peterkin *et al* (1990) have reported a 3 year primary patency of 76% for patients undergoing iliac angioplasty in combination with either femoropopliteal or femorodistal bypass.

Distal disease

This is one of the major causes of early graft failure, and even a technically perfect bypass will fail if the distal runoff is inadequate. Runoff is traditionally assessed by arteriography and different scoring systems have been devised in an attempt to identify those in whom the distal runoff is inadequate. In general however, the sensitivity of these methods in individual cases is poor. Continuity between the site of distal anastamosis and a patent pedal arch is generally held to be strongly predictive of early patency (Imparato *et al* 1974, O'Mara *et al* 1981), and preoperative confirmation of this is therefore desirable. In the presence of severe

disease in the femoropopliteal segment, however, arteriography often fails to display patent distal vessels (Campbell *et al* 1986).

A better idea of pedal arch status can be obtained with Doppler ultrasound (Campbell *et al* 1986, Shearman *et al* 1986), and the simple occlusion test described by Roedersheimer *et al* (1981) helps determine which vessels contribute to a patent arch. One disadvantage of standard Doppler is that it is not able to discriminate between a severely diseased vessel and one with minimal atheroma but very poor flow. A recent adjunct to Doppler assessment is Pulse Generated Runoff (PGR), which is reported to provide more information about vessel quality as well as improving the detection of patent vessels (Beard *et al* 1988).

The most accurate means of assessing runoff is probably measurement of the peripheral resistance (Parvin *et al* 1985). This is an attractive proposition as it quantifies the effect of any disease downstream of the proposed distal anastamosis, and is a theoretically more physiological means of assessing the potential of the runoff to support a graft. Several workers have explored this concept in order to define whether or not resistance values can be used to predict subsequent graft function (Stirnemann and Triler 1986, Ascer *et al* 1987, Parvin *et al* 1987).

Vein quality

Although the superior patency achievable with vein is well recognised the vein must be of good quality (Szilagyi *et al* 1979). Of major importance is the minimum diameter which can be used, and this is generally considered to be dependent upon the technique employed. Veins as narrow as 2 mm have been used successfully with the in situ technique, whereas 3.5-4 mm is generally considered to be the minimum acceptable for reversed veins (Leather *et al* 1988). The value of small veins is questionable however, since although the Albany group reported no difference in patency between grafts of 3.5 mm and above and grafts of 3 mm or less (Leather *et al* 1988), Moody *et al* (1992) found that veins narrower than 4 mm fared significantly

worse than larger veins. Also of importance are structural features such as anomalies of the long saphenous vein (Friedman 1988), varicosities and thickening. For this reason some form of preoperative assessment of the vein is desirable, so that potential problems can be anticipated.

Coagulation status

Systemic heparinisation is routine during femorodistal bypass to prevent thrombus formation, particularly distally, while vessels are controlled during construction of the anastamoses. The effect of postoperative manipulation of coagulation is unclear, however, particularly with regard to early graft failure. In a randomised study Kretschmer *et al* (1991) reported that oral anticoagulation significantly reduced the rate of failure of reversed vein femoropopliteal grafts, but the treatment was not commenced until the second postoperative week.

McDaniel *et al* (1988) found that a third of patients undergoing femorodistal bypass had increased platelet reactivity preoperatively, and that all patients had increased reactivity immediately postoperatively, returning to preoperative levels after one week. Although these data support the use of antiplatelet agents in these patients, a large randomised study found that a combination of aspirin and dipyridamole did not confer any patency advantage, when compared with placebo, in patients undergoing saphenous vein bypass (Edwards and McCollum 1991).

Poor graft perfusion

This is particularly important during the perioperative period since if graft flow falls below a critical level, or thrombotic threshold, then the graft and distal runoff will thrombose. Hypoperfusion is generally secondary to ischaemic heart disease being acutely exacerbated by the combined stress of surgery and anaesthesia (Harris 1987). The main requirement is for optimal fluid balance in the perioperative period when

the graft is at greatest risk of thrombosing. Peripheral perfusion may be improved by the use of epidural anaesthesia (Cousins and Wright 1971).

TECHNICAL FACTORS

Anastamotic errors

Probably the most technically demanding feature of femorodistal bypass is construction of the distal anastamosis to a small diameter vessel. Errors here usually result in luminal narrowing or intimal dissection, both of which produce abnormal, turbulent flow which predisposes to early thrombosis. An alternative to the standard continuous suture line used in vascular anastamoses is the use of interrupted sutures at the heel and toe in order to minimise the risk of narrowing. The use of magnifying loupes has been recommended as a means of reducing the incidence of errors (Leather *et al* 1981).

Endothelial and vein wall damage

Loss of a functional endothelial lining predisposes grafts to the risk of platelet aggregation and subsequent thrombosis, particularly in low flow states. A number of factors, such as overdistension, hypothermia and lack of vaso vasorum are thought to result in endothelial loss and damage during the preparation of reversed vein grafts (Cambria *et al* 1985). One of the proposed advantages of the in situ technique is that minimal handling of the vein minimises endothelial loss, and in fact the Albany group cite this as the principal reason for its adoption (Leather *et al* 1981). This proposition is supported by experimental evidence showing better endothelial preservation and higher prostacyclin and thromboxane A_2 production when compared with reversed vein grafts (Bush *et al* 1984). There is, however, conflicting

evidence indicating that passage of a valvulotome may cause considerable endothelial and smooth muscle damage, particularly at the distal end of narrow veins (Sayers *et al* 1991). Clinically apparent vein wall damage, as evidenced by perivenous bleeding or intramural haematoma, may also result from injudicious use of the valvulotome, and is a recognised cause of early thrombosis (Leather *et al* 1981, Gannon *et al* 1986A). It would seem reasonable to surmise that passage of the valvulotome produces subclinical endothelial damage in a greater proportion of veins than is generally accepted to be the case.

The clinical relevance of endothelial preservation is also put into doubt when one considers the proven lack of efficacy of antiplatelet agents in improving vein graft patency (Edwards and McCollum 1991), and the fact that the vein can be fully mobilised during in situ bypass, thus denuding it of a vasa vasorum, and still result in satisfactory early patency (Beard *et al* 1989).

Vein alignment

It is important to correctly align the vein prior to completion of the second anastamosis in order to avoid the problems of twisting and kinking either of which can result in disturbance of flow, predisposing to early thrombosis. With the in situ technique the vein is usually either left largely undisturbed in its bed or is fully mobilised under direct vision, thus minimising the risk of a twist occurring. Reversed veins are at greater risk, however, especially if the graft is tunnelled at any point. Vein kinking occurs if the vein is too long, and is typically seen in grafts angling in sharply just below the knee.

Persistent valve cusps

Inadequate valve disruption is a potential source of early failure with the in situ technique, since persistent cusps result in turbulent flow, and act as a nidus for

thrombus formation. Some form of assessment is therefore required to ensure that valve disruption is adequate.

Patent venous tributaries

This problem is also specific to the in situ technique and remains an area of controversy. Unligated tributaries can present a problem in around 16% of cases, leading either to arteriovenous fistulae, which communicate with the deep venous system and may reduce distal graft flow to such an extent that thrombosis occurs, or to areas of cutaneous venous hypertension which can be very painful (Cave-Bigley *et al* 1984, Gannon *et al* 1986A). They are particularly likely to occur when the vein is not fully exposed, which is the practice when minimum handling is considered to be important. Most surgeons are of the opinion that all tributaries should be identified and ligated, whereas others contend that selective ligation of large fistulae is all that is necessary (Leather *et al* 1988). In either case some form of assessment is required in order to locate persistent tributaries.

INTERMEDIATE FAILURE

The cause of failure during the intermediate period is important since around three quarters of vein graft failures occur during this interval (Wolfe and McPherson 1987A). Vein graft failure after the first month was previously attributed to neointimal hyperplasia, particularly around the distal anastamosis, or progression of atherosclerosis (Mannick 1979). More recently, however, attention has focussed on the development of intrinsic lesions within the vein itself, which were first brought to notice by Szilagyi *et al* (1973). A number of different lesions were identified, principal among which were fibrous strictures at varying sites, and were reported to

occur in 30% of reversed vein grafts. It was originally proposed that these lesions might progress sufficiently to result in graft occlusion, and this sequence of events is now generally accepted as being the principal cause of intermediate vein graft failure.

Graft stenosis

Following Szilagyi's initial report a number of centres began graft screening programmes, and these have confirmed that stenoses develop in 20 - 30% of vein grafts (Grigg *et al* 1988, Moody *et al* 1989). The majority of these lesions are detectable within 6 months of graft implantation, and have been shown to occur with equal incidence in reversed and in situ veins (Harris *et al* 1987). In most cases the stenoses are short (< 1 cm) but longer lesions do occur, and there does not appear to be a prediliction for any particular site within a graft to be affected, stenoses being evenly distributed between proximal, mid and distal segments (Harris *et al* 1988).

The rationale behind graft screening is that if stenoses are identified prior to graft occlusion then prophylactic correction should improve subsequent patency, and clinical experience supports this premise. It is also apparent, however, that not all stenoses lead to graft failure. In a prospective series Moody *et al* (1989) reported graft occlusion in 5 out of 22 stenosed grafts, compared with 5 of 58 non-stenosed grafts, indicating that 25% of stenoses threaten patency and that a stenosed graft has a threefold risk of occlusion. It is therefore necessary to adopt a selective approach to treatment. Using a screening programme and a selective treatment policy the same group reported a 12% improvement in graft patency in a prospective series of 79 grafts when compared with a previous series of 216 unscreened grafts (Moody *et al* 1990).

LATE FAILURE

The attrition rate after the first 1 - 2 years is of the order of 2 - 4% per annum in most series (Szilagyi *et al* 1979). Graft stenoses do not appear to be a significant problem after the first year and the principal factor responsible is generally acknowledged to be progression of atherosclerosis, particularly affecting the distal runoff (Whittemore *et al* 1981). Intervention should therefore be aimed at risk factors known to predispose to atherosclerosis, principal among which is smoking. The actual mechanism by which smoking accelerates PVD is poorly understood, but the strong association between continued smoking and poor outcome after vascular reconstruction is well recognised (Myers *et al* 1978, Greenhalgh *et al* 1981). Most vascular patients smoke, and although efforts to get them to stop, either before or after surgery, are largely unrewarding, up to 25% will stop if appropriately counselled (Power *et al* 1992).

Patients with disease progression often present with recurrent symptoms and a patent rather than occluded graft, and should be investigated in the standard fashion. The relatively small number of failures which occur mean that intensive screening programmes are not cost effective, and are inappropriate after the first 12 - 18 months (Taylor *et al* 1990).

(II)   PREVENTION AND DETECTION OF CAUSES OF FAILURE

Femorodistal bypass failure can be seen to be due to a variety of factors, all of which require appropriate management in order to guarantee a successful outcome. These are matched by an equal variety of methods which are available to detect the potential problems which may be encountered. The assessment of factors relating to early graft function will be considered in greater detail than those related to graft

function after the first month.

EARLY GRAFT FUNCTION

PREOPERATIVE INVESTIGATIONS

The advantage of preoperative methods is that patients identified as unlikely to do well, either on the basis of inadequate runoff or poor quality vein, could be spared the ordeal of an unsuccessful reconstruction and be offered instead the option of either conservative management or primary amputation, whichever is considered most appropriate. The difficulty with a preoperative test, however, is that there is always likely to be a degree of uncertainty over whether or not patients excluded from surgery could have undergone a successful bypass.

Arteriography

The major limitation of conventional arteriography in patients with severe proximal disease is undervisualisation of both distal calf vessels and pedal circulation (Fig 1.5) (Simms *et al* 1984, Campbell *et al* 1986). Outside centres with a special interest, however, it is still the case that patients are denied surgery on the basis of a preoperative arteriogram. Improved visualisation has been reported with the use of reactive hyperaemia and delayed films (Imparato *et al* 1974), but the major advance has been the development of intra-arterial digital subtraction angiography (IADSA), which is reported to provide a truer picture of the runoff (Kaufman *et al* 1984). The advantages of this technique will hopefully become more apparent as it becomes more widely available.

Where the distal circulation is visualised, demonstration of at least one patent calf vessel in continuity with an intact pedal arch is considered to indicate a

favourable situation (Imparato *et al* 1974, Dardik *et al* 1981). This is not an absolute requirement however, since successful reconstruction is possible in the face of a deficient pedal circulation. Dardik *et al* (1981) reported graft patency in 15 out of 32 cases in which the arch was either incomplete or occluded, and Corson *et al* (1984) reported bypass to discontinuous tibial vessels in 13 cases, all of which were patent after one month.

A further criticism relating to arteriography as a means of predicting graft function is that it is essentially a morphological investigation, providing little haemodynamic information. In an attempt to overcome this deficiency various scoring systems have been described in order to relate the appearances on the preoperative arteriogram to early graft outcome. In general, however, these have failed to gain popularity (Menzoian *et al* 1985). The Committee on Reporting Standards of the Society for Vascular Surgery and the International Society for Cardiovascular Surgery devised a thorough system based on the runoff distal to the proposed anastamosis, rather than of the limb as a whole (Rutherford *et al* 1986). Peterkin *et al* (1988) evaluated this system in a series of patients undergoing infrainguinal bypass. They found a reasonable correlation between the arteriogram score and intraoperatively measured resistance when the distal anastamosis was to the above knee popliteal or posterior tibial arteries, but not to the below knee popliteal or peroneal arteries. They were able to improve the correlation for the series as a whole by the introduction of multiple linear regression, which was used to provide weighting factors for the outflow vessels. In daily practice, however, such a system is too complex to gain widespread acceptance.

Doppler assessment

Doppler ankle pressure measurement is important in light of the defining criteria of critical ischaemia (Bell *et al* 1982), but the absolute pressure and ankle/brachial index are poor predictors of outcome following femorodistal bypass (Sumner and

Strandness 1979, Samson *et al* 1985).

In the severely ischaemic limb, however, careful Doppler examination is able to provide valuable information with regard to calf vessel patency and pedal arch status when compared with preoperative arteriography (Roedersheimer *et al* 1981). Simms *et al* (1984) studied a series of 58 limbs undergoing femorodistal bypass and reported that Doppler identified 30% more patent vessels. In a similar study Campbell *et al* (1986) reported that Doppler identified 18% more patent vessels in patients with severe ischaemia, but that 19 (17%) arteriograms were inadequate for assessment.

Roedersheimer *et al* (1981) described a method to evaluate the pedal arch in which patency of the arch is determined by insonating over the first web space on the dorsum of the foot (Fig 1.4). If the arch is deemed patent the tibial arteries at the ankle are sequentially compressed in order to determine the number of vessels in continuity and which is the dominant one. In their initial study there was agreement between the Doppler findings and arteriography (hyperaemic and/or intraoperative) in 21 out of 22 cases. Simms *et al* (1984) used this test to assess patients undergoing femorodistal bypass and found the arch to be occluded in nearly 70%. Following surgery, however, re-evaluation revealed that only 10% remained occluded, all of which were associated with early failure. There were 20 patients in whom an initially occluded arch was adjudged to be complete after reconstruction, all of which were patent at one year, and it was concluded that patency of the pedal arch was not a pre-requisite for a successful outcome. In a later series of 157 patients undergoing limb salvage surgery the arch was considered to be occluded in a smaller number, 61 (39%), suggesting an improvement in technique (Simms 1988).

The potential value of Doppler assessment was underlined by Shearman *et al* (1986), who described a non-invasive scoring system which was used to determine the feasibility of surgery in the absence of arteriography, and showed that the site of distal anastamosis could be predicted just as effectively. This has resulted in a

Fig 3.1   Insonation of the anterior communicating branch of the peroneal artery
with the foot dependant.

virtual abandonment of preoperative arteriography, with surgery being planned on
the Doppler findings, supplemented by an intraoperative arteriogram.

There are two important points to bear in mind with regard to Doppler
assessment of the critically ischaemic limb. The first relates to the peroneal artery
which is often the only calf vessel remaining relatively disease free (Dible 1966). It
is of prime importance, therefore, to assess the peroneal artery in these patients.
This entails insonating behind the lateral malleolus for the terminal portion of the

main trunk, or anterior to the lateral malleolus for the anterior communicating branch (Fig 3.1) (Campbell *et al* 1986). The second point is that severe damping may make signals difficult to detect with the limb supine. Campbell *et al* (1986) found that 20 out of 177 Doppler signals were only audible with the leg dependant, and Simms (1988) reported that in 96 patients with a patent pedal arch, 16 (17%) required the leg to be dependant in order for flow to be detected.

Pulse Generated Runoff (PGR)

This a recently developed adjunct to standard Doppler assessment in which the signals at the ankle and in the foot are accentuated by means of a below knee cuff driven by suprasystolic pulses of compressed air (Figs 3.2, 3.3). In a preliminary study Beard *et al* (1988) found that PGR detected up to 25% more patent vessels than standard arteriography, and that the PGR derived runoff score correlated better with peripheral resistance measured at operation than the arteriogram score, suggesting that it may be a more physiological test of runoff. The system was also reported to provide information regarding vessel quality, which was of benefit in selecting the best vessel for exploration.

More recently Scott *et al* (1990) used linear regression analysis to derive peripheral resistance values from the preoperatively determined PGR vessel and arch scores, and these were found to correlate well with the resistance measured at operation.
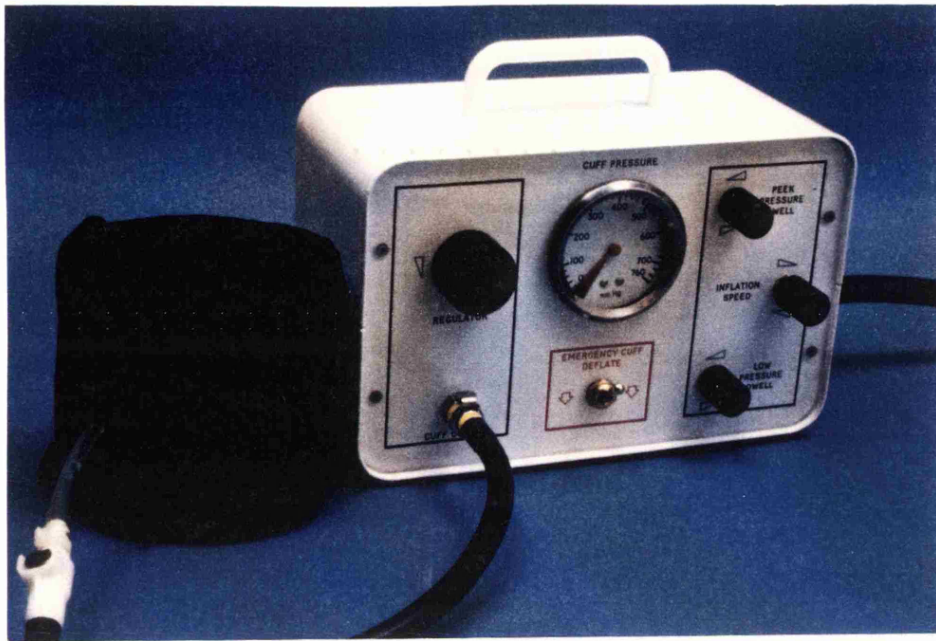
Fig 3.2   The control unit of the prototype PGR system. In clinical use a maximum
pressure of 300 mmHg was used. The unit is operated by a foot switch.
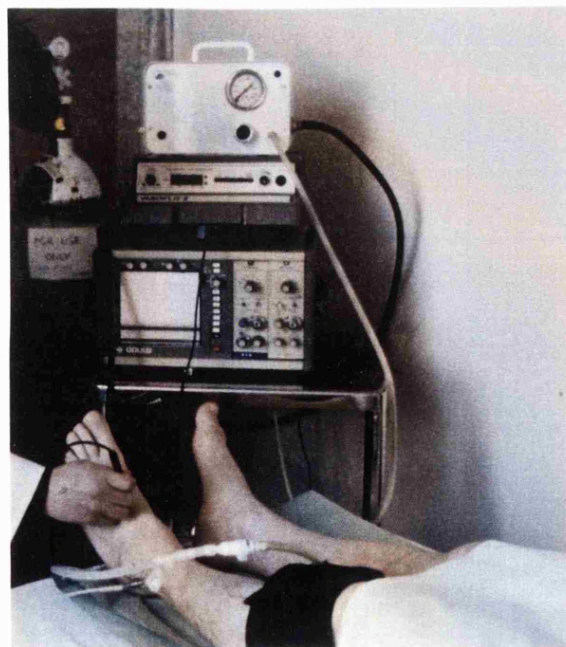
Fig 3.3   The modified PGR system in use. Compressed air from the cylinder (left)
is used to rapidly inflate the below knee cuff, thus augmenting any
Doppler signals at the ankle.

VEIN QUALITY

It is desirable, pre-operatively, to have some indication of the suitability of the long saphenous vein for the proposed surgery. This should ideally include an assessment of calibre and location. In the absence of a satisfactory vein a search can be made for veins elsewhere, since these are preferable to prosthetic materials (Harris *et al* 1986). If there is no suitable vein then the surgeon must choose between using a prosthetic graft such as PTFE, with its known inferior patency, and primary amputation.

Venography

The long saphenous vein can be demonstrated by injection of contrast proximally, anterior to the medial malleolus. This allows any anatomical variations to be assessed and gives an approximate indication of the course of the vein (Veith *et al* 1979). Although venography has its proponents in the US, and is recommended by Leather and his colleagues in Albany (1981), it is not routinely used in the UK.

Duplex assessment

Duplex scanning, which uses a combination of real time and Doppler ultrasound, has been used more recently and appears to have some advantages over venography (Leopold *et al* 1986, McShane *et al* 1988). In practical terms the procedure is quicker, non-invasive and can even be performed at the bedside (Figs 3.4, 3.5). In a study comparing venography with Duplex imaging Leopold *et al* (1986) reported that Duplex was more reliable in determining vein presence and continuity. In addition, Duplex allows the course of the vein to be marked on the skin. This simplifies operative exposure, whether the vein is being used in situ or reversed, minimising the risk of vein trauma and avoiding excessive undermining of skin flaps, particularly in obese legs, thereby reducing the risk of wound infection and flap necrosis (Beard

et al 1989). In their comparative study Leopold *et al* (1986) did not feel that either method was able to reliably predict the size of the vein once arterialised.
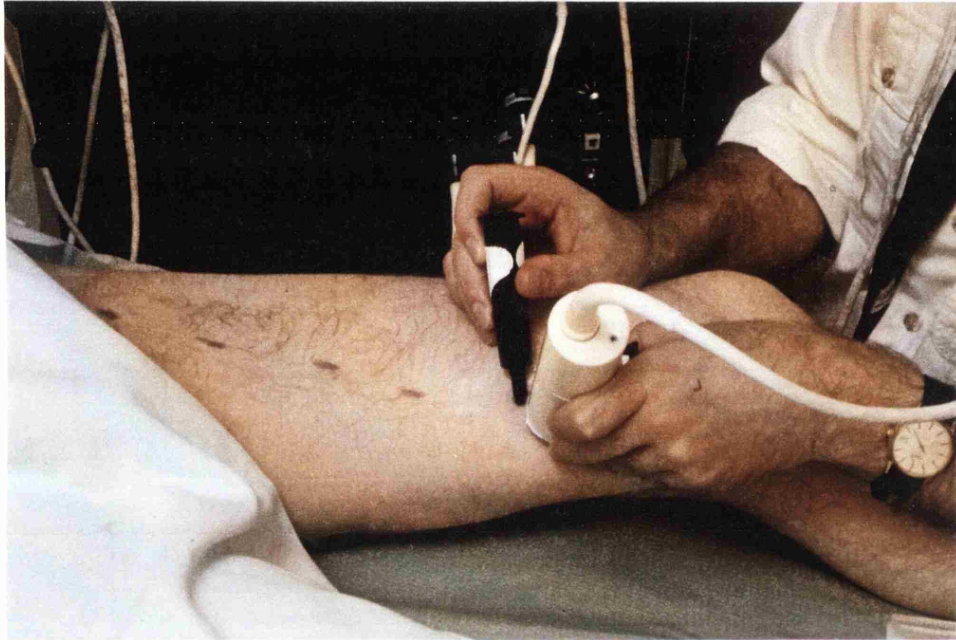
Fig 3.4   Marking the course of long saphenous vein preoperatively with Duplex.

Fig 3.5   On completion of scanning a permanent marker records the course of the vein as a continuous line.

INTRAOPERATIVE RUNOFF ASSESSMENT

The potential advantage of intraoperative tests is that by gaining direct access to the distal circulation it is possible to make a much more specific assessment of runoff in individual cases, thus providing a better indication of the feasibility of reconstruction. The disadvantage of this approach is that the final decision between reconstruction and amputation is made with the patient anaesthetised, not knowing whether they will wake up with the limb intact.

On-table arteriography

From the discussion above it is clear that conventional preoperative arteriography has a number of limitations in the severely ischaemic limb. These have led to the development of intraoperative prebypass arteriography (IPA) as a method by which to define the distal circulation more clearly (Dardik *et al* 1975).

Two slightly different techniques have been used. The first involves exposure of the common femoral artery and its bifurcation in the groin. The vessels are controlled and a catheter inserted into the common femoral artery. An x-ray film is wrapped in a sterile towel and placed under the lower leg and foot, and a single exposure is taken after rapid injection of a bolus (50 ml) of non-ionic contrast. Ricco *et al* (1983) reported the value of this approach in a series of 113 patients undergoing femorodistal bypass. In 46 (40%) cases there was either limited or non-visualisation of the runoff. IPA identified a suitable recipient artery in 42 (91%), and these patients underwent successful bypass. Primary below knee amputation was carried out in two cases and it was felt that avoidance of a distal incision was beneficial in these cases. Simms (1988) advocated use of the same technique as an adjunct to preoperative Doppler assessment.

The alternative approach involves dissection and cannulation of either the below knee popliteal artery or individual tibial vessels (Scarpato *et al* 1981, Patel *et*

al 1988). A sterile plate is again placed under the lower leg and foot and a static exposure taken after injection of a smaller bolus (10-20 ml) of contrast. Scarpato *et al* (1981), reported that IPA was beneficial in 42 out of 57 patients. In 7 cases the operative approach was altered, and in 35 a better appreciation of the runoff was achieved. Patel *et al* (1988) studied a series of 67 patients deemed unreconstructible on the preoperative arteriogram. In 56 cases IPA revealed patent tibial vessels in continuity with a patent pedal arch, enabling reconstruction to be carried out.

Using a combination of the two techniques, Flanigan *et al* (1982) reported that in 31 patients with inadequate preoperative arteriograms, IPA was beneficial in 91%, and in 66% reconstruction was to a vessel not detected preoperatively.

Fig 3.6   On-table arteriogram via the peroneal artery, demonstrating runoff into the foot not seen preoperatively (see Fig 1.5). The artery was exposed after resection of a segment of the fibula.

Peripheral resistance measurement

Demonstration of a disease free tibial vessel in direct continuity with a patent pedal arch clearly indicates a favourable situation, but there are cases in which this is not possible. The peroneal artery only communicates with the pedal arch via collaterals, and where this is the only patent vessel the ability of these to support a graft may be difficult to assess. Furthermore, Simms (1988) concluded that a patent pedal arch was not a pre-requisite for successful reconstruction, and Corson *et al* (1984) reported successful grafting in patients with discontinuous tibial vessels.

Peripheral resistance measurement has been proposed as a means of assessing the significance of disease distal to the proposed anastamosis and the extent to which any collaterals contribute to runoff. The concept of vascular resistance is derived by using an analogy to Ohms law for electrical resistance, and is given by the formula,

$$\text{Resistance} = \frac{\underline{\text{Mean arterial pressure (mmHG)}}}{\text{Mean blood flow (ml/min)}}$$

Simultaneous measurement of flow and pressure at the site of the distal anastamosis is therefore required, providing a quantitative measure of peripheral resistance in arbitrarily defined peripheral resistance units (PRU). A low peripheral resistance implies good runoff and the likelihood of a favourable outcome if technical errors are avoided.

Resistance is known to vary with changes in pressure and flow, so in order for valid comparisons to be made between patients one of the variables must be kept constant (Parvin 1987). For practical purposes a constant flow system is simpler to construct, with pressure being the variable. The method usually employed is to cannulate the proposed site of distal anastamosis and to record the intra-arterial pressure generated by infusion at a known flow rate using a syringe pump (Parvin *et al* 1985, Menzoian *et al* 1985, Cooper *et al* 1990). Parvin *et al* (1985) used four different flow rates ranging from 9.5 - 190 ml/min, and found 76 ml/min to be the best. Cooper *et al* (1989) used the same system, but only made measurements at 76 ml/min, before and after injection of papaverine, which had been used in limited fashion by Parvin and co-workers. Menzoian *et al* (1985) used the average of

resistance measurements made at 50, 75 and 100 ml/min. The constant infusion method can be criticised on the grounds that in the presence of a high resistance it is possible to generate very high pressures which can result in vessel trauma. It can be argued, however, that provided the infusion is within reasonable physiological limits the generation of an abnormally high pressure is an indication that the runoff will not support a bypass.

Other workers have used methods in which the pressure is kept constant. Stirnemann and Triller (1986) described a simple system in which pressure was maintained by a reservoir of saline situated 120 cm above the site of infusion. They measured the volume of saline infused over one minute, but did not convert it into resistance values. Beard (1987) and Scott *et al* (1990) used a system whereby the pressure was generated by handheld injection, and maintained at approximately 100 mmHg by viewing a transducer readout on a computer screen. The rate of infusion was measured with a flowmeter, the output of which was fed into the same computer, which then calculated the resistance. This system was somewhat complex and prompted development of simple handheld constant pressure infusor in which pressure was generated by compression of a spring to a pre-set level (Beard *et al* 1988B). Flow was calculated from the time taken to infuse 20 ml of blood.

Ascer *et al* (1987) described technique in which 20-50 ml of saline was infused into the graft after completion of the distal anastamosis. The intragraft pressure was measured and integrated on a purpose-built computer. The integral of pressure was divided by the volume infused to provide a value for outflow resistance. A similar technique was described by Vos *et al* (1989).

The resistance depends in part on the viscosity of the infusion fluid, the two most commonly used being saline (Stirnemann and Triller 1986, Ascer *et al* 1987, Vos *et al* 1989) and blood (Parvin *et al* 1985, Scott *et al* 1990). Saline is likely to give low values due to its lower viscosity and blood is preferable since it mimics the real life situation and eliminates the need to make any corrections for viscosity when comparing the results between different series (Bell and Parvin 1988).

Peripheral resistance values have been shown to correlate well with angiographic scores derived from both preoperative (Ascer *et al* 1984) and intraoperative (Parvin *et al* 1987) arteriograms, but of more significance is how the resistance relates to early outcome. Parvin (1987) found that at a resistance of more than 1.5 PRU all grafts failed within 3 months. Using the same system Cooper *et al* (1989) found that a post-papaverine resistance of 0.8 PRU was 100% predictive for early failure, and considered the technique to be particularly applicable for infrapopliteal grafts. Beard (1987) found a value of greater than 1.75 PRU predicted early failure with 66% sensitivity and 86% specificity. Using the constant pressure syringe a cutoff value of >2 PRU predicted early failure in 8 out of 12 cases (Beard *et al* 1988). Ascer *et al* (1984) reported that a resistance >1.2 PRU was associated with early failure, although Vos *et al* (1989) using a virtually identical technique, concluded that the overlap between successful and failed grafts meant that they were unable to produce a useful cutoff value.

Parvin (1987) reported significant differences between the resistance of patent and occluded grafts up to 6 months postoperatively, but at 1 year there was no difference. Ascer *et al* (1987B), however, reported that grafts with a high resistance had a significantly reduced 1 year patency.

The concept of peripheral resistance measurement is an attractive one, and it would appear that there is a group of patients in whom very poor runoff can be identified prior to reconstruction. Having established a value in PRU's above which graft failure is certain, or at least very probable, the surgeon should then consider alternative options if early thrombosis is to be avoided.

TECHNICAL ASSESSMENT

The identification of favourable runoff and a suitable vein significantly reduce, but do not eliminate entirely, the chances of early graft failure. Given such

circumstances, however, the outcome is dependent upon error free surgery, which can never be guaranteed and it is for this reason that some method of graft assessment is important. The best time to identify technical problems is at the time of the original operation. This not only simplifies their subsequent correction but avoids the rather fraught scenario of emergency re-exploration, which often takes place in the middle of the night.

Completion arteriography

This is obtained by cannulating either the host artery above the proximal anastamosis or the graft itself. Arterial inflow is temporarily arrested by clamps, a bolus of non-ionic contrast is injected and a single film taken of the distal anastamosis and runoff. It may be necessary to delay exposure for a short period in the case of very distal grafts (Liebman *et al* 1981).

The incidence of errors detected by this method has been reported to be as high as 25% (Dardik *et al* 1975), but is more commonly reported to be less than 10% (Liebman *et al* 1981, Scarpato *et al* 1981). The process of obtaining an arteriogram should take no longer than 10 minutes, and regular use of a simple technique improves its efficiency (Dardik *et al* 1978).

The most important aspects to consider following distal bypass are the distal anastamosis and the state of the runoff, and it is imperative that both are adequately visualised. Errors most commonly detected include stenosis of the distal anastamosis, intimal flaps (Fig 3.7) and distal thrombus (Liebman *et al* 1981). Any errors which are identified can be corrected and a further arteriogram obtained to confirm that all is well.

If the in situ technique has been used the arteriogram may reveal incompletely disrupted valve cusps or, in cases where the vein has not been completely exposed, persistent arteriovenous fistulae may be identified (Leather *et al* 1988). Problems may be missed, however, *eg* Bush *et al* (1983) reported thrombosis of 3

(10%) in situ grafts due to retained valve cusps, despite the use of arteriography. The main limitation with arteriography is that the information gained is morphological rather than haemodynamic, so that graft function is only indirectly assessed, but the technique is valuable in localising problems.
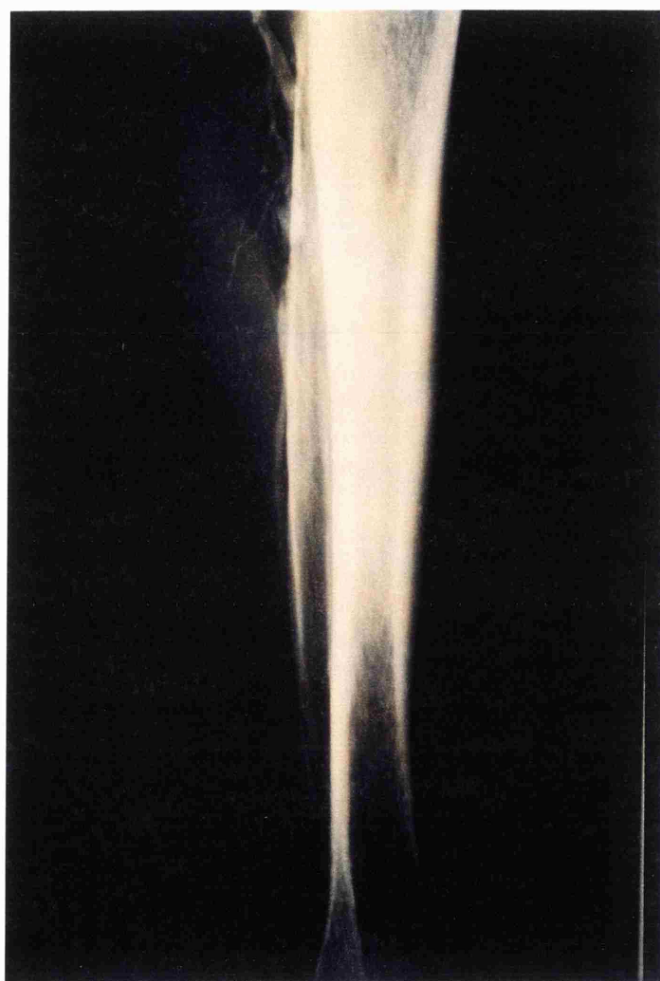
Fig 3.7   Completion arteriogram following a femoroperoneal bypass revealing an intimal dissection beyond the anastamosis which necessitated distal extension of the graft.

Graft flow

It is well recognised that adequate blood flow is necessary to maintain graft patency. Cappelen and Hall (1967) found patency to be higher in in situ grafts with flows greater than 100 ml/min, and Terry *et al* (1972) reported similar results for reversed vein grafts. Sauvage *et al* (1979) introduced the concept of a thrombotic threshold which states that graft thrombosis will occur once flow falls below a critical level. Unfortunately this threshold is dependent on a number of variables including graft diameter and systemic pressure, and while a flow in excess of 100 ml/min is strongly in favour of continued patency it is not sufficiently predictive in individual cases. Flow rates as low as 15 ml/min have been reported as sufficient to maintain patency of vein grafts. Bush *et al* (1983) reported mean blood flow of 161 ml/min, rising to 267 ml/min after administration of papaverine, in 30 in situ grafts. These values were higher than reports of reversed vein grafts and it was concluded that this was a further advantage of the in situ technique, although the reason for the finding was not clear, and there was no direct comparison made between the two methods.

Until recently the only instrument able to reliably measure graft flow was the electromagnetic flowmeter and although these are accurate if used properly they are also expensive, require frequent calibration and need an experienced technician to operate them. These factors have led most vascular surgeons to abandon routine intraoperative flow measurements. There is likely to be a renewal of interest in this area, however, with the development of a Doppler flowmeter by Beard *et al* (1988). This has been specifically designed to be "user friendly", and can be operated by a foot pedal, enabling it to be used by the surgeon with only minimal technical backup. The flowmeter also offers the advantage of providing an audible and visible waveform which provides the surgeon with additional information.

Graft pressure

Direct pressure measurements can be made fairly easily by needle puncture of artery and graft using standard equipment. Segmental pressures can be measured across the anastamoses and along the graft in order to localise any problems. Tweedie *et al* (1986) reported a pressure fall of greater than 20 mmHg to indicate a significant fault in bypasses to the popliteal artery, but did not consider the technique to be suitable if the distal anastamosis was beyond the tibioperoneal trunk. A further criticism is that no information is supplied concerning the runoff which must be assessed in some other way.

Graft resistance

This combines the advantages of the previous two methods, being the ratio of simultaneously measured graft flow and pressure, from the formula

$$\text{Graft resistance (PRU)} = \frac{\underline{\text{Mean pressure (mmHg)}}}{\text{Mean flow (ml/min)}}$$

thus providing a thorough assessment of graft haemodynamics. Albrechtsen (1976) found resistance to be of greater value than blood flow measurements alone in predicting early outcome. Previous workers had showed that following successful femoropopliteal bypass blood flow increases in the first 24 hours, compared with the value measured at the end of operation, with high flow being maintained for a variable period before declining to normal levels (Hall 1969, Cronenstrand and Ekestrom 1970). This response is thought to be due to progressive dilatation of the runoff bed in the early post-operative period with a consequent fall in peripheral resistance. Further discrimination between successful and failed grafts might, therefore, be expected if the runoff potential was also assessed. This involves measurement of graft resistance before and after administration of a vasodilator such as papaverine. Beard (1987) found that the resistance of all successful grafts fell below 1 PRU after the administration of papaverine, and that a value of >1 PRU predicted early failure with 66% sensitivity and 100% specificity.

A disadvantage of resistance measurement is that if the findings indicate a problem with the graft then further investigation, with *eg* arteriography, will be necessary in order to localise it.

Doppler analysis

Insonation of the completed graft with a sterile Doppler probe has been reported to be an effective means of identifying technical problems, particularly with regard to the in situ technique. Spencer *et al* (1984) used a continuous wave 5 MHz probe to insonate the entire graft, detecting retained valve cusps in 5 (20%) cases, and at least one arteriovenous fistula per case. Problems were evidenced by abnormal waveforms, although it was not possible to distinguish between the two. Fistulae were confirmed by the detection of flow in the soft tissue adjacent to an area of abnormal flow. Donaldson (1988) described a simpler method to detect persistent arteriovenous fistulae with a continuous wave 5 MHz probe. This involved proximal insonation with compression of the graft some 10 cm distally. Persistent flow in the presence of distal occlusion indicates the presence of a fistula between probe and point of occlusion, and this is localised by gradually moving the compressing finger closer to the probe.

Bandyk *et al* (1986) used a 20 MHz pulsed wave probe to insonate the entire graft, and was classified bypasses by means of spectral analysis of the Doppler waveforms. Successful grafts had a peak systolic velocity of greater than 40 cm/s and demonstrated a hyperaemic waveform with antegrade flow throughout diastole, indicative of a low peripheral resistance. Turbulent flow, indicative of an underlying problem, was identified at 7 (14%) distal anastamoses, and at 9 (5%) valve sites. Correction of these problems restored flow characteristics to normal. Only one patient with favourable criteria experienced early failure and this was attributed to heparin induced platelet aggregation.

Doppler pressures

These can usually be measured on graft completion using a standard cuff protected from the operative field by sterile towels, although this technique is limited to proximal calf reconstructions. It is well recognised, however, that there is often a considerable delay before the ankle-brachial pressure index reaches its maximum value (Wood *et al* 1985). It has also been shown that a low pressure index following surgery is not a reliable predictor of either technical error or graft failure. Bandyk *et al* (1988) found that of 65 patients with an abnormal ABPI on the first day following in situ bypass only 3 had technical errors requiring graft revision.

Pulse volume recorder (PVR)

Air plethysmography can be used to assess the pulse volume at the ankle following graft completion, which should be improved compared with the pre-operative recording (Baird 1979). There is often a delay, however, before the signal improves and although a good response is predictive of success, failure of the signal to improve does not necessarily imply a poor outcome. A further disadvantage is that the equipment is fairly cumbersome and although it is possible to exclude the cuff from the operative field, it is not applicable for more distal reconstructions.

Angioscopy

Vascular endoscopy is a relatively new modality which is still undergoing evaluation of its potential in relation to distal bypass. The main limiting factor has been the diameter of the angioscopes themselves as earlier models were 5 mm in diameter and not, therefore, applicable to assessing small calibre grafts. More recent experience with steerable 2.2 mm angioscopes suggests that this technique may be of some value in identifying incompletely disrupted valve cusps and in assessing the distal anastamosis (Loeprecht *et al* 1988).

Transcutaneous oxygen tension (TcPO$_2$)

The TcPO$_2$ of the dorsum of the foot is measured and compared to the TcPO$_2$ of the chest wall, the ratio being termed the regional perfusion index (RPI). This can be measured before and after surgery with a rise in the RPI indicating success. Gannon *et al* (1986C) made measurements intraoperatively on graft completion, with failure of a rise in the RPI following revascularisation being an indication for on-table arteriography. The main limitation of the technique is that the oxygen probes require up to 30 minutes to give a stable reading and, in keeping with the other indirect methods such as Doppler pressures and PVR, a negative result does not always predict graft failure.

POSTOPERATIVE METHODS

The host of pre- and intraoperative measures already outlined serve to stress the importance both of patient selection and the identification of technical errors at the original operation, in order to allow their correction. In spite of these measures, however, virtually all series report a small number of early failures, usually occurring within the first 24-48 hours.

Monitoring following surgery is generally less intensive, consisting in the main of clinical examination with the possible addition of Doppler pressure measurement. While the finding of a warm, pink foot with a palpable pulse obviously indicates a successful outcome, the picture is not always so clear cut. The sensitivity of clinical assessment alone can be improved by the use of one of the indirect methods listed above but the same criticism over the interpretation of a negative result still applies. In cases where revascularisation is clearly successful there is little debate, with any one of a number of methods being able to confirm the result. It becomes important, however, to assess graft status more thoroughly in cases where a positive outcome is not so apparent, particularly if intraoperative studies have indicated the graft to be at

risk of failure.

Arteriography

Arteriography is a good means of identifying technical problems and confirming patency, but is not routinely used in the early postoperative period. There are a number of reasons for this, foremost among which are its expense and the fact that it represents considerable disturbance to the patient. Teeuwen *et al* (1989) reported the use of intravenous digital subtraction angiography in the early post-operative period, thus eliminating the inconvenience of an intra-arterial injection, and suggested that problems were present more frequently than might have been expected. Such an approach may have a role to play in selected cases where patency is in doubt.

Duplex scanning

This has recently gained popularity as a means of screening vein grafts postoperatively for the development of fibrous stenoses. Duplex scanning can, however, also be used in the first few days after surgery in order to assess graft status (Hickey *et al* 1991). Scanning can be performed at the bedside and, although it is not feasible to assess the whole graft due to the presence of dressings, it is a fairly simple exercise to measure graft flow and also to assess the Doppler waveform. Blood flow should be at least equal to that measured intraoperatively and the waveform should display a hyperaemic pattern in successful cases. Where this is not the case further action may be taken to improve the flow pattern.

INTERMEDIATE GRAFT FUNCTION

The principle problem affecting intermediate graft function is the development of fibrous strictures and maintainence of patency during this interval is dependent upon reliable detection of these lesions so that they can be corrected before they result in graft occlusion. Following Szilagyi's report (1973) concerning the development of graft stenoses there was a surge of interest relating to graft follow-up. It soon became readily apparent that clinical follow-up alone, involving an enquiry into symptoms and examination of foot pulses and the graft where appropriate, was poorly sensitive and that adjunctive methods were required if screening was to be effective.

Doppler pressures

The predominant method used by early workers was serial ABPI measurement, with a fall being an indication that further assessment was required, usually in the form of arteriography. Berkowitz *et al* (1981) identified stenoses in 30 out of 134 femorodistal vein grafts. These patients had a significant fall in their ABPI from a mean of 0.83 down to a mean of 0.57, the mean fall being 0.25, although in three patients the fall was less than 0.1. It was concluded that an ABPI fall of greater than 0.2 was an indication for arteriography. More recently, however, measurement of the resting ABPI has been criticised on the grounds of poor sensitivity. Wolfe *et al* (1987A) found that only 4 out of 10 grafts with angiographic abnormalities had an ABPI fall of greater than 0.15. The addition of an exercise test has been advocated in order to unmask stenosed grafts with normal resting pressures but this too has been criticised. McShane *et al* (1987 A) reported that only 50% of grafts with an angiographically confirmed stenosis had a positive exercise test.

Duplex scanning

This has become a popular method for screening purposes. It has the advantage of being non-invasive and can be carried out with a minimum of inconvenience to the patient. The method usually applied is to image the graft by first localising the proximal anastamosis in the groin and then to scan along the whole of its length, while simultaneously sampling the Doppler waveform at numerous points. At the site of a stenosis the Doppler waveform changes its character, developing an increase in peak systolic velocity and a degree of spectral broadening (Fig 3.8). These changes occur within the stenosis and for a short distance (1-2 cm) distally, making it important to sample flow frequently. Grigg *et al* (1988) showed how it is possible to determine the degree of diameter reduction caused by a stenosis by calculating the ratio of the velocity immediately preceding the lesion to the velocity within it. A velocity increase of 50% was shown to reliably indicate a stenosis of
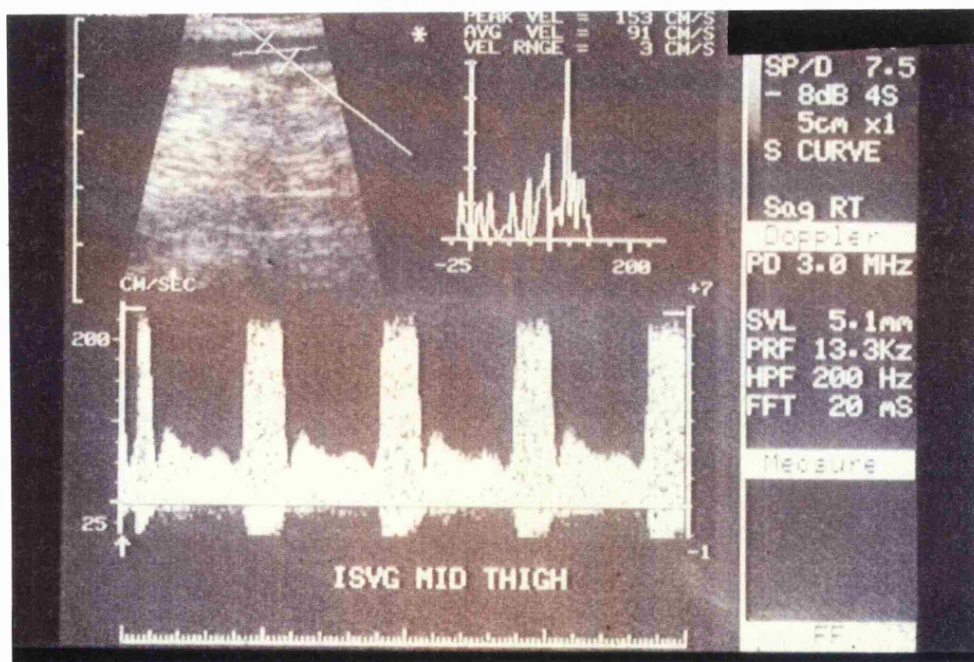
Fig 3.8   Duplex waveform from an area of stenosis in a vein graft. There is an increase in peak systolic velocity with marked spectral broadening throughout the pulse cycle. Note that the image of the graft (top) does not show any narrowing.

20%, with greater changes denoting a more severe lesion. It is therefore possible to localise and grade stenoses with Duplex. Using these criteria they successfully detected all stenoses identified angiographically in a series of 106 grafts. The disadvantages of Duplex scanning are that it is often difficult to accurately follow a graft below the knee and that the runoff is not adequately assessed (Wyatt *et al* 1991).

Bandyk *et al* (1988B) used Duplex slightly differently, preferring to analyse the Doppler waveform to a greater degree. In a series of 56 femorodistal vein grafts identified as having a stenosis, they considered the following to be important; transformation of triphasic waveform to either biphasic or monophasic, peak systolic velocity less than 45 cm/s, and a fall in the peak velocity of greater than 30 cm/s. This type of analysis, however, does not localise stenotic lesions and has not been widely adopted.

Angiography

This has acted as the gold standard for graft screening and was used by Szilagyi *et al* (1973) in their original paper. Conventional arteriography, however, is a far from ideal screening tool since it represents a considerable inconvenience to the patient and is costly, particularly if carried out frequently. It has tended to be used instead to investigate patients with a deterioration in symptoms or a significant ABPI fall. As outlined earlier, however, such an approach is not very sensitive and results in occlusions occurring in grafts with non-haemodynamically significant stenoses.

More recently the development of intravenous digital subtraction angiography (IVDSA) has meant that angiographic screening can be carried out much less invasively, on an out-patient basis (Wolfe *et al* 1987B, Moody *et al* 1989). IVDSA is a sensitive screening method, identifying stenoses in otherwise asymptomatic grafts, and also allows the runoff to be assessed. Although it is possible to guage some idea of stenosis severity by viewing diameter reduction, IVDSA provides only limited

information about the haemodynamic severity of a lesion.

Impedance analysis

This a new development in which the graft is assessed non-invasively by computer assisted analysis of pulsatile pressure and flow signals obtained with a pulse volume recorder and a Doppler flow probe respectively. The computer uses Fourier waveform analysis to derive an impedance score for the thigh and calf (Wyatt *et al* 1991). This technique was applied to a series of 56 femorodistal grafts, being compared to IADSA. An impedance score of >0.45 correctly identified 33 out of 34 grafts with a >50% stenosis in either the graft or runoff vessels. Following intervention in selected cases there was a significant fall in impedance. This is an exciting development which awaits further verification.

LATE GRAFT FUNCTION

Vein graft stenoses develop principally within the first year but can occur later, although they probably do not represent such a threat to patency at this stage. The major problem after the first 1-2 years is disease progression, usually affecting the runoff. Once a vein graft has established itself for this period of time it is more able to tolerate low flow states without thrombosing. Such a situation will present itself as a recurrence of symptoms, loss of previously palpable pulses or an obvious ABPI fall and for this reason fairly basic follow-up, in the form of clinical review and Doppler pressures, is probably all that is required to monitor late graft function. Exactly when a graft changes from "intermediate" to "late" is not entirely clear, although 2 years would seem to be the upper limit. Taylor *et al* (1990) have suggested that screening as outlined above is only justifiable for the first year. It is reasonable to follow vein grafts after this time, although on a less intensive basis

than during the intermediate phase, at 6 monthly or even yearly intervals, having instructed the patient to return earlier if problems develop.

(III)   MANAGEMENT OF FAILING AND FAILED GRAFTS

In an ideal world femorodistal bypass would only be performed in the presence of adequate runoff, with all grafts free of technical problems, resulting in guaranteed limb salvage. It is apparent from the above review, however, that this is not the case and perhaps the main reason for this is the desire among vascular surgeons to attempt reconstruction in all but the most obvious cases, in an effort to spare the patient from amputation. In accepting that failures do occur most surgeons recognise the fact that it is easier to rectify a failing graft than to retrieve a graft which has already thrombosed (Cohen *et al* 1986).

EARLY GRAFT FAILURE

POOR RUNOFF

Having identified a patient with poor runoff the surgeon is in a position to either abandon the idea of reconstruction or to take steps to try and augment what runoff there is.

Primary amputation

Peripheral resistance measurement overcomes many of the difficulties of other methods of runoff estimation providing a quantitative, haemodynamic assessment.

Although its proponents accept that complete separation between successful and failed grafts is not feasible, most centres are able to quote a resistance score above which all attempted bypasses failed. In this very high risk group primary amputation may well be the best long term option.

Sequential grafting

This is a useful option where there is more than one calf vessel patent, serving to maximise the available runoff. If the runoff is identified as poor prior to reconstruction, sequential grafting can be performed as a primary manoeuvre often by using a convenient branch of the vein, forming an inverted Y graft (McCollum 1988). If completion studies indicate that reconstruction is unsatisfactory with poor runoff being identified as the problem, then a sequential graft can be constructed (Bandyk *et al* 1986).

Distal arteriovenous fistula (dAVF)

The formation of a dAVF in relation to the distal anastamosis has been proposed by a number of workers as a means of augmenting graft flow in patients with poor runoff, thus preventing early thrombosis (Dardik *et al* 1983, Harris and Campbell 1983, Hinshaw *et al* 1983, Snyder *et al* 1985). The role of this manoeuvre, however, remains controversial, since enhanced flow through the graft may not be accompanied by improved distal perfusion.

Harris and Campbell (1983) constructed fistulae in patients undergoing tibial bypass in whom the pedal arch was incomplete on IPA. Mean graft flow increased from 84 ml/min to 236 ml/min when the shunt was open, compared with a mean flow rate of 152 ml/min in distal bypasses without a shunt in whom the pedal arch was intact. There was no difference in patency between the two groups after 12 months, and ischaemic lesions in the group with a shunt all healed if the graft remained

patent. A less favourable outcome was reported by Snyder *et al* (1985), who documented mean graft flow of 260 ml/min after construction of the AVF but reported that after 17 months follow up 17 (57%) patients had required a major amputation as a result either of graft/fistula occlusion or of non-healing in spite of a patent graft. Budd *et al* (1990) reported that the use of a dAVF had met with poor results and that its use had been abandoned.

The concept of a dAVF is certainly attractive, but a randomised study of its use in patients with poor runoff is required before it is more widely used.

Prostacyclin therapy

The synthetic prostacyclin analogue Iloprost (Schering AC, Berlin) has been shown to improve blood flow in femorodistal grafts. In a controlled trial Hickey *et al* (1991) showed that injection of a single intragraft bolus of 3000 ng significantly increased graft flow, the improvement being maintained a week later. An immediate effect on flow would be expected since Iloprost is a powerful vasodilator, but the mechanism whereby a single dose can produce such a prolonged response remains unexplained since the half-life of the drug is of the order of minutes. Further studies are required to determine whether the beneficial effect on flow can be used to improve the patency of high risk grafts.

TECHNICAL PROBLEMS

As emphasised earlier, the most important point in dealing with technical errors is prompt identification enabling correction at the time of surgery. Management of specific problems is fairly straightforward.

With regard to the in situ technique, persistent arteriovenous fistulae should be identified and ligated, and residual valve cusps disrupted by re-passage of the

valvulotome. An unsatisfactory anastamosis should be revised, using a vein patch or jump graft extension if necessary. Thromboemboli in the graft and runoff can usually be removed with a Fogarty embolectomy catheter. A vein segment identified as too narrow, or which has been damaged by the valvulotome, should be excised and replaced. Correct alignment is best achieved by allowing arterial blood down the vein after completion of the proximal anastamosis which unravels any twist, and thereafter by maintaining the established orientation of tributaries.

It is important to check the graft position with the knee extended to ensure that it is not excessively kinked, in which case it may be necessary to divide some of the medial hamstring tendons.

Once an error has been identified and revised, further assessment is required in order to confirm that the situation has resolved. The overriding message is that attention to detail is vital.

POSTOPERATIVE FAILURE

In the event of early occlusion the first decision to be taken is whether or not the graft should be re-explored. If completion studies indicate that their are no technical errors and nothing further can be done to improve the runoff, then there is little to be gained from reoperating (Bandyk *et al* 1988). If, on the other hand, completion studies were favourable, exploration of the graft is more likely to uncover a redeemable cause such as a missed valve cusp or distal embolus.

Revisional surgery

It should be emphasised that once a vein graft occludes it is often difficult to adequately remove all the thrombus since it becomes adherent to the endothelial lining. It is therefore important to intervene early before the process becomes

advanced. The standard approach is to expose the distal graft and perform a thrombectomy with a Fogarty catheter through either the distal anastamosis or a separate graftotomy. Harris (1987) recommends flushing clot away with heparinised saline in order to avoid damage to the vein which may be caused by embolectomy catheters. The aim initially is to re-establish the inflow and clear the runoff, following which it is necessary to elucidate the cause of failure, usually with an arteriogram. Any remediable cause should be corrected as above. In the absence of an obvious cause it may be prudent to anticoagulate the patient (Stept *et al* 1987).

Haemodynamic failure

This a well recognised entity in which the graft remains patent but there is a failure of the runoff to direct sufficient blood to the ischaemic area. Instead, blood passes preferentially back up the limb on reaching the distal anastamosis, effecting a proximal steal. Beard (1987) found that a steal of more than 33% of total graft flow was associated with graft failure.

When this situation occurs the runoff should be investigated with an arteriogram since it may be possible to improve distal perfusion with a distal jump graft or a sequential bypass, although in practice the situation is usually beyond salvage.

INTERMEDIATE GRAFT FAILURE

GRAFT STENOSIS

In spite of a lack of controlled evidence it is generally accepted that intervention to treat stenoses prior to graft occlusion is worthwhile. The main questions to be answered are which stenoses should be treated, and what is the best method.

Stenosis selection

Evidence from prospective studies indicates that only 20-25% of stenoses identified with either Duplex or IVDSA progress to graft occlusion if left untreated (Moody *et al* 1990). Since the mechanisms of stenosis causation and progression are not understood there is no single test indicating which lesions require treatment. There are, instead, a number of guidelines derived from prospective studies which are considered to identify lesions likely to threaten graft patency, and these are (Grigg *et al* 1988, Moody *et al* 1990):

- Stenosis associated with clinical deterioration, or ABPI
  fall greater than 0.2
- Greater than 50% reduction in cross-sectional area
- Lesions developing within 6 weeks
- Lesions demonstrating progression on serial examination

Stenosis treatment

Having decided that treatment is indicated the choice lies between surgical repair and percutaneous transluminal angioplasty (PTA) (Fig 3.9).

Surgical repair is usually in the form of a vein patch, although occasionally an interposition graft or distal jump graft are required (Harris and Moody 1991). Proponents of surgical repair quote its durable record with patency rates from 76-82% at 5 years (Cohen *et al* 1986, Bandyk *et al* 1987).

The obvious advantage of PTA is that it is far less invasive but doubt has been expressed about its efficacy since although it may be initially successful, there is a higher incidence of restenosis and occlusion (Berkowitz *et al* 1981, Thompson *et al* 1989). More recent studies, however, have stressed the importance of high inflation pressures to deal with stenoses (Moody *et al* 1990, Brennan *et al* 1991) and indicate that PTA is of considerable value as a first line therapy.

Fig 3.9   Sequential arteriograms showing an area of stenosis in relation to the distal anstamosis of a femoroperoneal graft before (left) and after (right) PTA.

GRAFT OCCLUSION

Once occlusion has occurred in the intermediate period there are two problems to tackle; the graft and runoff must be cleared of thrombus and the underlying cause identified and corrected. Intervention at this stage appears to be justified, and Whittemore *et al* (1981) reported 50% 5 year limb salvage after secondary surgery.

Thrombolysis

Clot dissolution with a fibrinolytic agent is preferable to surgical thrombectomy in femorodistal vein grafts, since it is difficult to fully remove all of the thrombus and the embolectomy catheter may cause trauma to the graft and runoff vessels. In order to achieve clot lysis it is necessary to guide a catheter into the graft and infuse the drug directly into the thrombus (Towne and Bandyk 1987). There is no concensus as to which lytic agent should be used, with streptokinase (Walker and Giddings 1988), urokinase (Durham *et al* 1989) and tissue plasminogen activator (t-PA) (Graor *et al* 1988) all having been used.

One point which is clear from the various studies is that although thrombolysis is an effective means of restoring patency, rethrombosis is likely if the underlying cause is not identified and corrected. Graor *et al* (1988) reported 86% patency at 30 days in 33 thrombosed grafts treated with t-PA, 30 of whom had undergone revisional surgery after thrombolysis. Similarly, Belkin *et al* (1990) achieved long term patency in 22 grafts following thrombolysis, 19 of which had undergone either surgery or PTA.

Thrombectomy

The results following surgical removal of thrombus do not appear to be as good as those achievable with thrombolysis. Graor *et al* (1988) compared the two methods, reporting a 30 day patency of only 42% in the thrombectomy group compared with 86% after thrombolysis. This was in spite of the fact that 34 of the 38 patients underwent a revisional procedure following thrombectomy. Cohen *et al* (1986) reported a 50% 1 year patency in a group of 25 patients undergoing thrombectomy and patch angioplasty.

It has been proposed that thrombolysis produces a "cleaner", less thrombogenic surface (Towne and Bandyk 1987, Hopkinson 1991)) which would explain its superior efficacy.

LATE GRAFT FAILURE

Management of the failing or failed graft after the first two years is largely similar to that applied to the intermediate category, and can be summarised briefly.

Failing grafts are invariably due to distal disease progression and present with recurrence of symptoms, usually claudication. If symptoms are troublesome then further assessment in the form of arteriography is indicated. Treatment is guided by the site and degree of disease, although distal revision of a previous distal graft may be difficult.

Late occlusion of a graft may not present with limb threatening ischaemia since any areas of tissue necrosis should have healed, and in fact the exact date of occlusion is often difficult to ascertain since it may only be detected at the subsequent clinic visit. Any significant delay in presentation precludes surgical thrombectomy, but thrombolysis is worth trying if significant symptoms are present.

DISCUSSION

In reviewing the problems posed by femorodistal vein graft failure a number of recurrent themes are apparent. The three principal areas of interest have been those of patient selection, intraoperative technical assessment and postoperative graft screening. The motivation behind research into the problems posed is the desire among vascular surgeons to ensure that limb salvage surgery is offered to as many as possible, and that their endeavours are rewarded with optimal graft patency. What is clear is that surgeons professing an interest in the management of patients with severe chronic lower limb ischaemia need more than clinical experience and good luck in order to achieve the best results.

The results of Leather and co-workers in their specialised unit have proved

difficult to equal in the UK, but they do serve as a gold standard by which to be compared. In an effort to emulate their graft patency and limb salvage rates it is clearly important to keep abreast of the numerous developments which are taking place. The surgeon must make a considered choice as to which of the proposed methods of *eg* runoff assessment to adopt, and this will inevitably be based on the confines presented by resources, both financial and practical. In order to improve, however, new modalities need to be introduced and critically evaluated.

A further problem lies in deciding how to assess the impact of any methods which are introduced. In ideal circumstances this would be carried out in a prospective fashion, with patients randomly allocated to either the standard or new method and the results compared. In practice, however, many developments such as PGR, are intended to be adjunctive to traditional methods, rather than replacing them entirely. It is common, therefore, to compare the results following introduction of new methods with those from a retrospective series, accepting that there are limitations to the conclusions which may be drawn from such a study. The next chapter, therefore, reviews the results of in situ vein grafting at the Leicester Royal Infirmary.

CHAPTER 4

RETROSPECTIVE REVIEW OF FEMORODISTAL

IN SITU VEIN GRAFTS

INTRODUCTION

During the period May 1981 to July 1988 a total of 136 in situ vein grafts were performed at the Leicester Royal Infirmary. This represents 35% of a total of 373 infrainguinal reconstructions carried out in the same period (Budd *et al* 1990). The case notes for 6 patients were lost, leaving data available for review on 130 grafts.

The in situ grafts were looked at separately because during the period in question this was the principal technique used for vein grafts where the distal anastamosis was below the knee. In the same period 47 reversed saphenous vein grafts were performed, of which only 21 were to below knee vessels (13 popliteal and 8 crural). These grafts have not been included in the analysis mainly because the numbers were considered to be too small when compared with the in situ group, particularly at the crural level. In addition it was an opportunity to assess the potential technical problems posed by the in situ method, particularly with regard to early graft failure.

Patients and methods

All patients undergoing infrainguinal bypass with in situ saphenous vein were retrieved from the vascular database at the Leicester Royal Infirmary. This contained information on all patients undergoing a vascular procedure from January 1980 onward. In addition to details of the operative procedure, the database contained demographic information, recorded the indication for surgery and listed relevant risk factors. More detailed information was obtained by a review of the case notes, particularly with regard to follow-up. Graft patency was confirmed at the most recent clinic visit by the presence of a palpable pulse within the graft or by the presence of improved Doppler pressures, where appropriate.

A preoperative arteriogram was obtained in all patients and the majority also had intraoperative arteriography as well, pre-bypass or completion or both. Calf vessel runoff was judged on the basis of the best available record, and frequently this was limited to comments in the operation notes or the x-ray report since in a large number of cases the films were missing.

Sufficient information was gathered for 121 patients, with 9 undergoing bilateral procedures. There were 89 men and 32 women with an age range of 21-89 years (median 66 years). The indication for surgery was severe claudication in 20 (15%), rest pain in 56 (43%), non-healing ulcers or gangrene in 53 (41%), and in one case for a popliteal aneurysm. For the purposes of this analysis patients with either ischaemic rest pain or tissue necrosis were considered to be undergoing limb salvage surgery.

The decision to operate was principally based on clinical assessment and the preoperative arteriogram. Doppler pressures were measured in only 67 (52%) patients in the whole series, although were recorded more frequently, in 62%, in the presence of ulceration or gangrene. The median ankle pressure and ABPI for the different groups, where available, are shown below in table 4.1.

With regard to risk factors, 64 patients were current smokers, 44 were hypertensive, 14 had had a previous myocardial infarction, 15 suffered from angina

or heart failure and 41 were diabetic.

Operations

In order to confirm the distal runoff status and suitability of the chosen site for distal anastamosis, a prebypass on-table arteriogram was obtained wherever possible. The distal anastamosis was to the below knee popliteal artery in 64 (49%), to the above knee popliteal artery in 5 and to an isolated popliteal segment in 3. There were 58 (45%) infrapopliteal grafts, 20 to the tibioperoneal trunk and 38 to a single calf vessel. On graft completion a further on-table arteriogram was performed in order to assess technical adequacy.

In the majority of cases the proximal anastamosis was to the common femoral artery, associated with an endarterectomy in 2 and a preoperative iliac angioplasty in 3. In 15 cases the proximal anastamosis was to the lower end of an aortobifemoral (8), iliofemoral (6) or femorofemoral crossover (2) graft. Eight patients had undergone a previous ipsilateral femoropopliteal graft with either PTFE or HUV.

Indication No (%)	Median pressure (range)	Median ABPI (range)
Claudication 10 (50%)	90 mmHg (30-130 mmHg)	0.57 (0.24-0.74)
Rest pain 24 (43%)	68 mmHg (0-118 mmHg)	0.43 (0-0.74)
Tissue loss 33 (62%)	60 mmHg (0-95 mmHg)	0.37 (0-0.63)

Table 4.1 Preoperative ankle pressures / ABPI

There was unfortunately insufficient data to enable a qualitative comparison between on-table and pre-reconstruction arteriography. In the main the only available data related to the number of vessels visualised, allowing runoff to be classified only as single or multiple. There was virtually no data regarding arteriographic assessment of the pedal arch.

RESULTS

Outcome in terms of graft patency, limb salvage and patient survival was determined by Life Table analysis at 3-monthly intervals, with an initial assessment after the first month (Underwood 1984). Patency was ascertained by clinical examination in out-patients, Doppler pressures being recorded too inconsistently to be of value for this purpose.

There were 7 postoperative deaths, 3 from myocardial infarction, and one each from CVA, cardiac failure, acute renal failure and bronchopneumonia, giving a 30 day mortality of 5%.

Overall patency

The cumulative secondary patency rate at 1, 2 and 3 years was 56%, 49% and 45% respectively, the limb salvage rate 72%, 70% and 68%, and patient survival rate 83%, 77% and 74% (Fig 4.1).

In order to determine the relative importance of various risk factors on graft patency multiple regression analysis was performed using proportional hazards (Cox 1972). Only the operative indication (p < 0.05) and degree of runoff (p < 0.02) were found to be significant (Figs 4.2, 4.3). Grafts performed for claudication had a superior patency than grafts performed for either rest pain or critical ischaemia

Numbers at risk

PS	130	124	113	102	91	83	76	71	66	54	48	46	44
LS	130	114	97	79	70	61	54	50	46	39	34	34	33
GP	130	100	81	60	51	45	38	36	32	26	22	22	21
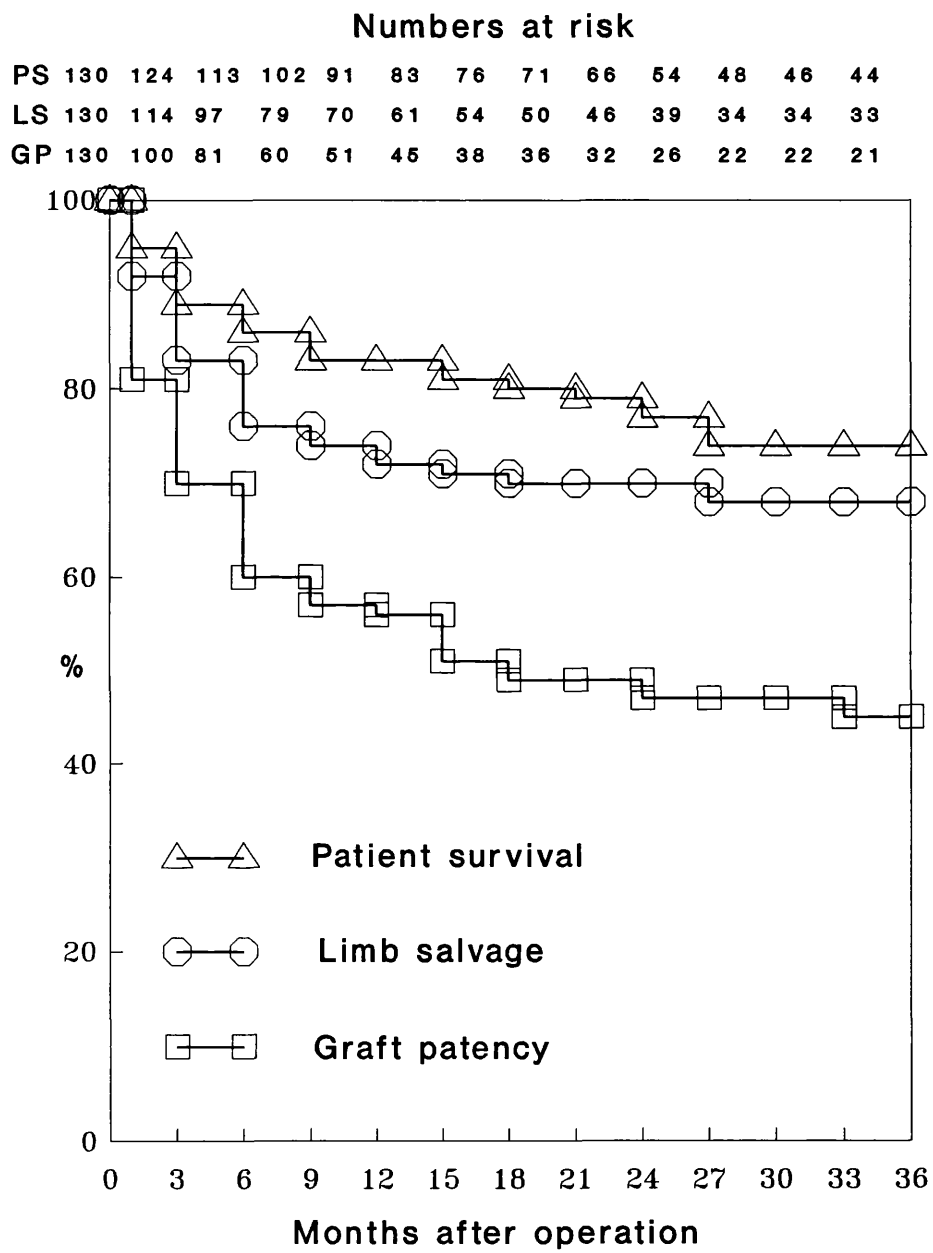
Fig 4.1   Cumulative life table curves for graft patency (GP), limb salvage (LS) and patient survival (PS).

Numbers at risk

Cl	19	19	14	14	13	12	12	10	10	10	9	9	9	8
RP	56	56	47	36	23	21	18	16	16	15	13	10	10	10
Ga	54	53	38	31	23	17	14	11	9	7	4	2	2	2

P < 0.05

Claudication

Rest pain

Gangrene

Months after operation
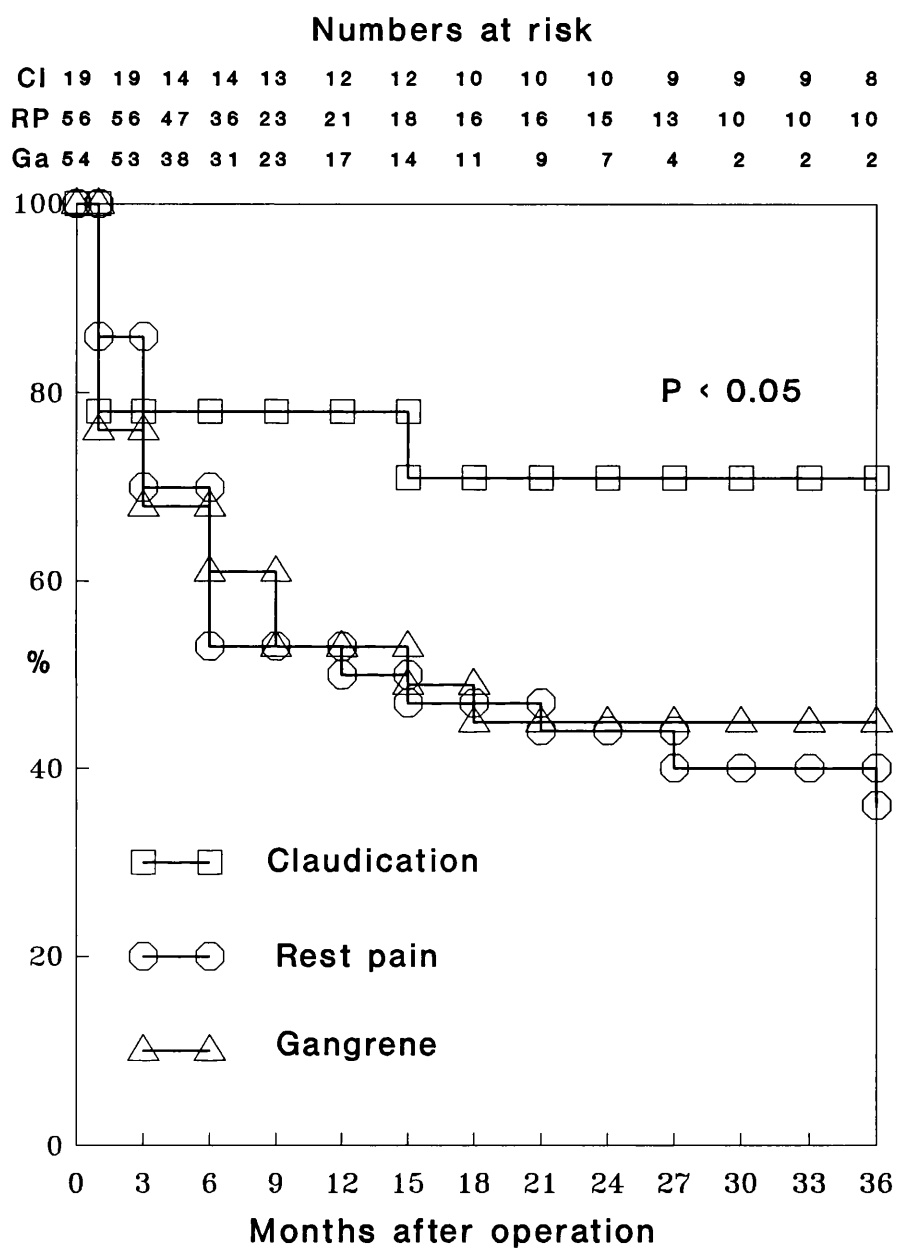
Fig 4.2   Patency rates according to the operative indication.

Cl - claudication, RP - rest pain, Ga - gangrene.

Numbers at risk

BKP	64	64	50	42	31	26	24	22	21	19	16	14	14	13
TPT	20	19	15	13	9	8	7	5	4	3	3	3	3	3
SV	38	38	30	21	14	11	9	7	7	6	4	1	1	1
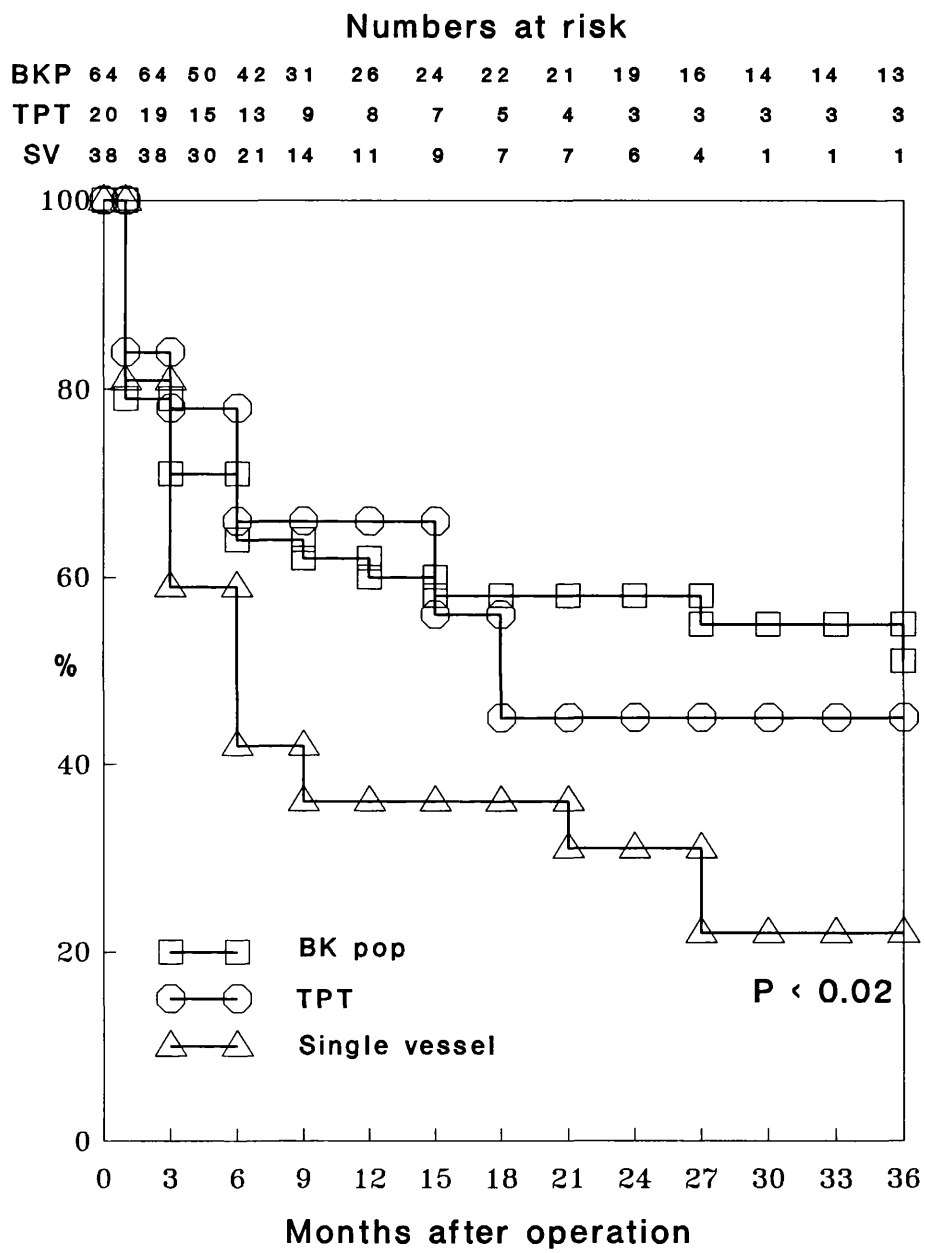
Fig 4.3   Patency rates according to degree of runoff.

BKP - below knee popliteal (2/3 vessels),

TPT - tibioperoneal trunk (2 vessels),

SV - single vessel.

(78% at 1 yr *v* 50% and 53% respectively). Grafts with 2 or 3 vessel runoff fared better than grafts with single vessel runoff (64% 1 yr patency *v* 36%). Other factors such as smoking and diabetes were not found to have an independently significant influence on graft patency.

The majority of graft failures occurred within 6 months. The largest interval fall, of 19%, occurred within the first month, with additional falls of 11% and 10% at 3 and 6 months respectively. Although grafts continued to fail after 6 months the interval falls were much smaller.

Early failure

A total of 39 grafts failed within the first 30 days. There were 36 occlusions and 3 cases in which the graft remained patent without clinical improvement. Twenty-six of the occluded grafts were explored, with patency being restored in 16. Graft exploration was undertaken if it was felt there was a reasonable chance of restoring patency, especially when early thrombosis was unexpected. In a number of cases the completion arteriogram revealed a poor runoff situation which it was not felt could be improved upon, and in these cases a decision not to explore the graft in the event of early occlusion was made at the end of operation. The findings in the in the reoperated group (Table 4.2) consisted of 9 technical problems, 2 inadequate veins and in 15 no specific cause was documented, thrombectomy alone being performed. The primary failure rate at 1 month, therefore, was 30%, with a secondary failure rate of 18%.

It can be seen that in the majority no specific cause for thrombosis was found and thrombectomy alone was carried out, although this was only successful in 8 out of 15 cases. Only one patient was formally anti-coagulated after simple thrombectomy and the graft remained patent. Where a specific fault was recognised and corrected after the graft had been thrombectomised the outcome was better, with 8 out of 11 grafts remaining patent. In the two cases where the problem was

Cause	No.	Succ	Fail
None found - thrombectomy alone	15	8	7
Distal anastamosis fault			
- jump graft	3	2	1
- vein patch	2	2	
Persistent cusp	2	2	
Unligated vein branch	1		1
Distal vein twist	1	1	
Poor quality vein			
- whole replaced	1		1
- proximal replaced	1	1	

Table 4.2   Operative findings in grafts explored after early occlusion, indicating subsequent outcome.

considered to be poor quality vein the affected portion was replaced by PTFE and neither did well subsequently. In one, the entire vein was replaced and this graft occluded after one month, and in the other the proximal portion of the vein was replaced, the graft staying patent for a further 3 months. In both cases the affected limb was ultimately amputated.

In the 13 grafts which were not re-explored and the 10 grafts which failed despite reintervention, there were 16 major amputations. Six of these were above-knee and 10 below-knee, resulting in an initial BK:AK ratio of 1.67. Four of the below-knee amputations, however, were subsequently revised to above-knee after a range of 10-18 days, producing a final BK:AK ratio of only 0.6 following early failure. Three amputations (2 above and 1 below-knee) were necessary in patients with a patent graft. In addition, 3 of the 7 postoperative deaths in the series occurred

after early failure, 2 of which followed unsuccessful graft revision and subsequent amputation.

There were 7 cases in which the limb survived in spite of early graft failure. The indication for surgery in this group was claudication in 3, rest pain in 2 and ischaemic ulcer in 2. Graft failure did not result in any deterioration, and in fact 2 of the claudicants reported improvement in their walking distance on subsequent follow-up.

Intermediate failure

Of the 107 grafts which were patent after 1 month, 31 occluded within the first year, giving an intermediate failure rate of 29%. This group accounted for 50% of failures in the whole series and 74% of failures occurring after the first month. Failure during this period was not a benign event, with 16 (52%) requiring a major amputation (BK:AK ratio 1.29), the remainder being left with stable ischaemia.

Ten of the grafts failing in this period had undergone revision during the first month, and of this group 7 occluded within 4 months of the original surgery.

Six patients underwent graft revision at intervals ranging from 3 to 30 months following implantation. Intervention was prompted by a deterioration of symptoms in 5, and in 1 case a distal graft stenosis was picked up incidentally at 15 months during arteriographic investigation of the opposite leg.

DISCUSSION

This series serves to underline the problems posed by femorodistal bypass, since even with the inclusion of a moderate proportion of claudicants the cumulative secondary patency rates are inferior to most reported series (whether or not they are

more representative of wider, unreported experience is open to debate). The reasons for this are inevitably multifactorial and analysis reveals that the majority of ground covered in the previous chapter is implicated. Painful though it may be, analysis of this type is crucial since it is the starting point whereby steps can be taken to improve results. It should also be borne in mind that while one is always aiming to emulate the gold standards prominently displayed in the literature, reality decrees that improvement is achieved gradually, with previous experience being a more relevant benchmark.

While the overall results are poor the underlying problems are the same as those highlighted elsewhere, with the majority of failures falling in the early and intermediate categories. It is to these areas, therefore, that attention must be focused. The late failure rate was of the order of 5% per annum which is comparable with other reports.

Early failure

As discussed previously, the principal factors to consider are patient selection and technical assessment.

During the early part of the series particularly, patient selection was based largely on clinical indications and a preoperative arteriogram, neither of which are sufficiently discriminative. Doppler pressures were not routinely measured, and although it is acknowledged that they are not a sensitive predictor of outcome, they allow accurate patient classification, particularly in view of their central role in the definition of critical ischaemia (Bell *et al* 1982). This deficiency automatically hampers any comparison between this and other series', and emphasises the need for thorough preoperative investigation in order for meaningful interpretation of results.

The general policy, therefore, was to select patients according to need, and in the majority of cases the surgery was undertaken for what was considered to be limb

salvage. The limitations of this definition in providing an accurate reflection of limb viability has been discussed earlier. It was interesting to note, however, that there was no significant difference in patency between grafts performed for rest pain and those performed for tissue loss. This might be explained in part by the fact that one third of the rest pain group in whom the ankle pressures were available had true critical ischaemia, but may also reflect the fact that technical errors are likely to affect both groups equally, thus cancelling out some of the expected difference due to disease severity.

It is disappointing that the impact of on-table arteriographic runoff assessment could not be properly assessed, although the general impression was that the on-table x-ray provided more information than the preoperative arteriogram. Unfortunately there was no information regarding cases which were abandoned as a result of inadequate runoff demonstrated by on-table arteriography.

In the later part of the series a number of patients were included in a study assessing the value of peripheral resistance measurement using an infusion of heparinised blood (Parvin et al 1985). It was concluded that a resistance of > 1.5 PRU, or > 0.75 PRU after papaverine, was associated with graft occlusion within 3 months. The infusion pump which was used was experimental and a number of flow rates were used, the predictive data being derived from measurements carried out at 76 ml/min. The results were not subsequently evaluated on a prospective series, but the promising nature of resistance measurement resulted in the construction of a prototype infusion pump suitable for clinical use.

It is surprising that despite the use of completion arteriography there were 9 technical errors which led to early thrombosis. There are a number of possible reasons for this, including inadequate visualisation of graft and/or runoff, lesions missed on uniplanar views, and misinterpretation of x-ray findings. These are supported by the relatively high success rate following intervention which reduced the early failure rate to 18%, although ideally reintervention could have been avoided if the errors had been detected at the original operation. If completion

arteriography is used as the sole method of graft assessment then criteria for acceptability should be established and the graft revised until a satisfactory arteriogram is obtained.

The decision not to intervene in 13 cases was based largely on arteriographic findings at operation. In these cases the graft was considered to be technically satisfactory with failure being due to inadequate runoff, and in the absence of alternative runoff vessels further exploration was not felt to be indicated. In this situation completion arteriography played a positive role in management.

The serious consequences of early failure were clearly demonstrated with 16 out of 23 patients requiring an amputation. The poor BK:AK ratio of 0.6 reflects the finding by others that a failed reconstruction often results in a more proximal amputation (Szilagyi et al 1979, Dardik et al 1982, Sethia et al 1986). The 7 cases of early failure which did not result in amputation serve to illustrate two important points. The first is that patients with claudication are by no means immune to early graft failure, although there were fortunately no instances in which a patient with claudication ended up with an amputation. The second point relates to inappropriate labelling of patients as candidates for limb salvage on purely clinical grounds, and emphasises the need for objective evaluation of disease severity.

A final point concerning early graft failure and its consequences relates to economics, a factor which cannot be ignored in the present climate. It is clear from the studies previously cited (Mackey et al 1986, Raviola et al 1988, Cheshire et al 1991) that primary reconstruction is a cost effective option when compared with primary amputation. The in-patient cost of a failed bypass followed by a major amputation is, however, more expensive than the cost of a primary amputation alone, and, if one is to promote the cost benefit of reconstructive surgery to hospital managers, it is important that graft failures are kept to a minimum. In this respect the crucial points are, once again, appropriate patient selection and attention to operative detail.

Intermediate failure

This series confirms the findings of others that failure between months 1 to 12 can be a significant problem. Unfortunately there is little in the way of objective data to indicate the actual cause of failure in the 31 grafts in this series since follow up was essentially clinical. In view of the close association which has now been established between the development of fibrous stenoses and failure during this interval however, it is reasonable to assume that this was the likely cause in a significant proportion. Another important factor which emerges from this series, however, is the deleterious effect of revisional surgery within the first month. This is illustrated by the 10 cases in which revision resulted in a patent graft at 30 days but which subsequently failed by 12 months. The fact that 7 of these had failed within 4 months of the original surgery is a clear indication that grafts undergoing early re-exploration represent a high risk group even after patency has been restored.

The assumption that the remainder of graft failures in this category were due to stenosis formation is not entirely without support, since in 5 of the 6 grafts in whom secondary intervention took place after the first month, the underlying problem was a stenosis. In 4 cases investigation was prompted by a deterioration in symptoms and in 1 the stenosis was an incidental finding during investigation of the contralateral limb, confirming that symptom deterioration is present in only a minority of grafts found to have a stenosis.

CONCLUSIONS

This retrospective series clearly illustrates the potential pitfalls which may be encountered when an aggressive programme of femorodistal reconstruction is undertaken. In order to tackle the deficiencies which have been identified three general areas can be considered.

1. Patient selection - a more co-ordinated approach is necessary in order to allow accurate classification of disease severity, while at the same time placing emphasis on methods aimed at providing thorough assessment of calf vessel and pedal arch patency.

2. Operative assessment - both prebypass arteriography and resistance measurement need to be studied further in order to determine their additional role, if any, in runoff assessment. Completion arteriography needs more critical evaluation, and should ideally be compared with haemodynamic measurements to determine which is superior in assessing technical adequacy.

3. Postoperative assessment - relatively little is known regarding the haemodynamics of early graft failure, and it is possible that close monitoring during this period could identify grafts at risk of failure. In addition, the problem of failure after the first month has assumed considerable prominence due to the recognition of graft stenoses. Some form of screening programme to identify these lesions seems sensible since clinical assessment alone would appear to be inadequate, although it is not clear which methods represent the "best buy" in terms of practicality, stenosis detection and cost.

The following chapter outlines the programme of pre-, intra-, and postoperative measures which were introduced in a prospective series of patients undergoing femorodistal vein bypass in an effort to improve our understanding and management of factors relating to early graft failure.

CHAPTER 5

PATIENTS AND METHODS

INTRODUCTION

All patients presenting to the Vascular Surgical Unit at the Leicester Royal Infirmary between September 1988 and August 1990 with either rest pain or critical ischaemia and a palpable femoral pulse were initially eligible for inclusion. All patients fulfilling these criteria underwent preoperative non-invasive assessment but data analysis has been restricted to those patients in whom intraoperative studies were carried out. These were only performed in patients undergoing autologous vein bypass, either reversed or in situ, in which the distal anastamosis was to the below-knee popliteal artery or beyond. Early postoperative monitoring was similarly restricted to femorodistal vein grafts performed in the prospective group.

PATIENTS

Fifty-six patients fulfilled the initial entry criteria of whom 42 subsequently underwent femorodistal vein bypass. In the 14 patients excluded, management was by above-knee bypass in 9 (4 vein, 5 PTFE), distal bypass with PTFE in 4 and profundaplasty in 1.

The study group was made up of 24 men and 18 women aged between 51 and

89 (med 75 yrs). Fourteen patients (33%) were diabetic. Using the definition outlined in the European Concensus Document (1989) the patients could be divided into 3 groups; 6 with rest pain alone (ankle pressures 75-120, med 90 mmHg), 16 with tissue necrosis and ankle pressures > 50 mmHg (range 55-100, med 75 mmHg); and 20 with critical ischaemia (ankle pressures 0-50 mmHg, med 40 mmHg). An alternative classification based on the findings from the Joint Vascular Research Group (Wolfe 1986), in which the ankle pressure was not found to be of prognostic significance once ulceration or gangrene had developed, divided the study group into two; 6 with rest pain (ankle pressures 75-120, med 90 mmHg), and 36 with critical ischaemia (ankle pressures 0-100, med 47.5 mmHg).

An in situ bypass was performed in 33 cases, using the technique described by Beard *et al* (1989), in which the entire vein was mobilised, allowing ligation of all branches under direct vision and avoiding undue tension on the graft, particularly with regard to the proximal anastamosis. Reversed saphenous vein was used in 8, one being a composite graft with arm vein, and in the remaining case a reversed arm vein was used. The proximal anastamosis was to the common femoral artery in 33 and to the superficial femoral artery in 9. The distal anastamosis was to the below-knee popliteal artery in 9, to the tibioperoneal trunk in 5, to a single calf vessel in 28 (anterior tibial 8, posterior tibial 1, peroneal 19), and in 2 cases to the dorsalis pedis artery.

PREOPERATIVE ASSESSMENT

Patients were initially assessed through a combination of history, examination and measurement of the ankle/brachial pressure index (ABPI). All those considered to be suitable candidates for reconstruction were further investigated with arteriography, adjunctive Doppler methods, and Duplex vein mapping.

Arteriography

A conventional transfemoral arteriogram was performed preoperatively in all cases, with particular emphasis placed on visualisation of the distal calf vessels. Digital subtraction angiography was not available during the study period.

A simple scoring system was used to evaluate the three principal calf vessels. A vessel which was patent and disease free from origin to ankle scored 2, with 1 point being awarded if patent but diseased, and 0 points if occluded or inadequately visualised. The pedal arch was rarely visualised on the arteriogram and could not therefore be assessed.

Doppler ultrasound

The initial ankle pressure measurement was performed with the patient sitting up in bed or on an examination couch, the legs being horizontal. All 3 calf vessels were insonated at ankle level and pressures measured with a sphygmomanometer cuff placed around the lower calf. The highest value obtained was divided by the brachial systolic pressure in order to provide the ABPI, and was also used to categorise the severity of ischaemia.

Two modifications of this standard approach, dependant Doppler and Pulse Generated Runoff (PGR), were used in order to determine the most effective means of non-invasive runoff assessment. Of particular importance in this respect was the ability of each method to assess calf vessel communication with the pedal circulation, since this information is directly relevant when planning surgery.

Dependant Doppler assessment

This was carried out with the patient sitting upright on the examination couch with the legs over the side, the feet being supported on a step. The three calf vessels were insonated at ankle level scoring 1 point if flow was detected and 0 if flow was absent. Flow in the pedal arch was then sought by insonating in the first web space

on the dorsum of the foot. If the pedal arch was found to be patent the compression test of Roedersheimer was applied in order to determine which of the calf vessels were in communication (Fig 5.1). The arch was considered to be complete if supplied by two or three vessels, incomplete if only supplied by one and occluded if no signal was obtained. A complete arch scored 2, an incomplete arch 1 and an occluded arch 0 points. The combined vessel and arch score produced, therefore, a limb score of between 0 and 5.
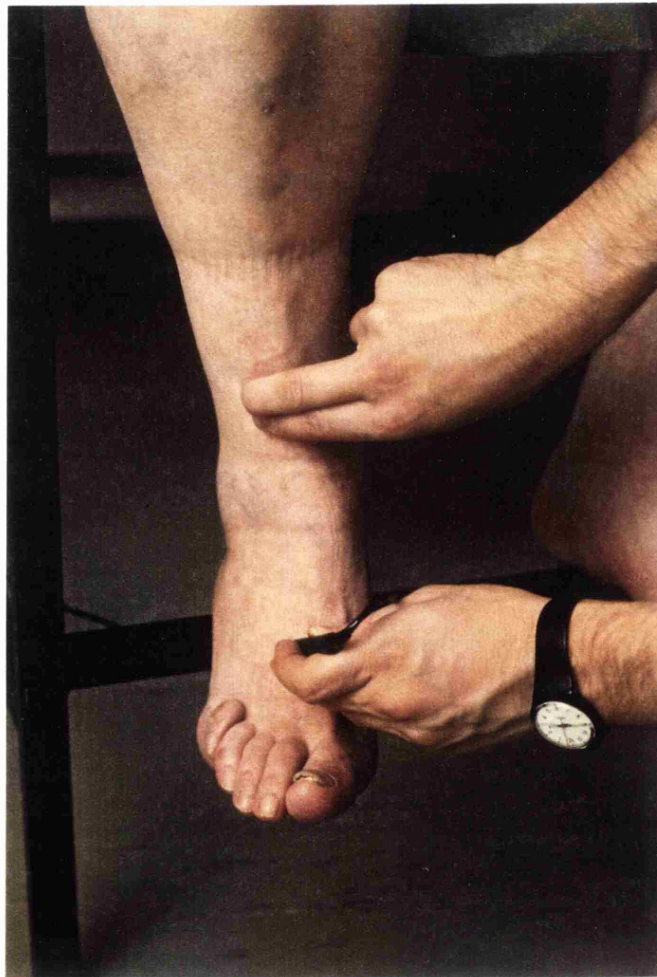
Fig 5.1 Application of the compression test of Roedersheimer with the limb dependant.

PGR assessment

The recently introduced PGR system (Beard *et al* 1988) was used to assess the calf and pedal circulation in a similar fashion, although the leg was kept horizontal as per the standard method. A similar scoring system to that used with the dependant Doppler technique was employed, based on the fact that PGR is reported to be able to differentiate between vessels which are patent but diseased and those which are relatively disease free (Beard *et al* 1988A). In the latter group the pressure wave generates a biphasic Doppler signal whereas in diseased vessels the signal is monophasic, allowing individual vessels to be scored 2 or 1 points respectively if found to be patent. This resulted in a possible calf score of 0 to 6. The pedal arch was scored in the same manner as for dependant Doppler, producing a possible limb score of 0 to 8.

Duplex vein mapping

Early into the study period it became policy to map the long saphenous vein preoperatively with Duplex, using a 7.5 MHz probe. The main purpose was to assess vein quality, particularly calibre below the knee, and to mark its position (Figs 3.4, 3.5). In the event of the vein being absent or of poor quality alternative sources of vein *eg* the arms, could be scanned.

INTRAOPERATIVE STUDIES

This includes pre-reconstruction methods of runoff assessment and various methods looking at graft function on completion.

On-table arteriography

The proposed site for the distal anastamosis was selected largely on the basis of the preoperative arteriogram and standard Doppler assessment. On-table arteriography was used to confirm the suitability of this choice, ensuring in particular a disease free runoff to the ankle and ideally identifying communication with a patent pedal arch. The proposed vessel was exposed and controlled with rubber slings. The artery was then cannulated with a 21 guage butterfly needle and an x-ray plate covered with a sterile towel was placed under the lower leg and foot. A single static film of the runoff was then taken after injection of 15 ml of the non-ionic contrast medium Niopam. If the chosen site was found to be unsatisfactory then further films were obtained after cannulation of either a site lower down the same vessel or an alternative vessel, in order to identify the most suitable location for the anastamosis.

The arteriogram was scored in a similar fashion to the preoperative arteriogram, with each visualised vessel scoring between 0 and 2. In addition the pedal arch was scored in the same manner as that used for the augmented Doppler studies *ie* 2 if complete, 1 if incomplete, and 0 if occluded, thus producing a possible limb score of between 0 and 8.

Prebypass infusion resistance

Two different methods of resistance measurement were used, one in which the flow remained constant and one in which pressure was the constant variable.

Constant flow

The machine used was purpose built by the Departments of Medical Physics and Medical Engineering at the Leicester Royal Infirmary and was based on earlier resistance measurement work carried out with a Harvard pump (Parvin 1985). The design consisted of a metal housing containing an electric motor, an amplifier connected to a pressure transducer and a chart recorder. Mounted on top of the housing was a syringe pump designed to accommodate a 100 ml glass syringe (Fisons,
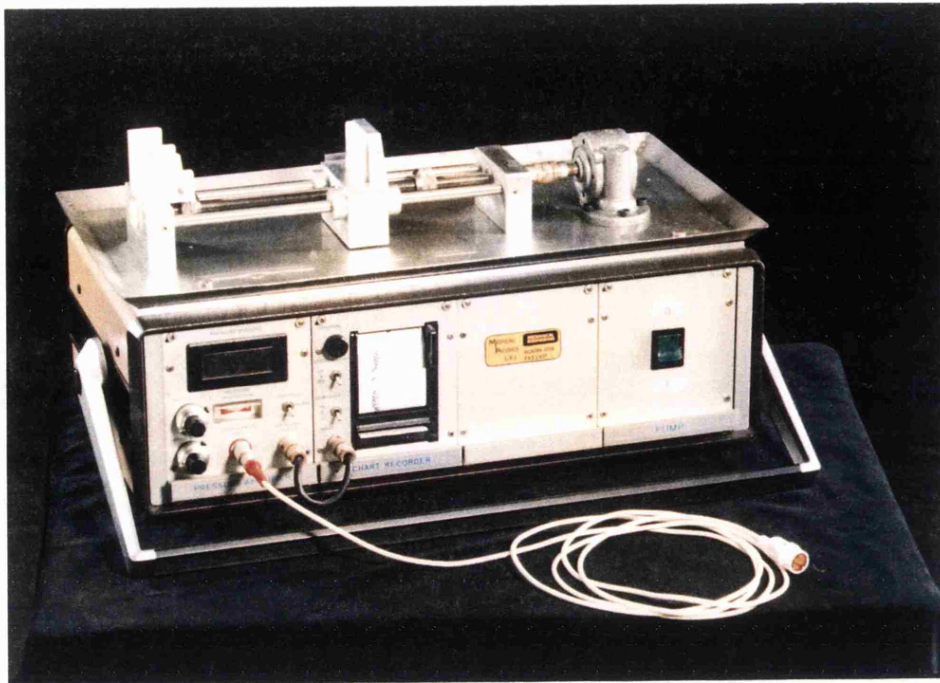
Fig 5.2   The constant flow resistance machine.
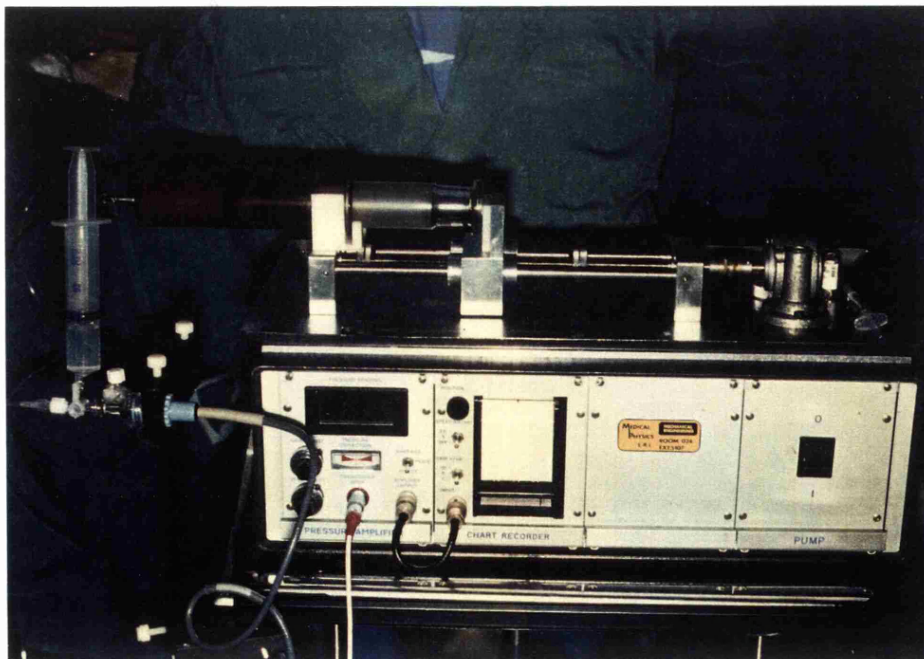
Fig 5.3   The machine in use in theatre. The glass syringe filled with blood is
seen mounted on top, and the pressure transducer is seen on the left.

Loughborough, UK). The system was calibrated to provide a constant rate infusion of 100 ml/min.

Just prior to measurement 60 ml of blood was drawn from the femoral artery into the glass syringe into which 500 units of heparin had been instilled. An extension line from the syringe was primed with blood and connected into a 3-way tap. A pressure line from the machine was similarly connected into the back of the 3-way tap. A soft 6 or 8 Fr umbilical catheter was used to cannulate the artery depending on the vessel calibre. This was carefully trimmed in order to reduce the catheter resistance. Prior to vessel cannulation the system was run in air so that the pressure generated by the catheter could be backed off to zero on the chart recorder, thus negating any resistance in the system. The catheter was then introduced via a small arteriotomy and held in place by a soft rubber sling (Fig 5.4). The pump was then turned on and the pressure generated in the artery was measured on the chart
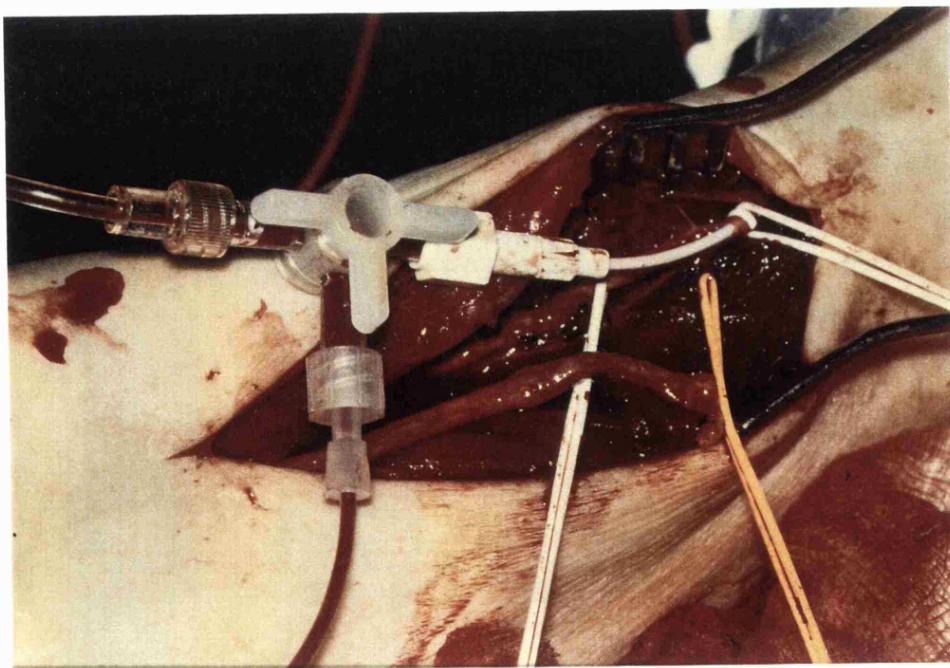
Fig 5.4   Measuring the resistance of the proximal peroneal artery. The cannula is held in place by the rubber sling. The two lines entering the 3 way tap lead to the constant flow machine and the pressure transducer.

recorder, from which resistance was easily calculated by dividing the figure by 100, giving a value in PRU's. In order to determine the possible effect of vasodilatation on improving the predictive power of resistance measurement, separate runs were carried out before and after the injection of 20 mg of papaverine with each run requiring 20-25 ml of blood.

Constant pressure

A version of the hand-held syringe pump developed by Beard *et al* (1988B) was used in this part of the study. This consisted of a stainless steel spring-loaded plunger into which a disposable 20 ml plastic syringe was fitted (Figs 5.5, 5.6). The device was calibrated so that a pressure of 100 mmHg could be maintained fairly constantly by keeping the marks on the plunger at a pre-determined steady state during infusion. Measurements were made via the cannula used for the constant flow studies. Heparinised blood was again used for the infusion, and the time taken to infuse 20 ml was recorded with a stopwatch. The actual capacity of the syringes used was of the order of 25 ml, and the first few millilitres were infused in depressing the plunger to the pre-set mark on the barrel, thus generating a pressure of 100 mmHg. The rate of infusion was calculated from the formula,

$$Rate \ (ml/min) \ = \ 20 \ ml \ \times \ (60 \ s \div \ t)$$

where t is the time taken to infuse 20 ml, and the resistance could then be read from a graph in which time was plotted against resistance.

This alternative method of resistance measurement was chosen for two main reasons. The simplicity of the technique was particularly attractive, enabling measurements to be made in the absence of experienced technical backup, and secondly, measurement using a constant pressure method is a theoretically more physiological means of determining intravascular resistance, avoiding the risk of vessel damage due to the generation of high intravascular pressure with a constant flow method. The main drawback with such a system is the inaccuracy inherent in

Fig 5.5   The constant pressure syringe loaded with a disposable plastic syringe.

Fig 5.6   A close-up view of the syringe barrel. On the left are the calibration marks
to which the plunger is depressed to maintain constant pressure. On the
main barrel the markings indicate the resistance in PRU for a measured
infusion time.

any method in which there is such a heavy reliance on hand-eye co-ordination.

The syringe was also adopted on the basis of the original study by Beard *et al* (1988B) in which it was used to measure peripheral resistance in a series of patients undergoing femorodistal bypass.

Completion arteriography

This was performed principally to assess the distal anastamosis and runoff. It was not necessary to look for unligated vein tributaries since the vein was always fully exposed and branches were dealt with under direct vision. On completion of the distal anastamosis all clamps were released to allow flow to be established. The graft was then cannulated with a 21 guage Venflon either through the stump of a reasonable calibre side branch (Fig 5.8) or through the hood of the graft just below the proximal anastamosis. An x-ray plate covered with a sterile towel was then placed under the calf and foot in order to include the lower end of the graft and runoff into the foot. Arterial inflow was then controlled with clamps and a single static film taken after injection of a 15-20 ml bolus of Niopam.

The film was carefully examined to exclude errors such as narrowing at the anastamosis or distal embolus. Any problems detected on the arteriogram were corrected where possible, with further films being obtained to confirm their resolution.

Graft blood flow

Graft flow was measured at a convenient point, usually in the upper graft, after a short period during which flow was established on release of clamps. Measurements were carried out with a Cliniflow electromagnetic flowmeter (Carolina Medical Electronics, Carolina USA) (Fig 5.7). In the latter part of the series a new Doppler flowmeter was also used, enabling the two methods to be compared (Appendix A).

The EM flowmeter was supplied with a series of resterilisable clip-on probes

of varying size. In order to achieve reliable readings it was important to ensure that a snug fit between the flow probe and the graft, without causing any constriction. A technician was required in theatre in order to calibrate the machine prior to use and also to supervise measurements. The mean flow rate was measured and outputted to a Gould 3-channel chart recorder.

Graft flow was measured before and after injecting a bolus of 20 mg papaverine into the graft.
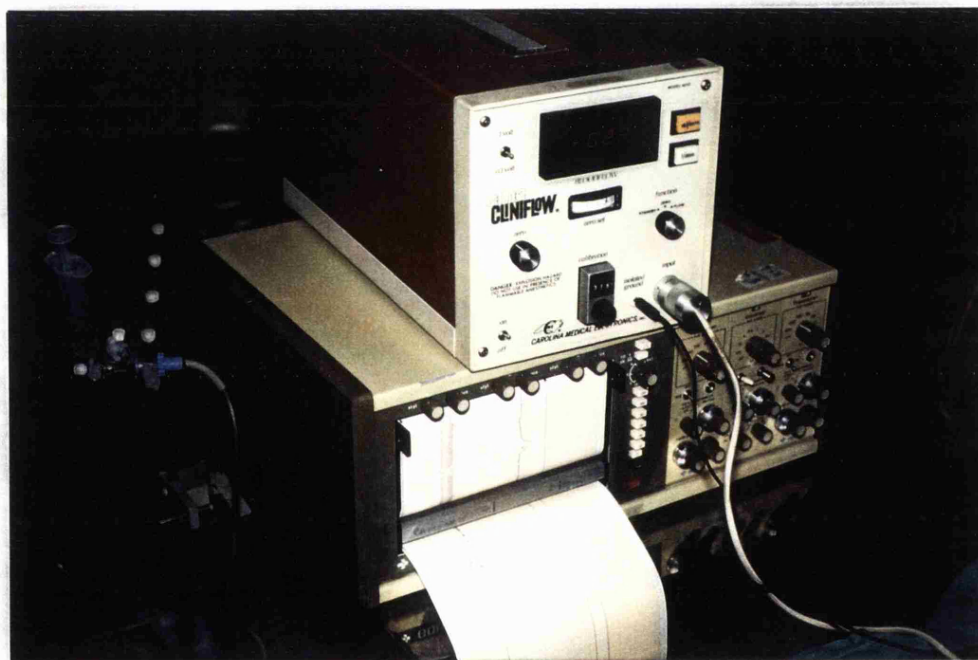
Fig 5.7   The electromagnetic flowmeter and chart recorder. To the left is the pressure transducer which was also fed into the chart recorder for measurement of graft resistance.

Graft resistance

This was determined from the ratio,

$$\text{Resistance (PRU)} = \frac{\text{Mean intragraft pressure (mmHg)}}{\text{Mean graft flow (ml/min)}}$$

with mean graft flow as measured above being used in the calculation.

Intragraft pressure was determined by cannulating the graft with a 21 guage venflon, either through a side branch (Fig 5.8) or occasionally through the hood of the graft. A manometer line was used to connect the venflon to a pressure transducer, the output of which was fed into the multi-channel chart recorder used for recording flow from the EM flowmeter, so that the two traces were
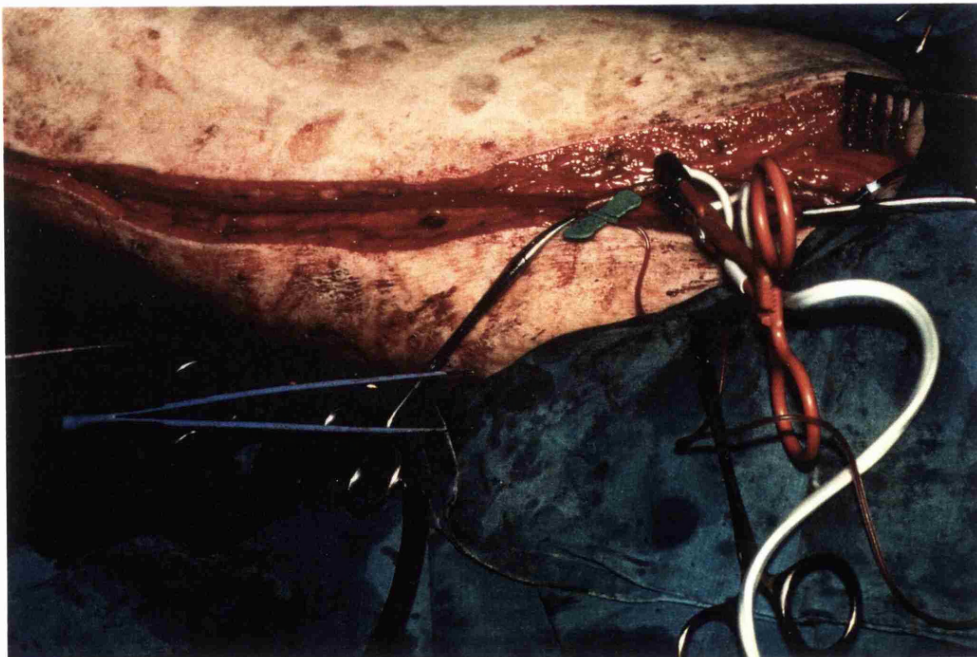
Fig 5.8   Measurement of graft resistance. The EM flow probe can be seen around the upper graft, and adjacent to this the graft has been cannulated via a side branch by a 19 guage butterfly needle. This is used both as a pressure line during resistance measurement and as a means of obtaining a completion arteriogram (see Fig 6.8).

chronologically synchronised (Fig 6.8).

The pressure reading was also diverted into the Doppler flowmeter which was able to automatically calculate resistance from simultaneous measurement of flow, the result being printed out by the chart recorder on the machine.

For the purposes of this study the EM flowmeter derived values were used when analysing the role of resistance measurement in predicting outcome since this constituted a larger group. In a smaller group it was possible to analyse resistance values as determined by the Doppler flowmeter (Appendix A).

POSTOPERATIVE ASSESSMENT

In the early postoperative period graft assessment consisted of clinical examination and Doppler pressure measurement where possible, although this was frequently hampered by the presence of wounds on the lower leg and foot. In order to improve assessment during this period a new Doppler monitoring system was developed. Following discharge all patients with a patent graft were incorporated into a graft surveillance programme run in the Vascular Studies Unit.

Continuous Doppler monitoring

This was developed in order to study graft haemodynamics in the immediate postoperative period to determine the role of more intensive monitoring at this critical stage. The system consisted of a modified Sonicaid BV380 bidirectional continuous wave Doppler unit connected via a timer and control unit to a cassette tape recorder which recorded the forward and reverse audio Doppler signals onto separate channels. Recordings were made initially with a Uher CR160 machine using standard cassette tapes which was later replaced with a Sony TCD-D10 digital
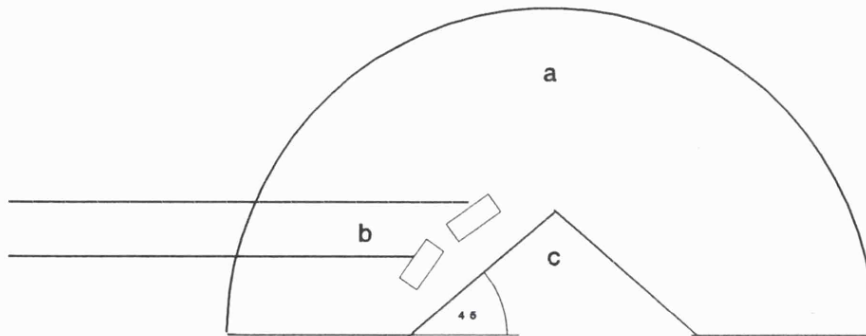
Fig 5.9 Diagram of the Doppler probe. The main resin body (a) houses the two piezoelectric discs (b) situated adjacent to the hollow (c) on its undersurface.
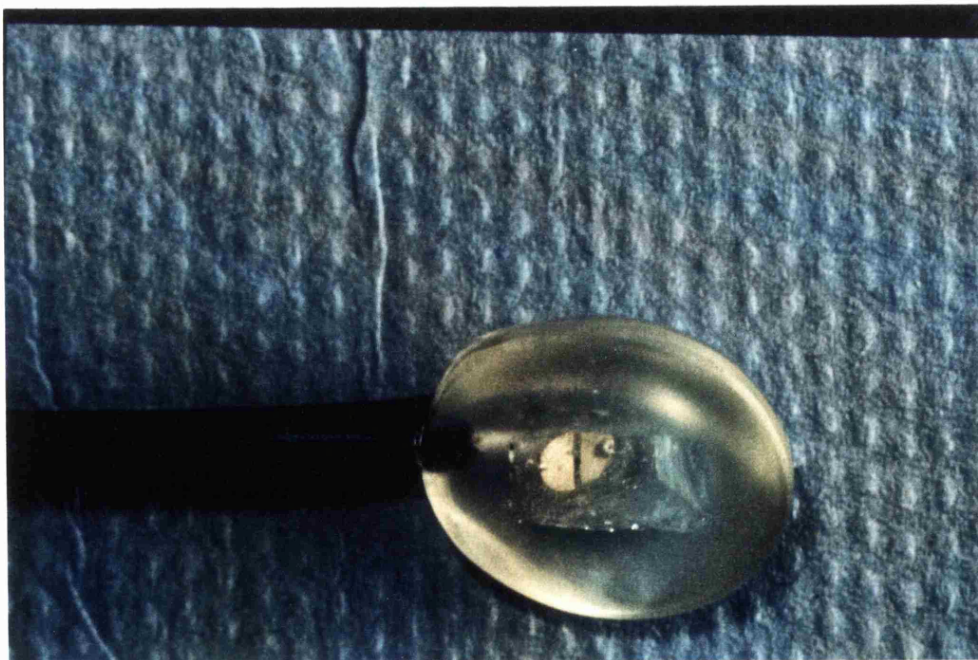
Fig 5.10 The probe in close up. The transducer discs can be seen adjacent to the hollow.

audio tape (DAT) unit (Sony Sound Tec Corp., Tokyo, Japan). The DAT unit had the advantage of automatically recording the date and time of recordings and also had a wider dynamic range. Prior to its introduction any alterations to the recorder, such as tape changes and temporary periods of switching off, had to be documented separately.

A 4 MHz Doppler probe was specifically designed for use with the system. It consisted of two piezoelectric ceramic discs, one transmitting and one receiving, set in a central hollow in a dome shaped mould of cold curing epoxy resin (Figs 5.9, 5.10). The discs were arranged in such a fashion that the generated ultrasound beam subtended an angle of 45 degrees to, and with the centrelines crossing 2 cm from, the flat undersurface of the probe. This design was specifically aimed at insonation of grafts lying superficially in the leg. Early experience showed that it was not possible to record satisfactory signals from grafts lying deeper than 3-4 cm, thus precluding monitoring of tunnelled grafts.

The timer unit controlled a relay which simultaneously switched on the Doppler and tape units when activated, and switched them off again after one minute (Fig 5.11). The timer unit could be set to activate the relay at either 15 or 30 minute intervals, providing intensive, intermittent periods of Doppler recording which were stored on tape. As well as the automatic mode it was possible to activate the system manually in order to allow additional recordings to be made as desired. When the unit was in record mode a volume switch made it possible to listen to the Doppler signal providing a ready means of instant graft assessment.

The ideal probe position for recording purposes was in the mid to lower thigh, so in order to allow ultrasound "access" to the graft the wound in this area was closed with a subcuticular suture and covered with a clear adhesive dressing. Monitoring was commenced immediately postoperatively once the patient was stabilised in the theatre recovery area. The hollow was filled with acoustic gel and the probe placed over the graft with the system switched on, its position being altered until the strongest signal was obtained. It was then fixed in position by means of a
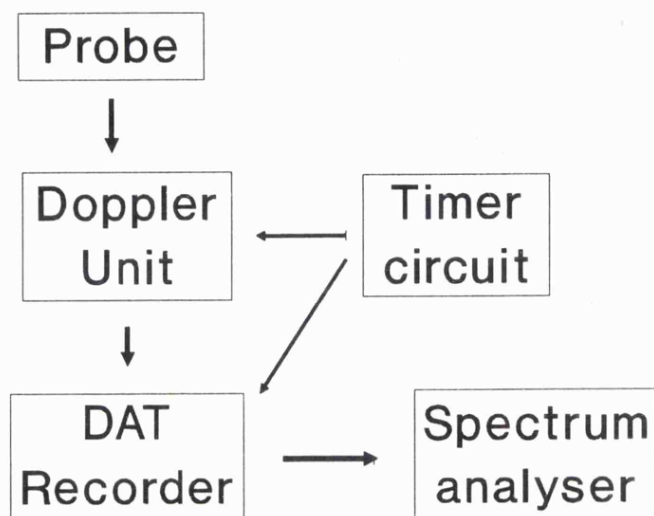
Fig 5.11   Schematic representation of the continuous monitoring system.
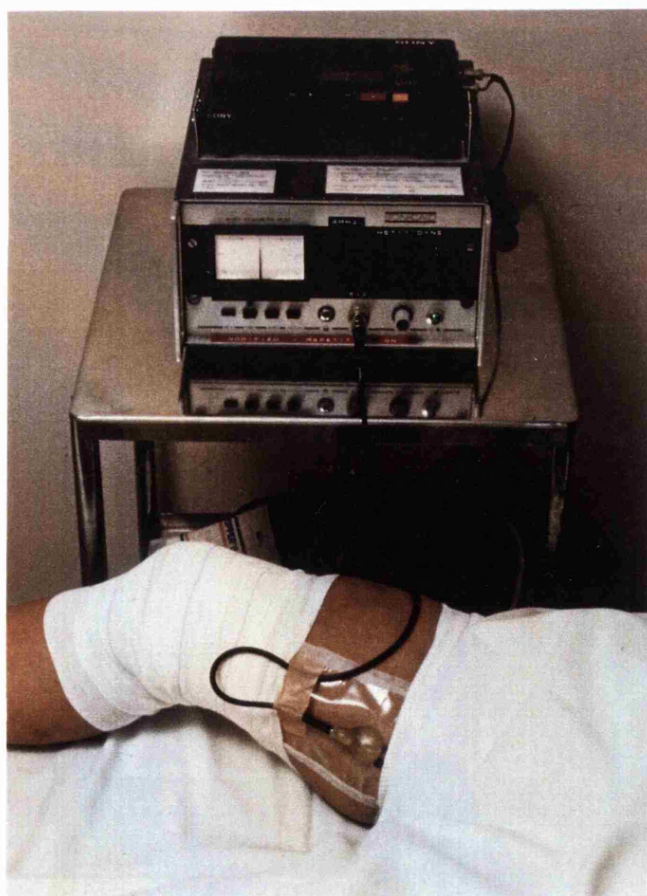
Fig 5.12   The system in use showing the probe attached in mid thigh.

double-sided adhesive ring, and the lead further secured with tape to prevent probe dislocation (Fig 5.12). Once positioned satisfactorily an initial one minute recording was made before setting the system to automatic mode.

On completion of recording the tapes were replayed through a real-time fast Fourier transform analyser providing a number of parameters for analysis, from which we used the maximum frequency and intensity-weighted mean frequency (IWMF) envelopes. From these it was possible to calculate the pulsatility index (PI) and time-averaged mean velocity (TAMV) respectively for each recording period. The PI is defined as the peak to peak excursion of the maximum frequency envelope divided by the mean value over the cardiac cycle (Fig 5.13). This ratio is low in the presence of hyperaemic flow (Fig 5.14), where there is forward flow throughout the pulse cycle and is increased in the presence of increasing peripheral resistance as flow becomes more pulsatile. It was therefore used as an indirect means of monitoring graft resistance.

The IWMF takes into account the proportion of blood cell reflectors moving at different velocities over the pulse cycle and is converted into a velocity by using the Doppler equation,

$$V = \frac{c \, Fd}{2Ft \cos\theta}$$

where c = speed of sound in blood, Fd = Doppler shift frequency, Ft = transmitted frequency, θ = angle of insonation (assumed to 45 degrees). When the IWMF is used in this equation the velocity parameter which is derived is known as the
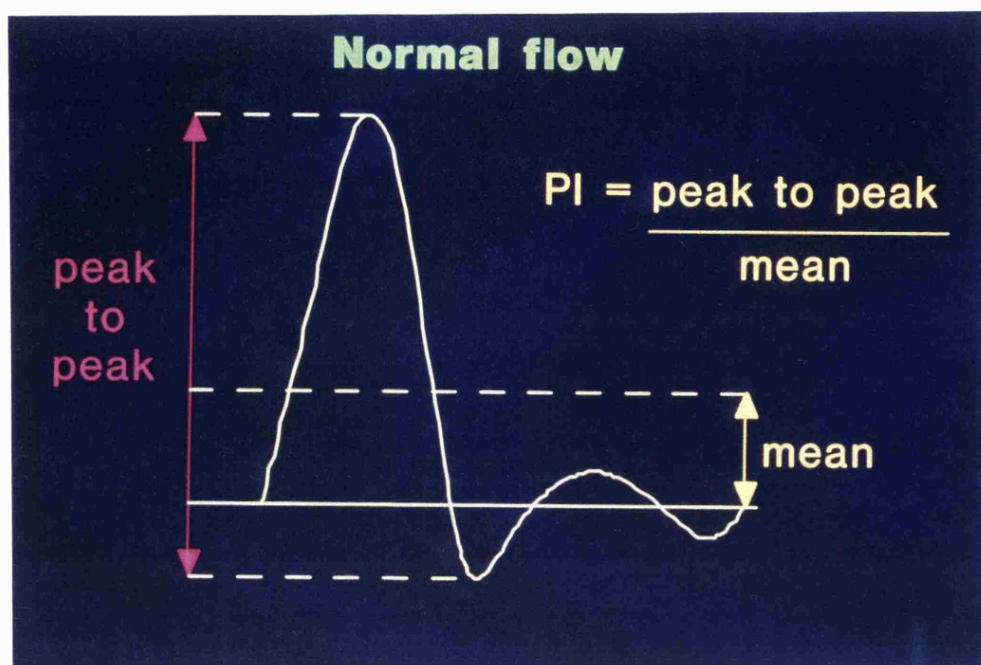
Fig 5.13 In a normally pulsatile artery the Doppler waveform is triphasic, with a reverse diastolic component. The peak to peak excursion is large compared with the mean frequency, and the pulsatility index (PI) is high.
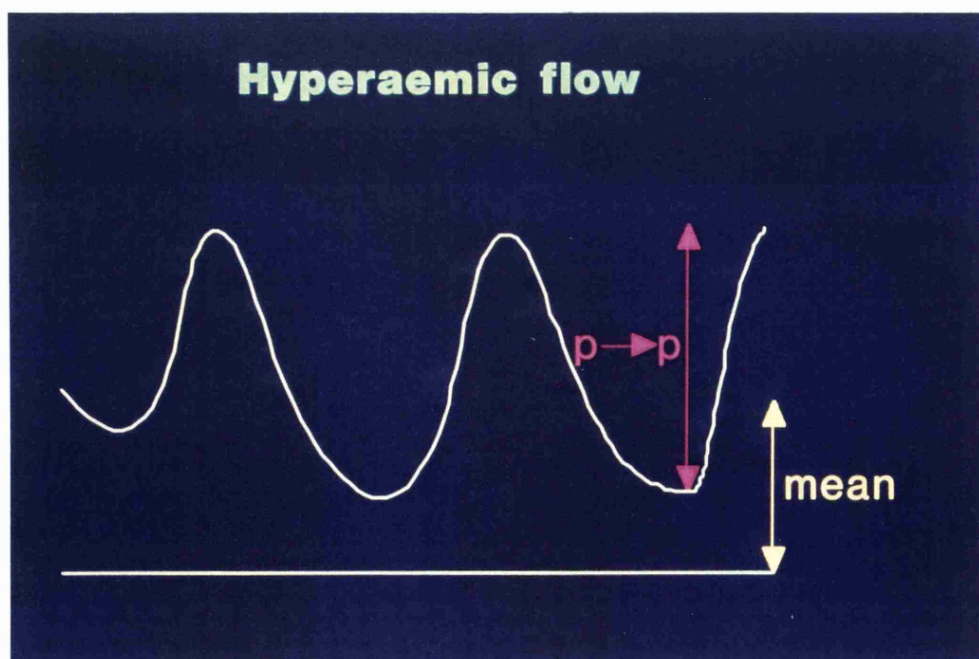
Fig 5.14 In a state of hyperaemic flow there is antegrade flow throughout the pulse cycle and the peak to peak excursion is considerably reduced compared with the mean value, leading to a lower pulsatility index (PI).

time-averaged mean velocity (TAMV). This parameter was chosen as it is directly proportional to volume flow,

Volume flow = **Time-averaged mean velocity** × *Cross-sectional area*

from which it follows that changes in flow are mirrored by changes in TAMV, allowing graft blood flow to be closely observed.

Graft surveillance programme

The aim of this thesis was to determine those factors responsible for early graft failure, in view of the considerable impact which this has on the overall success of femorodistal bypass. As a natural consequence, however, graft follow-up was extended beyond the first month as part of a co-ordinated graft surveillance programme. This was established in order to assess the durability of grafts patent at 1 month, using objective methods rather than simple clinical assessment, and also in recognition of the problems presented by the development of fibrous stenoses after the first month.

Patients were reviewed initially after one month and then at 3, 6, 9, and 12 months. At each visit clinical assessment was accompanied by Doppler ankle pressure measurement, exercise testing (where possible), and Duplex scanning. Any potential areas of stenosis were assessed more closely to determine their severity using peak velocity ratio criteria and examining the degree of spectral broadening.

Grafts considered to be at risk as a result of stenosis development were further assessed by conventional arteriography. First line treatment was with percutaneous transluminal angioplasty (PTA) provided the lesion was accessible, and this was carried out at the same time as the arteriogram in order to minimise the number of invasive procedures. Lesions not suitable for PTA were managed surgically.

CHAPTER 6

RESULTS

CLINICAL OUTCOME

Thirty-two grafts were patent with clinical improvement after 1 month and there were 10 early failures (7 occlusions, 3 haemodynamic failures). The subsequent clinical course in the cases of early failure is outlined in Table 6.1. Secondary procedures were undertaken in 7 out of 10 but none resulted in clinical improvement and amputation was required in 9, amounting to an early failure rate of 24%. There were 3 above-knee and 6 below-knee amputations, producing a BK:AK ratio of 2:1. In one case it was considered that the failed reconstruction converted the subsequent amputation from below-knee to above-knee. One patient was left unchanged with rest pain.

There were two deaths in the series, 1 due to cardiac failure and 1 to a combination of sepsis and a dense CVA. Both deaths occured after amputation (1 above- and 1 below-knee) for graft failure and resulted in a 30 day mortality of 4.8%. In addition there were 2 major complications; 1 patient with extensive ischaemic heart disease suffered a cardiac arrest and was successfully resuscitated, 1 patient with pre-existing chronic renal impairment developed acute renal failure requiring a short period of dialysis, in both cases the graft remained patent. The patient with renal failure died 6 months after operation with a patent graft, and was the only death in the intermediate period.

Pat	Outcome	Action	Outcome
1	Occluded after 2 days	Thrombectomy and distal revision	Reoccluded BKA
2	Patent, no improvement	None	AKA
3	Occluded after 2 weeks	None	Rest pain
4	Occluded after 4 hours	Thrombectomy and distal revision	Reoccluded BKA
5	Patent, no improvement	Thrombectomy and distal revision	Reoccluded BKA
6	Occluded after 10 days	Thrombectomy and distal revision	Reoccluded AKA
7	Occluded after 1 day	Thrombectomy	Reoccluded BKA
8	Occluded after 2 days	Thrombectomy	Reoccluded BKA Left hemiplegia Died
9	Occluded after 2 days	Thrombectomy and revision	Patent, no improvement BKA
10	Patent, no improvement	None	AKA Died

Table 6.1   Summary of the outcome for the 10 cases of

early graft failure

VARIABLE	SUCCESS	FAILURE	p value
Age	77 (51 - 89)	75 (59 - 81)	0.24
Diabetic	7 / 32	7 / 10	**0.015**
Standard Doppler	2 (0 - 3)	2 (1 - 3)	0.49
ABPI	0.32 (0 - 0.77)	0.56 (0.15 - 0.69)	**0.03**
Critical ischaemia			
BJS	27 / 32	9 / 10	1.0
ECD	18 / 32	2 / 10	0.1
Dependant Doppler			
limb	4 (1 - 5)	3.5 (1 - 5)	0.17
arch status	1 (0 - 2)	1 (0 - 2)	0.25
PGR			
limb	3 (1 - 5)	4 (2 - 5)	0.2
arch status	1 (0 - 2)	1 (0 - 2)	0.49
Preoperative arteriogram			
vessels	1 (0 - 3)	1 (1 - 2)	0.07
modified	2 (0 - 5)	1.5 (1 - 2)	0.07
On-table arteriogram	3 (1 - 8)	2 (1 - 4)	**0.02**
Infusion resistance			
Pre-papav	0.89 (0.36 - 1.35)	2.05 (0.67 - 4.0)	**0.003**
Post-papav	0.76 (0.36 - 1.3)	1.22 (0.45 - 4.0)	**0.005**
Graft flow			
Pre-papav	104 (35 - 400)	52 (15 - 260)	**0.001**
Post-papav	187.5 (46 -450)	88.5 (30 - 280)	**0.007**
Graft resistance			
Pre-papav	0.9 (0.19 - 1.66)	1.62 (0.28 - 4.0)	**0.0001**
Post-papav	0.48 (0.12 - 1.43)	1.12 (0.26 - 3.0)	**< 0.0001**

Table 6.2   Summary of the results for all 42 cases expressed as a median and range for each variable, and separated into success and early failure. Statistical analysis was by the Mann Whitney U test, except for diabetic status and classification of critical ischaemia which were analysed by Yates-corrected Chi^2 test.

PREOPERATIVE ASSESSMENT

Patient factors

In keeping with most series the patints in this study were elderly, although age itself was not a discriminating factor. The 6 oldest patients in the series, with ages ranging from 82 to 89, all underwent successful surgery.

There was a high proportion of diabetics, 33%, which is again a common finding, and these patients fared significantly worse than non-diabetics, accounting for 7 out of 10 early failures. The presence of diabetes itself, however, was not an independent risk factor, since it was closely related to the degree of distal disease and available runoff *ie* diabetic patients tended to require a more distal graft in the face of poorer runoff. From a practical point of view, however, the message is clear in that careful judgement must be exercised in offering distal bypass to diabetic patients, and the 50% failure rate noted in this series is probably a realistic benchmark to quote when advising patients.

The classification of disease severity was somewhat disappointing in that neither the BJS nor the ECD criteria for defining critical ischaemia were able to predict the outcome of surgery. On initial inspection the BJS criteria appeared more relevant, being 90% sensitive for graft failure, compared with a mere 20% for the ECD definition. This performance is tempered, however, by a specificity of only 16%, compared with 44% for the ECD definition. Overall the BJS definition was only 25% predictive (33% accuracy) for early graft failure, whereas the ECD criteria were only 10% predictive (38% accuracy). When the patients with tissue necrosis and ankle pressures > 50 mmHg were included with the critical ischaemia patients in the ECD group the numbers were identical to the BJS group.

Doppler methods

Using the standard Doppler technique 90 out of a possible 126 (71%) vessels were considered to be patent at ankle level. In 2 cases there was no detectable signal. Assessment of the pedal arch with the standard technique was largely unsatisfactory with acceptable signals only found in 16 (38%) cases. One notable point relates to signal quality since in most cases a degree of damping was obvious. Spectral analysis was not used, however, with signals being assessed audibly only in order to mimic the normal clinical situation. Grading on this basis would inevitably be subjectively biased and it was considered best to keep the scoring system as simple as possible *ie* 1 if patent and 0 if occluded. For the sake of uniformity the same scoring system was used in the dependant Doppler (DD) and PGR groups.

Both DD and PGR detected 102 out of 126 vessels (81%) and although there was some disagreement between the two methods, both detected at least one patent vessel in all 42 limbs. There was considerable improvement in signal quality, albeit on a subjective basis, which was confirmed by the fact that both methods were superior in assessing pedal runoff.

In terms of vessel patency DD and PGR were in agreement in 32 (76%) cases and in the 10 cases in which there was disagreement neither method was superior, DD detecting more vessels in 6 and PGR in 4 (Fig 6.1). It is interesting to note that in spite of the severity of ischaemia in the study group the majority had good runoff. When the two methods were in agreement 29 out of 32 were adjudged to have either 2 or 3 patent vessels. Where there was disagreement between the two techniques one or the other detected 3 vessel runoff in all 10 cases.

The signal augmentation provided by both DD and PGR enabled pedal arch status to be confidently assessed and graded. There was agreement between the two in 31 (74%) cases, a patent arch being detected in 23. In the 11 cases of

DD

		3	2	1
	3	**18**	2	2
PGR	2	6	**11**	
	1			**3**

Fig 6.1 Comparison of calf vessel patency when assessed by DD and PGR.

Agreement shown in bold type.

DD

		C	I	O
	C	**8**	1	
PGR	I	6	**15**	
	O	1	3	**8**

Fig 6.2 Comparison of pedal arch status when assessed by DD and PGR.

Agreement shown in bold type (C = complete, I = incomplete, O = occluded).

disagreement DD indicated a more favourable runoff situation in 10. There were 4 cases in which PGR failed to detect a pedal arch considered patent on DD assessment (Fig 6.2).

There was no difference between the DD derived limb scores (vessel plus arch score) of successful and failed grafts, and the same was true for PGR. When the two methods were compared DD limb scores were significantly higher than PGR limb scores in successful cases (p = 0.005, Wilcoxon signed rank), but there was no difference in failed cases. When pedal arch assessment was considered alone there were no differences between the successful and failed groups for either method.

For more practical purposes it is important to assess whether or not the vessel to which the distal anastamosis was fashioned was identified as being patent. DD confirmed patency correctly in 34 (81%) cases and PGR in 38 (90%). The commonest error occurred when single or 2 vessel runoff was identified but the subsequent anastamosis was to the below knee popliteal artery, which occurred in 3 out of 4 cases with PGR and in 5 out of 8 with DD. Direct continuation in the runoff is difficult to assess with non-invasive methods although if distal patency is confirmed morphological assessment is indicated to clarify the situation further. DD failed to identify the bypass vessel as patent in 3 cases and PGR in 1. These differences were not significant.

Arteriography

Preoperative arteriography visualised 58 (46%) out of 126 calf vessels, with pedal runoff demonstrated in only 15 (36%) out of 42 cases, due to a combination of either poor flow or more commonly because the foot was not included on the films. All 3 doppler methods were significantly better than arteriography in terms of vessel detection, with PGR and DD also providing significantly better assessment of pedal runoff (Tab 6.2).

<u>Vessel detection - 126</u>

```
Arteriography - 58    v    SD  -  90      p < 0.0001
                      v    PGR - 102      p < 0.0001
                      v    DD  - 102      p < 0.0001
```

<u>Pedal arch assessment - ? patent</u>

```
Arteriography - 15    v    PGR - 30       p = 0.001
                      v    DD  - 34       p < 0.0001
```

Table 6.3   Comparison of preoperative arteriography with doppler methods (Chi^2 analysis).

Although the detection rate was lower with arteriography there were still only 5 limbs in which no vessel at all was seen and a successful bypass was subsequently carried out in 4 of these, indicating that failure to demonstrate distal runoff on arteriography is not necessarily a contraindication to limb salvage. In addition there were 6 cases in which either single (5) or two (1) vessel runoff was identified in the mid or distal calf without demonstrating continuity with proximal inflow and the subsequent bypass was to the below knee popliteal artery. At least one disease free vessel patent to the ankle was only seen in 3 of these 6.

In the remaining 31 cases the vessel to which the distal anastamosis was ultimately fashioned was visualised on the arteriogram, but was poorly demonstrated in 13. In these instances the vessel was either considered to be diseased or its full course was not adequately demonstrated. In general preoperative arteriography gave a poor overall impression of distal runoff and was only judged to be an adequate guide to the site of reconstruction in 18 (43%) cases.

INTRAOPERATIVE METHODS

(i) Pre-reconstruction

On table arteriography

Delivery of contrast directly into the distal circulation at a pre-selected level produced a marked improvement in runoff definition. The arteriograms obtained were used as the final decider for siting the distal anastamosis and in 32 cases demonstrated continuous runoff into the foot via at least one disease free vessel. In the remaining 10 cases the only demonstrable runoff vessel was considered to be disease free but narrow in 6 and of poor quality in 4. In the presence of poor runoff on the on table arteriogram 4 / 10 grafts failed compared with 6 / 32 in the group with good runoff.

On table arteriography visualised patent pedal vessels in 36 (86%) cases. In 6 of these a complete pedal arch was demonstrated but in the majority the distal part of the foot was not included on the films and the arch status could not be properly determined. The more usual picture was of patent vessels running into the foot proximally with a variable degree of minor vessel filling, particularly around the heel (Fig 3.6).

Infusion resistance (IR)

Continuous flow

Refinement of the technique originally developed by Parvin (1985) resulted in considerable improvement in the time needed to carry out measurements (10-15 min), enabled post-papaverine measurements to be reliably made, and the new pump allowed instant access to the results (Fig 6.3). In the presence of a very high
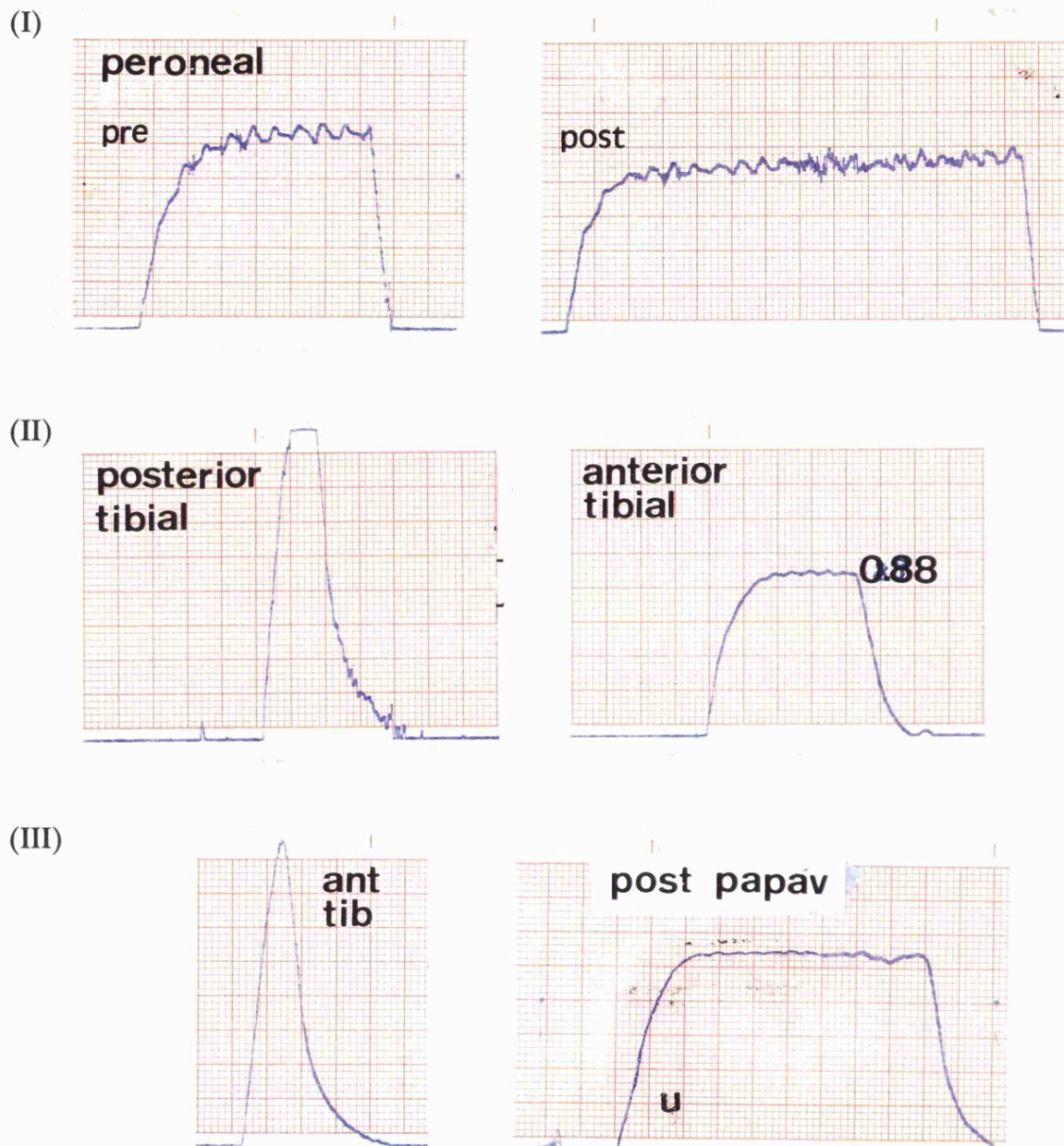
Fig 6.3 Three examples of resistance measurements. In (I) the resistance is being measured in the proximal peroneal artery. There is a small fall in resistance following administration of papaverine. (II) An example in which two vessels were seen on the on table arteriogram, the resistance of the anterior tibial is clearly more favourable. (III) An initially high resistance (> 1.8 PRU) is reduced after administration of papaverine.

resistance the chart recorder showed a rapid, steep upstroke and in these cases the pump was switched off and the resistance graded roughly according to where the recording stopped, although the true value was not actually measured. This was done in order to prevent damage to the vessel as a result of the high pressures generated and also to prevent damage to the glass syringe. In earlier studies rapid generation of very high resistance led to the syringes shattering.

There was a significant difference ($p = 0.003$) between the IR before papaverine in successful (med 0.89, range 0.36 - 1.35 PRU) compared with failed (med 2.05, range 0.67 - 4.0 PRU) grafts. For practical purposes, however, the scatter seen in Fig 6.4 indicates that the predictive power of this measurement is limited when considering individual cases. At a cutoff value of > 1.4 PRU the IR was 100% predictive for early failure, achieving 60% sensitivity.

The results for IR after papaverine in successful (med 0.76, range 0.36 - 1.3 PRU) and failed (med 1.22, range 0.45 - 4.0 PRU) grafts are seen in Fig 6.5. Again there was a significant difference ($p = 0.005$) between the two groups, associated with a wide scatter. A cutoff value of > 1.3 PRU was 100% predictive for graft failure but was only 50% sensitive. In 34 cases papaverine induced a fall in resistance (range 0.02-1.52 PRU), which in the majority was only modest, being < 0.2 PRU in 27 cases. The degree of fall was not related to outcome although interestingly the one spurious case, with a fall of 1.52 PRU (the next highest was 0.5 PRU) was in a graft which failed. In 5 cases there was no recordable effect, 4 having an initial IR > 3.0 PRU all of which failed and one with a favourable IR of 0.36 in which the outcome was successful. In the remaining 3 cases a small rise was noted. Two of these, with rises of 0.02 and 0.04 PRU, had a successful outcome, and one, with a rise of 0.14 PRU, subsequently failed.

The use of papaverine, therefore, failed to improve the predictive power of IR measurement. For both sets of data improved sensitivity could only be achieved at the expense of a reduction in specificity.
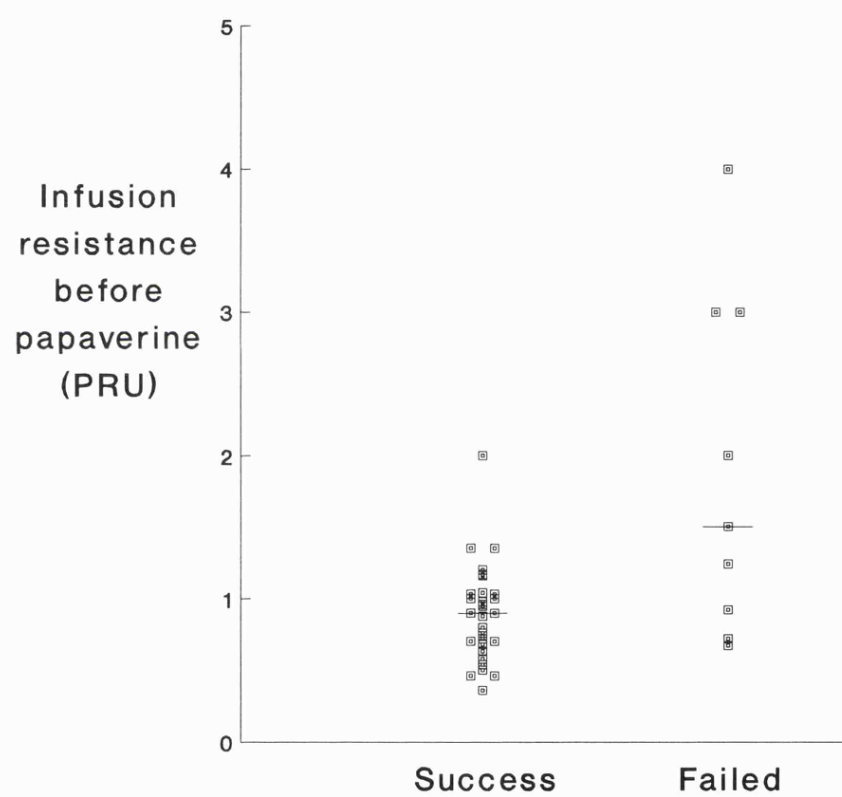
Fig 6.4   Infusion resistance before papaverine, success *v* failure.

Mann Whitney U Test, p = 0.003
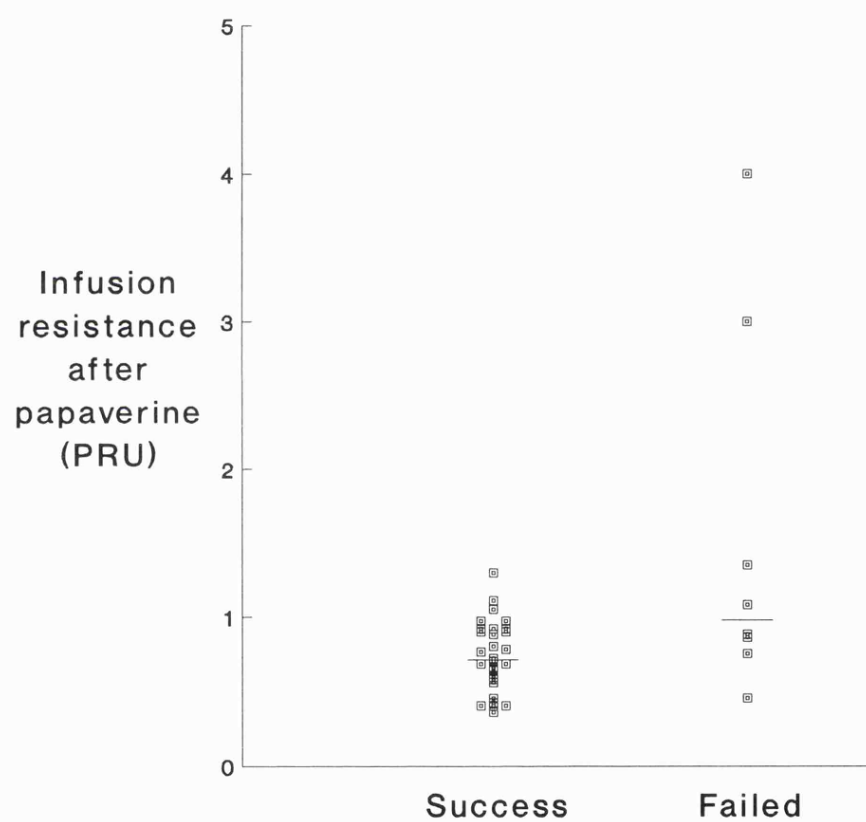
Fig 6.5   Infusion resistance after papaverine, success *v* failure.

Mann Whitney U Test, p = 0.005

There was no significant correlation between the IR before papaverine and either the DD or PGR limb scores, indicating that neither method could be used to predict resistance preoperatively. Similarly the correlation between the IR after papaverine and either of the non-invasive methods failed to reach significance. Comparison between the two sets of IR measurement and the preoperative arteriogram scores also failed to show any significant correlation.

Continuous pressure

In spite of this favourable report, however, the device proved to be completely unreliable when applied in this study. It was not possible to reliably generate any sort of constant pressure due to uneven catching between the metal components in the main barrel, and measurements were made in only three cases before the technique was abandoned. The problem appeared to be related to differential expansion of the individual components during the sterilisation process. Attempts to modify the principal components in the Dept of Medical Engineering failed to improve the running of the syringe. A number of measures were tried in the laboratory, with different lubricants being used, but further bench testing confirmed the clinical finding that the system was unable to generate and maintain a constant physiological pressure. In view of these findings no further clinical studies were undertaken.

(ii) Post reconstruction

Graft flow

There was a significant difference ($p = 0.001$) between graft flow before papaverine in successful (med 104, range 35 - 400 ml/min) and failed (med 52, range 15 - 260 ml/min) grafts (Fig 6.6). In terms of predictive power, however, resting graft flow was a poor discriminator between success and failure due to considerable overlap.
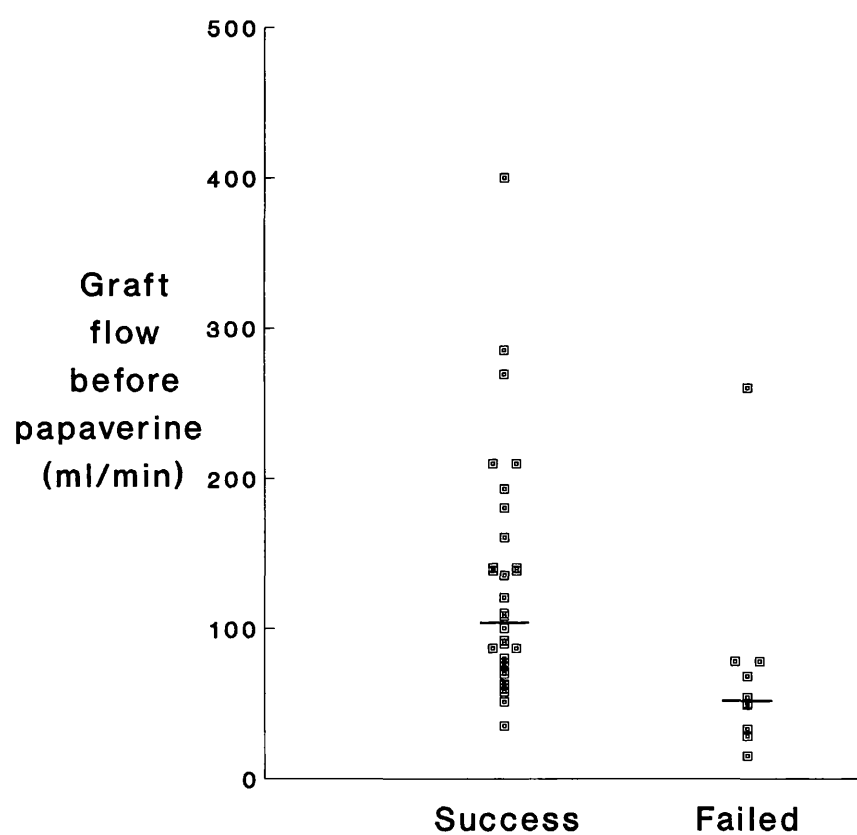
Fig 6.6   Graft flow before papaverine, success v failure.

Mann Whitney U Test, p = 0.001
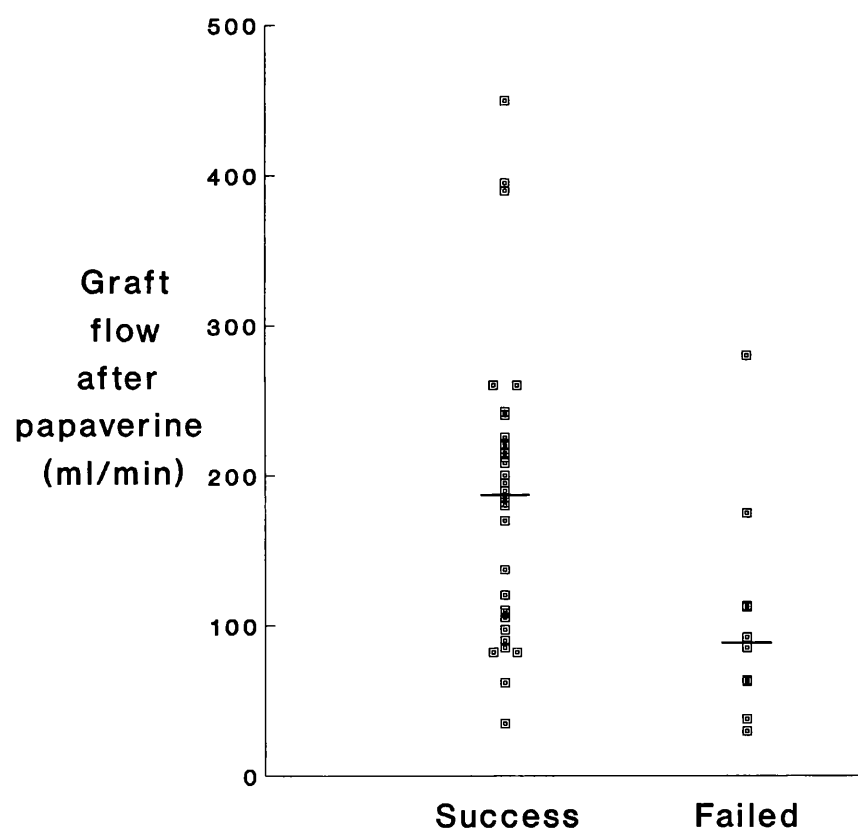
Fig 6.7   Graft flow after papaverine, success *v* failure.

Mann Whitney U Test, p = 0.007
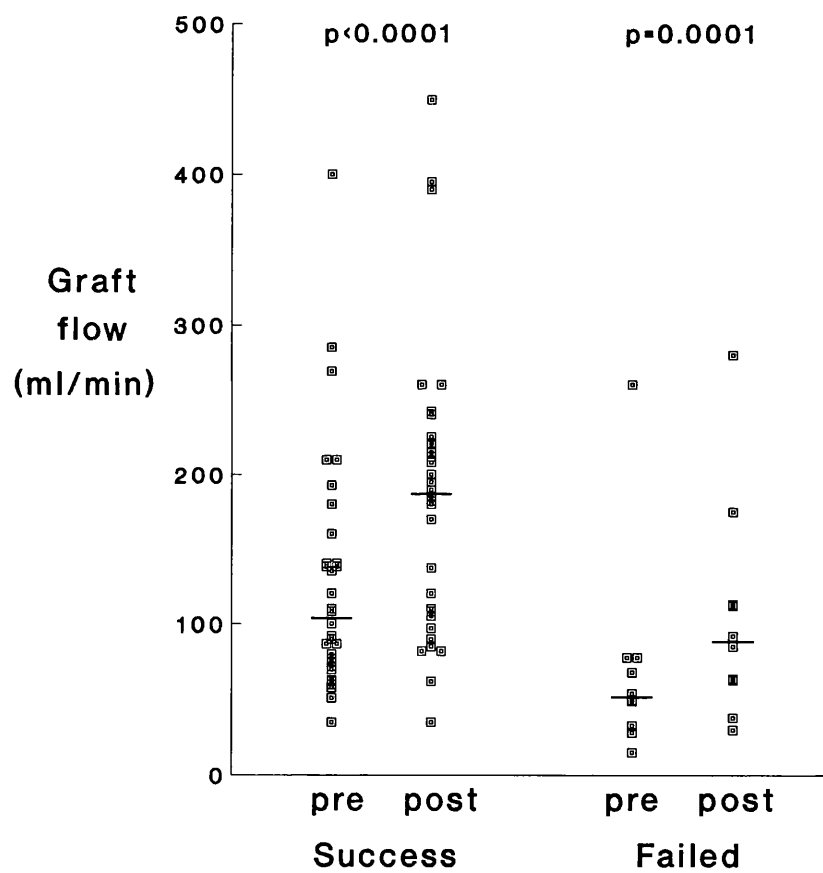
Fig 6.8   Graft flow before and after papaverine in successful and failed grafts. The differences are highly significant (Wilcoxon signed rank test for matched pairs), but indicate that papaverine does not improve the separation between the two groups.

A flow of 80 ml/min appeared to represent a watershed since 21 out of 22 grafts with a flow above this level were successful. The scatter seen in Fig 6.6, however, meant that of the 20 grafts with a flow < 80 ml/min, 9 failed and 11 were successful. Failure could only be predicted with certainty with a flow of < 35 ml/min, but this only identified 3 out of 10 cases, all 3 having had a pre-papaverine IR > 1.4 PRU. Raising the cutoff level to 50 ml/min only increased the sensitivity to 40% by the addition of 1 more case, and reduced the specificity to 97%.

The addition of papaverine actually resulted in poorer discrimination between the two groups (Figs 6.7, 6.8). Although the difference between successful (med 187.5, range 46 - 450 ml/min) and failed (med 88.5, range 30 - 280 ml/min) grafts was again significant (p = 0.007), there was still considerable overlap in the low flow range. Four out of the 10 cases of early failure and 25 out of 32 successful grafts had a post-papaverine flow of > 100 ml/min leaving 13 grafts with a post-papaverine flow of < 100 ml/min, 6 of which failed and 7 of which were successful. For practical purposes there was no clinically useful cutoff level which could be used to reliably identify high risk grafts.

Graft resistance (GR)

Measurement of GR (Fig 6.9) improved the separation between success and failure compared with measurement of flow alone. Prior to the administration of papaverine there was a highly significant difference (p = 0.0001) between successful (med 0.9, range 0.19 - 1.66 PRU) and failed (med 1.62, range 0.28 - 4.0 PRU) grafts (Fig 6.10). A GR of > 1.7 PRU was 100% predictive of early failure, with 5 out of 10 cases identified in this manner (50% sensitivity), all 5 having a pre-papaverine IR > 1.4 PRU. A lower level of > 1.25 PRU identified 9 out of 10 early failures, thus improving the sensitivity to 90%, and reducing the specificity to 91%.

In a similar fashion to the IR measurements the administration of papaverine
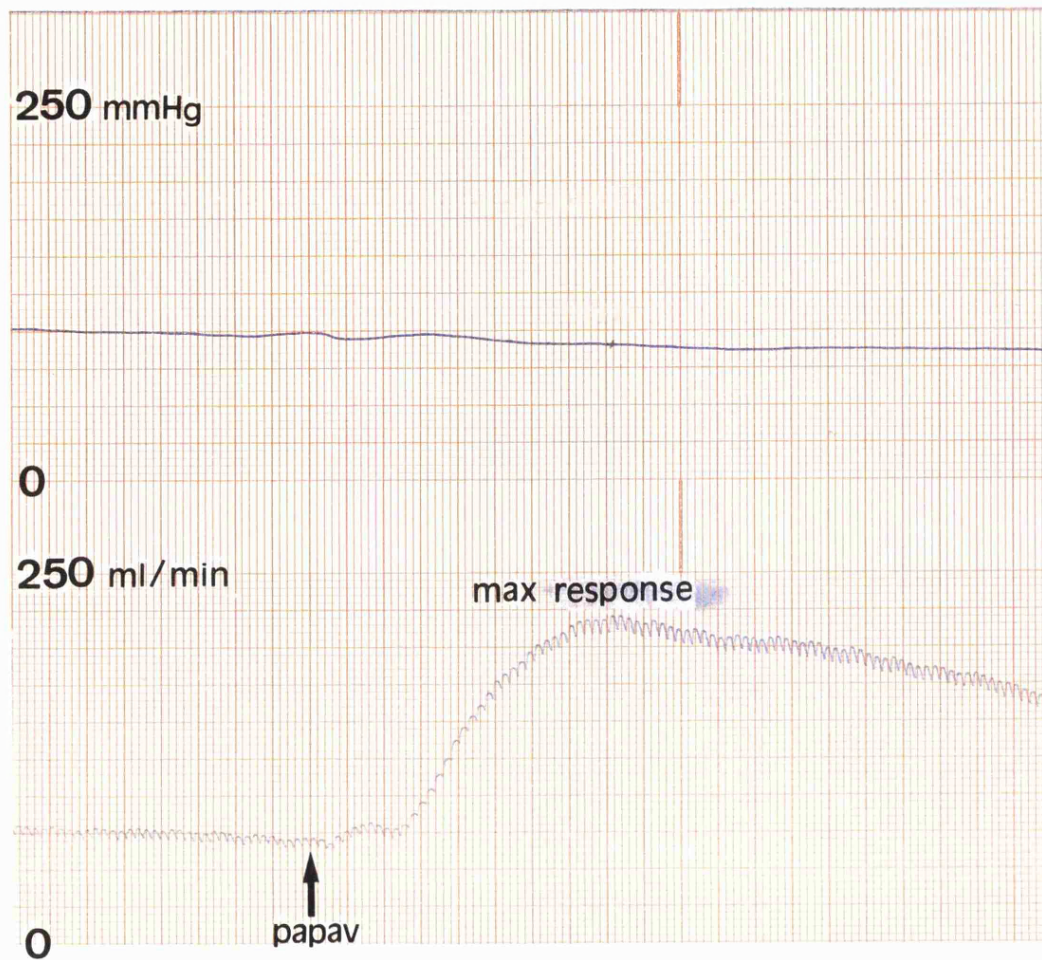
Fig 6.9 Completion measurements of mean pressure (top) and mean flow (bottom) before and after administration of an intragraft bolus of papaverine.

failed to improve on the separation seen in the pre-papaverine group, and was a poorer predictor of outcome (Figs 6.11, 6.12). The difference between successful (med 0.48, range 0.12 - 1.43 PRU) and failed (med 1.12, range 0.26 - 3.0 PRU) grafts, was again highly significant, but there was more overlap in the higher range when compared with fig 6.10. A cutoff value of >1.5 PRU was 100% predictive of early failure, but only achieved 30% sensitivity. A more reasonable cutoff level of 1.0 PRU resulted in a specificity of 94% and sensitivity of 64%.
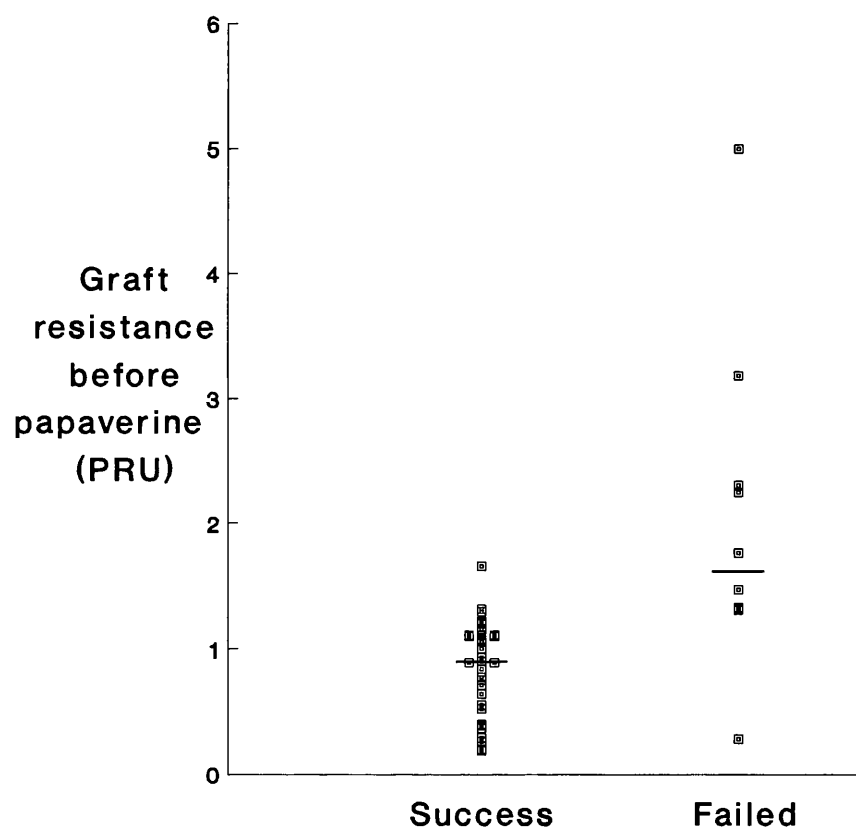
Fig 6.10   Graft resistance before papaverine, success *v* failure.

Mann Whitney U Test, p = 0.0001
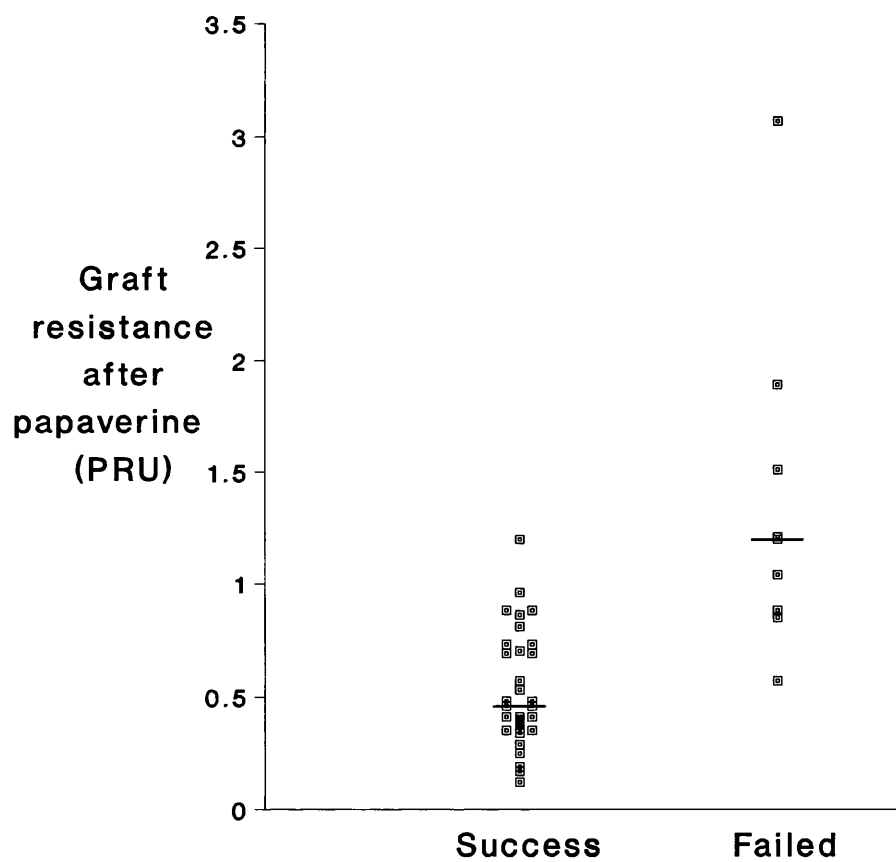
Fig 6.11   Graft resistance after papaverine, success v failure.

Mann Whitney U Test, $p = <0.0001$
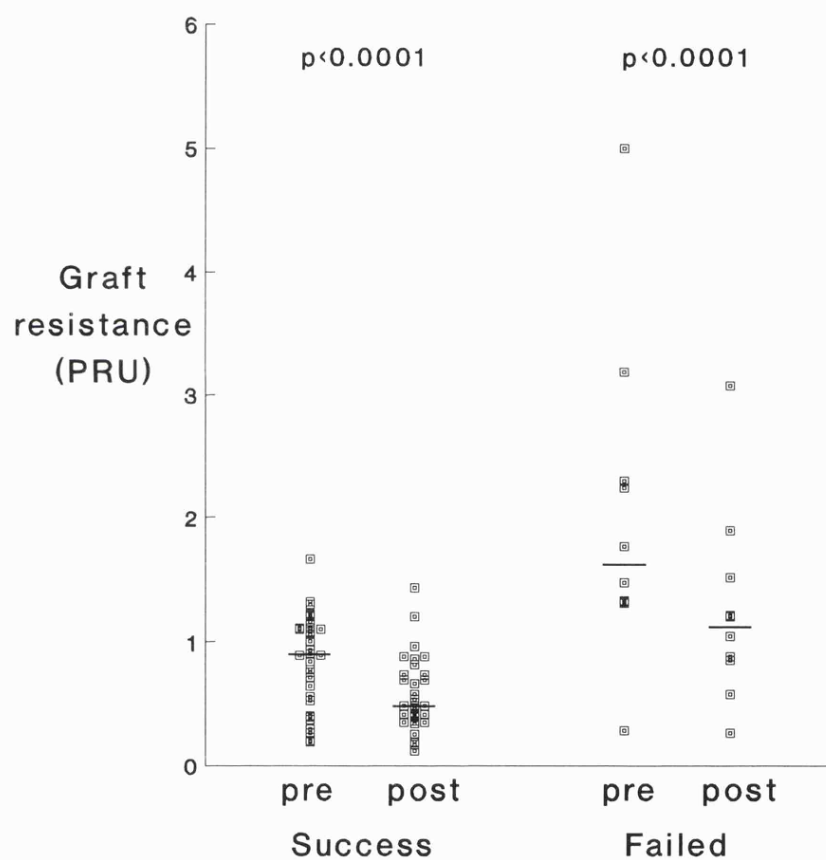
Fig 6.12 Graft resistance before and after papaverine in successful compared with failed grafts. The differences are highly significant (Wilcoxon signed ranks test for matched pairs), but indicate that papaverine has a similar effect in both groups without improving separation.

In terms of clinical relevance, therefore, the pre-papaverine results were again the most relevant, with three categories being identified;

(1) *High risk* - GR > 1.7 PRU, all grafts failed.

(2) *Borderline* - GR 1.25-1.7 PRU, 4 out of 7 failed.

(3) *Favourable* - GR < 1.25 PRU, 32 out of 33 successful.

Completion arteriography

A satisfactory arteriogram was obtained in 40 / 42 cases. In 31 of these the appearances were considered to be acceptable and to represent the best achievable result, with continuity seen between at least one good quality runoff vessel and the pedal circulation. In the majority (24 / 31) the pedal arch was adjudged to be incomplete, principally because there was only single vessel runoff. A complete arch was demonstrated in the other 7.

There were 9 cases in which the arteriogram revealed potential problems, 5 due to poor runoff and 4 to technical errors. In the former group the distal graft and anastamosis were considered to be satisfactory with the poor runoff having already been seen on the pre-reconstruction on-table arteriogram, and it was felt that the situation could not be improved upon. Four of these 5 grafts subsequently failed. In the latter group there was 1 intimal dissection and 3 distal stenoses. Three out of 4 errors were recognised and corrected at the time, with an acceptable result confirmed on repeat arteriography. In the other case the significance of a stenosis in the proximal anterior tibial artery was not fully appreciated and the graft subsequently failed. The main reason for accepting the situation in this case was the finding of a post-papaverine graft resistance of 0.57 PRU. In retrospect, however, the pre-papaverine flow (68 ml/min) and resistance (1.31 PRU) were truer indicators of outcome.

There were two unsatisfactory arteriograms, one failing to include the foot and one failing to demonstrate the runoff at all due to a timing error. In both cases a

further arteriogram was not taken, reconstruction being considered to be adequate on the basis of haemodynamic measurements. In the first case a good runoff vessel was seen down to the distal calf and the pre-papaverine flow (260 ml/min) and resistance (0.28 PRU) were very favourable, in spite of which the graft occluded after 5 days. In the second case the pre-papaverine flow (50 ml/min) and resistance (1.3 PRU) were more suggestive of a poor outcome and the graft occluded after 2 weeks. It remains a matter of conjecture whether or not a remediable cause would have been demonstrated had the arteriogram been adequate.

POSTOPERATIVE MONITORING

Continuous Doppler monitoring

Satisfactory recordings were obtained from all but one graft with the intensive monitoring system. In this single case the thigh was markedly obese and it was not possible to obtain a satisfactory signal from the graft, which unfortunately occluded after 2 weeks. Analysable data was therefore available for the 32 successful grafts and 9 out of 10 failed grafts. Recordings from the early cases revealed a high level of background noise produced by monitoring equipment in the theatre recovery area which resulted in the data being unsuitable for analysis. In subsequent cases this problem was avoided by switching off the monitors during recording periods.

Successful grafts

The majority of successful grafts (29/32) were characterised by a mean PI of <2 and a mean TAMV of >10 cm/s. In 17 cases the TAMV was greater than 20 cm/s, which is equivalent to a flow of 235 ml/min in a vein with a diameter of 5 mm. This combination of a low peripheral resistance and good volume flow is indicative of
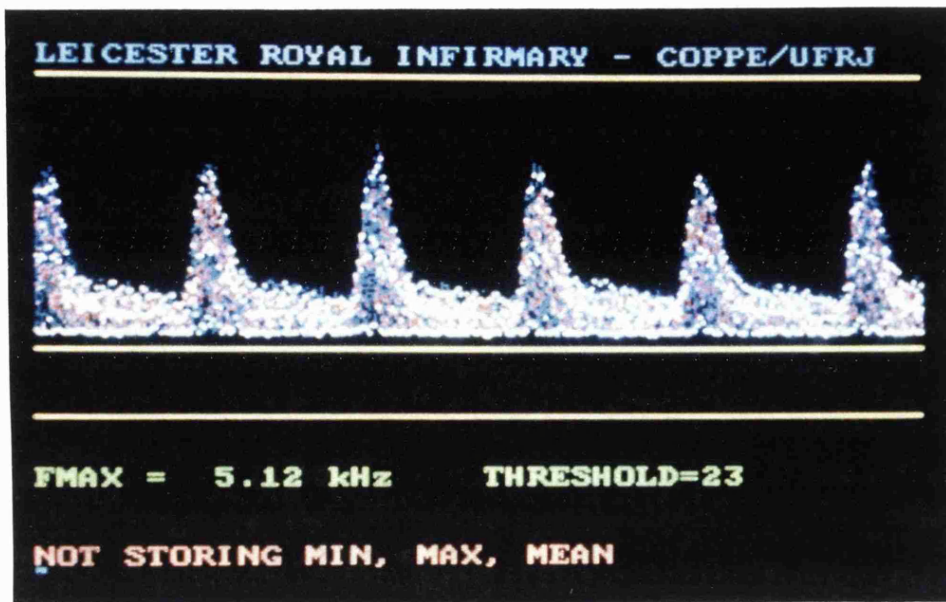
Fig 6.13 Hyperaemic Doppler waveform in a successful graft.
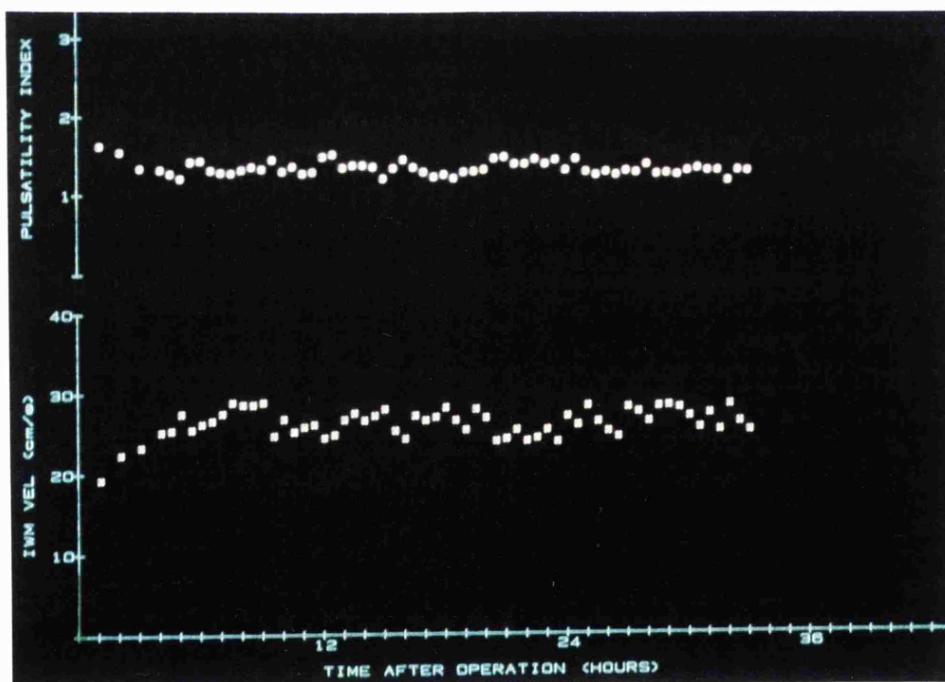
Fig 6.14 Graph of pulsatility index (top) and intensity weighted mean velocity (bottom) against time, following successful reconstruction. There is an early fall in PI and a corresponding rise in IWMV as hyperaemic flow is established over the first 6 hours. Flow is relatively stable following these early changes.

hyperaemia and this would be expected following successful reconstruction for severe ischaemia. This hyperaemic pattern established itself during the first few hours postoperatively and thereafter remained stable, apart from minor fluctuations, throughout the recording period (Figs 6.13, 6.14).

The remaining three grafts exhibited surprisingly poor flow characteristics (Fig 6.15), with the TAMV persistently below 10 cm/s and the PI ranging between 2 and 3. In spite of this "low flow" state clinical improvement was observed in all 3 cases, with patency sustained thereafter.
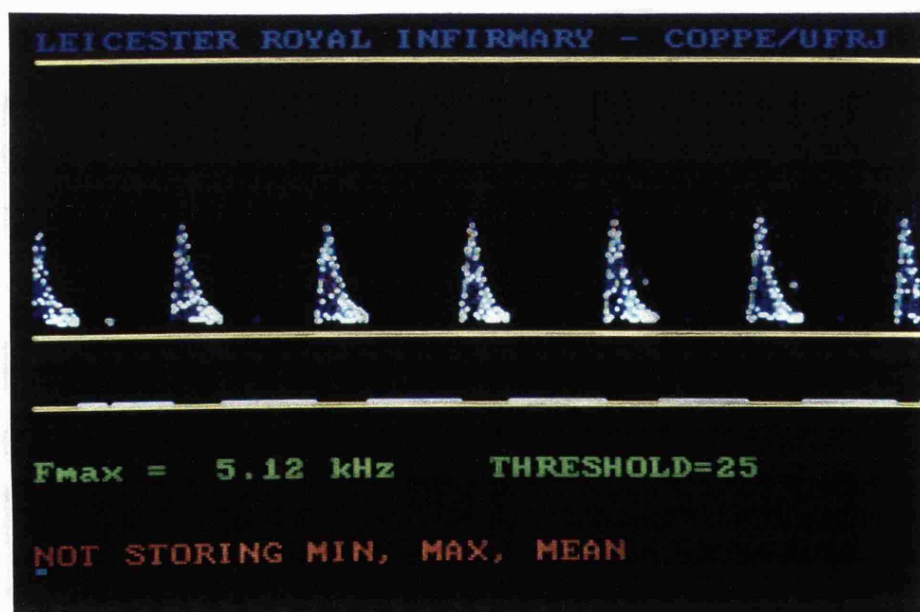
Fig 6.15 Doppler waveform demonstrating the "low flow" conditions seen in 3 cases which were nevertheless successful. Compare with Fig 6.13.

Failed grafts

Twelve sets of data were available from the nine failed grafts in which successful recordings were made, monitoring being carried out in 3 cases after revisional surgery. Three categories indicative of failure emerged;

(1) grafts developing a very pulsatile signal (PI >6), occluding within a few hours,

(2) grafts exhibiting progressive departure from initially "successful" characteristics and occluding after a few days,

(3) grafts with poor flow characteristics which remained patent but did not result in clinical improvement (haemodynamic failure).

Group 1 There were four cases in which hyperaemic flow was never established, with the rapid development of abnormally pulsatile flow being seen instead (Fig 6.16). This was characterised by a large component of reverse diastolic flow which would not be expected in these circumstances, reflected in an abnormally high PI which rose rapidly in the first few hours. The consequence of this extremely high resistance was a low TAMV representing negligible flow, followed by graft thrombosis within a few hours.

Group 2 In two cases the initial flow patterns appeared to be favourable, one demonstrating "low flow", and the other hyperaemia. In both cases, however, a progressive, unexpected departure from the original pattern towards more pulsatile flow (PI >3, TAMV <10 cm/s) was observed within the first 24 hours. This resulted in graft occlusion after 3 and 9 days respectively (Fig 6.17).

During the initial work with the system a similar early departure from initially hyperaemic flow was witnessed in a graft performed for claudication (Brennan *et al* 1991), although this patient has not been included in this thesis. This graft went on to long term patency, suggesting that the early changes from an initially favourable haemodynamic pattern are of particular importance in grafts performed for critical
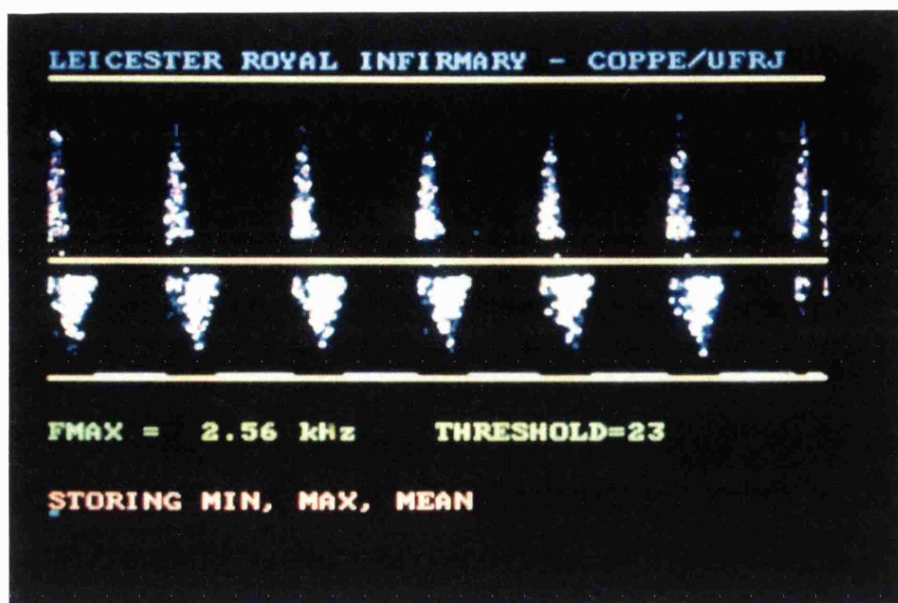
Fig 6.16   Abnormally pulsatile waveform in a graft failing within a few hours. Note the large component of reverse diastolic flow.
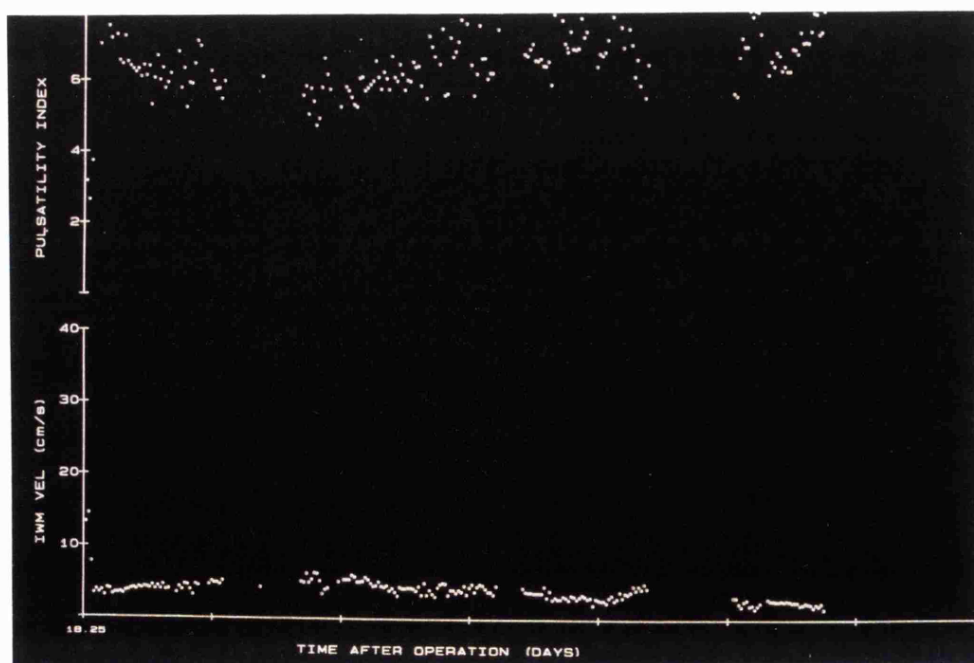
Fig 6.17   Graph of pulsatility index (PI) and intensity weighted mean velocity (IWMV) against time showing an early departure from initially favourable haemodynamics. This graft failed after 9 days.

ischaemia, as was the case with the two grafts described here.

In addition there were two further grafts, one failing after 5 and the other after 10 days, in which hyperaemic flow was seen during the first 24 hours, with monitoring being discontinued thereafter. These cases were both studied during the early part of the series when the reliability of the system was being assessed and monitoring periods were consequently restricted. In both cases there was no indication of subsequent failure but the timescale involved suggests that if monitoring had been continued for longer, changes similar to those seen in the two cases in this group may have been observed. In both cases the intraoperative measurements were considered to be favourable. In the first case re-exploration revealed that the distal vein was narrow and had been damaged, presumably as a result of valvulotome trauma, and in the second case there was a stenosis distal to the anastamosis on the completion arteriogram which was not corrected. These cases serve to illustrate the point that technical inadequacies can result in an initially favourable result, but that flow and pressure measurements should not be used as a reason for not correcting problems at the first sitting. In both cases the result of this course of action was a below knee amputation.

Group 3   This group contained four cases of haemodynamic failure, with the TAMV in all 4 being persistently below 10 cm/s. In 3 out of 4 this poor flow was accompanied by a PI >3.5, which was higher than that seen in the successful grafts displaying similarly poor flow. In two of these the distal anastamosis was to the anterior tibial artery at ankle level, and in the third to the below knee popliteal artery in the presence of poor runoff. In the fourth case the original graft to the peroneal artery had thrombosed (one of the cases from *Group 1*), and the distal anastamosis was subsequently resited to the below knee popliteal artery, again in the presence of poor runoff. In this case the PI reached a maximum of 2.5, and hence the graft remained patent, but prior thrombosis of the principal runoff vessel precluded any improvement in distal perfusion.

When the data from the monitoring system are considered as a whole, five distinct haemodynamic patterns were observed:

(i) Stable hyperaemia (PI < 2, TAMV > 10 cm/s) was seen in 31 cases, 29 of which remained patent.

(ii) "Low flow" (PI < 3, TAMV < 10 cm/s) was seen in 4 cases, 3 of which remained patent, with one case of haemodynamic failure.

(iii) Rapid onset of highly pulsatile flow was seen in 4 cases, all of which occluded within 24 hours.

(iv) Progressive departure from initially hyperaemic flow was seen in 2 cases, both of which occluded after a few days.

(v) High resistance poor flow, in which the PI was > 3.5, was seen in 3 cases, all of which resulted in haemodynamic failure.

If patterns (i) and (ii) are accepted as indicative of a successful outcome, with any deviation from this taken as a sign of impending failure, then it can be seen that the system reliably predicted outcome in 41 out of the 44 (93%) sets of recordings.

Graft surveillance

Analysis of the data from the graft screening programme is not included in this thesis, but the 12 month follow-up is briefly summarised in order to emphasise the impact of this aspect of femorodistal bypass.

Of the 32 grafts patent at one month 29 were incorporated into our surveillance programme, with 3 being followed up at their referring hospital. Clinical outcome in these 3 was by letter from the referring consultant, with all 3 being patent at one year. Of the 29 recruited to our own programme a significant stenosis was detected on Duplex scanning and confirmed with arteriography in 8 (28%) cases, 5 being in situ and 3 reversed. One reversed graft with a proximal anastamotic narrowing was corrected surgically (Fig 6.18), and the remaining 6 lesions (2 mid, 5 distal) were corrected by PTA. Treatment was successful in 7 cases

adjudged by patency on Duplex and continued clinical improvement, but in one case PTA of a distal lesion was associated with partial thrombosis of the runoff, presumably due to embolisation, and although the graft remained patent the patient was left with rest pain.
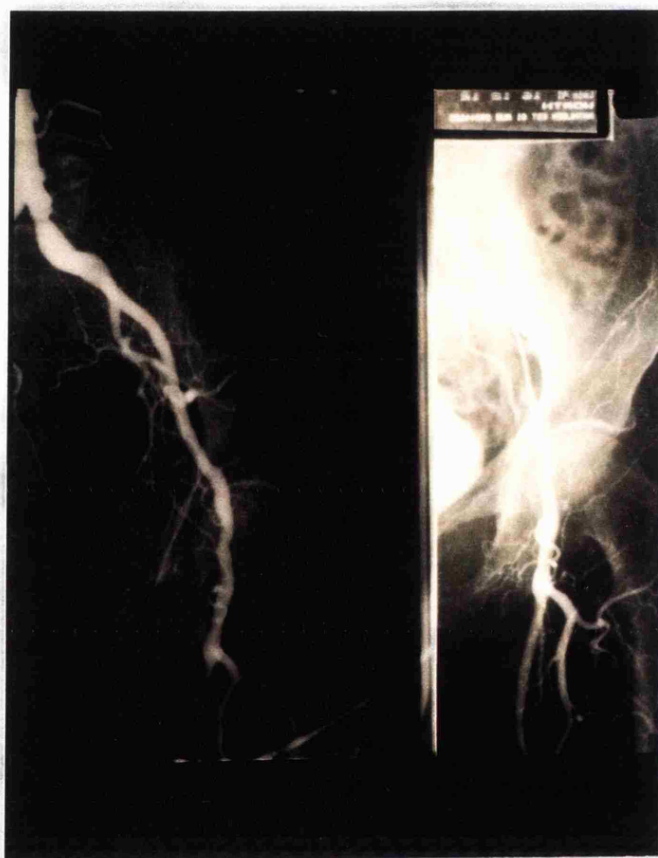
Fig 6.18 A stricture associated with the proximal anastamosis of a reversed vein graft before (left) and after (right) surgical correction with a vein patch.

CHAPTER 7

DISCUSSION AND FUTURE DEVELOPMENTS

The primary early failure rate of 24% in the prospective series was lower than the 30% rate seen in the retrospective study. Revisional surgery following graft failure, however, failed to improve patency in the prospective series but resulted in a secondary patency of 15% in the retrospective group. The differences can be explained by a number of factors, the most obvious of which is disease severity. There was a much higher proportion of patients with critical ischaemia in the prospective group with more extensive distal disease, reflected in the fact that in 29 out of 42 (69%) reconstruction was to a single calf vessel, compared with only 29% in the earlier study.

Analysis of the data revealed that in 7 (Nos. 2, 3, 4, 5, 8, 9, 10) out the 10 cases of early failure the only identifiable cause was inadequate distal runoff. In one case (6) the graft was sited proximal to a stenosis and the fault, although recognised, was not corrected due to favourable post-papaverine measurements both prior to and after reconstruction. In the remaining 2 cases (Nos. 1, 7) subsequent exploration revealed that the distal vein segment was inadequate, resulting in irretrievable thrombosis.

That none of the early failures in the present study were salvageable, compared with 19 in the retrospective group, is at first sight disappointing but indicates that the careful intraoperative assessment that was applied led to the best achievable result at the first sitting, and that simple thrombectomy with or without distal revision may not improve matters in the event of thrombosis or haemodynamic

failure.

In both series the severe consequences of early failure following femorodistal reconstruction were clearly illustrated by the amputation rate, 80% and 90% respectively. There was, however, an improvement in the BK:AK ratio from 0.6 to 2.0, suggesting that even in the presence of severe disease early graft failure does not necessarily compromise healing of a BK stump.

PREOPERATIVE ASSESSMENT

Doppler - standard and augmented

Measurement of Doppler ankle pressures is now mandatory in order to stratify disease severity in patients with severe lower limb ischaemia, with particular emphasis on the identification of those with critical ischaemia. The significance of pressure measurement in the presence of tissue necrosis may not be as important as first thought (Wolfe 1986), but it acts as a means whereby patients can be compared in different centres and should, therefore, continue to be carried out. This very point is highlighted in this thesis where direct comparison between the retrospective and prospective series' was hampered by the incomplete preoperative data available in the former. It was, however, disappointing that neither of the classifications of critical ischaemia used in this study were able to predict outcome with any degree of accuracy. This implies that clinical judgement remains of the utmost importance when selecting patients for femorodistal bypass.

That ankle pressure measurements were not able to predict outcome following reconstruction in this study, is a finding in agreement with others (Samson et al 1985, Beard 1987), but this should not undermine their importance with regard to clinical reporting. Alternative methods of assessment such as transcutaneous PO_2 and laser Doppler are hampered by the same difficulties. These limitations highlight the need for a means of non-invasive assessment of the severely ischaemic limb which can

reliably determine whether or not reconstruction is feasible in a given case, and if so, to what level should the distal anastamosis be sited.

Augmentation of Doppler signals is an attractive notion, since by determining individual vessel patency and pedal arch status, it provides a degree of both morphological and physiological assessment. Both of the methods used in this study were clearly better than standard Doppler assessment in terms of vessel detection and particularly with regard to pedal arch assessment, both being equally effective. In practical terms it is probably reasonable to conclude that signal augmentation is able to provide a more realistic picture of the distal runoff situation than either standard Doppler or conventional arteriography, and this in turn should give the surgeon greater grounds for optimism when considering the feasibility of reconstruction.

It was disappointing, however, that the limb scores derived using either method did not discriminate between subsequent success and failure, and did not correlate with the peripheral resistance measured at operation. In the original work with the PGR system Beard *et al* (1988) reported a significant correlation between the PGR limb score and peripheral resistance measured at femorodistal bypass, although they did not include assessment of the pedal runoff when calculating the scores, whereas one might expect this to be a significant factor. Scott *et al* (1990) developed a linear regression model to calculate peripheral resistance from the PGR score, this time including a factor for the pedal arch and found good limits of agreement between the two in cases of single or three vessel runoff. This work should be interpreted with some degree of caution, however, since the score was derived from the whole limb, whereas in many cases the ultimate bypass is to a single vessel, and it is the runoff from the point of distal anastamosis which is relevant. In the absence of correlation at a simpler level the data in this thesis would not support these findings.

It would obviously be desirable to have a simple non-invasive test which could reliably predict peripheral resistance since this would provide the surgeon with crucial information regarding the advisability of attempting bypass. It is difficult at

this stage, however, to envisage the situation where the decision to amputate a leg is based on a mathematical calculation. The problem of the reliability with which a given test can predict resistance in the individual case still remains. In the 42 patients studied in this thesis none had a PGR score of zero and only one had a score of 1, this particular case subsequently going on to have a successful outcome.

Doppler signal augmentation would seem to have a role to play, although at present this is limited to providing better runoff assessment generally and in selecting the dominant runoff vessel. The simple technique of dependant Doppler proved surprisingly reliable compared with PGR, although the latter was marginally superior in selecting the bypass vessel. There were, however, no significant differences between the two methods.

Preoperative arteriography

An arteriogram demonstrating the distal circulation sufficiently well to be relied on as a reasonable guide to subsequent surgery was obtained in less than half of the series, confirming the unreliability of this investigation in patients with severe ischaemia. The limiting factor is the critical reduction in flow created by the extensive atherosclerosis which explains the superiority of DSA imaging in this situation. This facility was not available at the Leicester Royal Infirmary during the study but there are plans for its introduction in the near future.

The danger of placing too much reliance on arteriography was exemplified by the 5 (12%) cases in whom there was no demonstrable runoff since 4 went on to have successful surgery. The poor overall performance of preoperative arteriography lends credence to the suggestion that in the presence of a palpable femoral pulse the preoperative arteriogram is unnecessary (Shearman et al 1986), and by extrapolation may even be detrimental if patients are denied surgery on the basis of inaccurate assessment. The alternative is to base surgical exploration on Doppler studies, and the results obtained in this study with signal augmentation would support such a premise.

The counter to this argument is that arteriography may reveal lesions suitable for angioplasty, although there is evidence that PTA generally has little to offer in patients with critical ischaemia due to the presence of long occlusions and tibial disease (Cooper and Welsh 1990).

Vein mapping

The principal advantage of preoperative vein mapping related to intraoperative mobilisation of the vein, which was considerably eased particularly in obese legs. The technique is both simple and rapid, although a radiologist or an experienced technician is required in order for it to be performed accurately. One factor not addressed in this study was the qualitative value of the technique. The vein tends to be narrow below the knee, but the capacity for distension under arterial pressure is difficult to determine, and hence the suitability of the distal vein was only assessed intraoperatively.

A simple modification of the technique such as inflation of a cuff placed around the thigh to diastolic pressure might distend the distal vein and provide more relevant information regarding the potential for distension, and ultimate suitability of the vein for use. Any modifications would increase the time taken to perform the assessment, however, and would need to be done in a prospective series before their value could be assessed.

INTRAOPERATIVE ASSESSMENT

(i) Pre reconstruction

On table arteriography

In patients undergoing femorodistal bypass this probably represents the gold standard in terms of morphological assessment, providing a thorough evaluation of

the proposed site for distal anastamosis and its continuity with the runoff bed. The obvious drawback is that it is extremely invasive, requiring an anaesthetised patient, although it should be realised that the outcome in the majority of patients is a successful bypass. In terms of decision making prior to femorodistal reconstruction a study comparing on table arteriography with DSA would be of great interest.

The information provided by on table arteriography was clearly superior to that gained from the preoperative arteriogram and it was therefore disappointing that it was poorly predictive of outcome. Poor runoff was 81% specific for graft failure but only achieved 40% sensitivity. In practical terms this meant that there were 6 patients in whom a successful reconstruction was carried out and yet the only identifiable runoff was adjudged to be of poor quality. This serves to illustrate the difficulty of assessing the haemodynamic significance of runoff vessels identified morphologically.

Infusion resistance

Peripheral resistance measurements have been shown to predict the outcome of distal vascular reconstruction by a number of workers using different methods and this finding was reiterated in this study using a purpose built pump. There was a clearly significant difference in IR values both before and after the administration of papaverine, but to be of practical use there is a need to be able to state categorically whether or not the runoff will support a graft in an individual case. It is clearly possible to do this since there is a group with very high resistance, > 1.4 before papaverine in this study, in whom subsequent failure seems certain no matter how good the surgery. Unfortunately this high degree of specificity is achieved at the expense of a sensitivity of 60%, but it should be appreciated that the multifactorial nature of vein graft failure means that a measurement made prior to reconstruction cannot make allowances for subsequent errors.

If an aggressive policy towards surgical intervention is adopted in patients with severe ischaemia then it seems that there will be a significant group, 6 (14%) in this

study, in whom the peripheral resistance measured prior to reconstruction is unfavourable. The important question then becomes how should these patients be subsequently managed ? The logical conclusion would be to proceed to primary amputation since the outcome after graft failure is invariably a salvage amputation anyway. This presents something of an ethical dilemma, however, with the proposition that patients go to theatre in the hope of success but wake up having had an amputation. A more acceptable solution would be to proceed no further and simply close the leg wound, explaining the findings to the patient afterwards and carrying out any necessary amputation at a later date.

It must be said, however, that there is still a general reluctance to accept the limitations of surgery in this high risk group and the preference in our unit is to go ahead with reconstruction as intended, but if the graft subsequently fails the situation is accepted and exploration is not undertaken. A number of procedures have been proposed in addition to standard reconstruction in an attempt to ameliorate the problems of poor runoff. Formation of a sequential graft to an additional outflow tract is a possibility but, as illustrated in this study, it is rarely the case that there are other patent vessels available. Fashioning of a distal arteriovenous fistula (dAVF) has been proposed by a number of authors as a means of increasing graft flow, and hence maintaining patency in the face of poor runoff. The evidence that distal perfusion is satisfactorily improved is equivocal however and this manoeuvre is not used widely. In Leicester the use of a dAVF was prompted by the favourable results reported by Dardik *et al* (1983) regarding their value in maintaining patency of HUV grafts to tibial vessels. Unfortunately the results were singularly disappointing (Budd *et al* 1991), and the technique is no longer used. Of potentially more value is the use of Iloprost (Schering AG, Berlin), a potent vasodilator which has been shown to improve femorodistal graft flow for up to one week following a single bolus injection (Hickey *et al* 1991). What is not clear, however, is whether this effect is applicable in cases of very high resistance, and further work is required to clarify this point.

It was interesting that the administration of papaverine did not improve the separation between successful and failed grafts. This may be because, in the patient group studied, any runoff vessels supplying critically ischaemic tissue are already maximally dilated, and that any fall in resistance induced by papaverine is not clinically relevant.

The two main criticisms levelled at resistance measurement are that it is an invasive procedure and that the technique is cumbersome. Its invasive nature can hardly be denied but the data in this study firmly supports the notion that there is no other single test which can clearly separate out the very high risk group which present so many problems. As to the technique itself, this has undergone considerable refinement in terms of time taken, amount of blood used, and instant access to the resistance measurement, but it still requires a technician to set up the pressure line and operate the pump. The potential of peripheral resistance measurement to identify very high risk patients does not seem to be in doubt but in order to become more acceptable, there is a need to develop a simpler, more user friendly method. It was therefore very disappointing that the simple continuous pressure infusor, which was developed to fit these criteria, proved to be completely unreliable in this series. The concept behind the system is very attractive, but modifications in it's design are clearly required before it can be used to provide reliable readings relevant to clinical practice.

(ii) Post reconstruction

Graft flow

Resting graft flow was seen to be a poor discriminator between success and failure due to the overlap seen in the low flow range. The fact that a flow of 80 ml/min or less was almost equally compatible with a good or bad outcome effectively negated any potential for graft flow to reliably predict graft failure, when looked at in isolation. This was largely due to the fact that the low thrombotic threshold of vein

grafts meant that a flow as low as 35 ml/min was compatible with a successful outcome, and it is clear that relatively low flows are seen when grafting to distal vessels. Other factors which also need to be considered are the perfusion pressure and activation of coagulation factors.

On the plus side it should be noted that although a low flow could be regarded as at best equivocal, a high flow (>80 ml/min in this study) was a virtual guarantee of success.

Graft resistance (GR)

The more comprehensive assessment provided by the combination of simultaneous flow and pressure measurement enabled graft outcome to be predicted with more certainty than flow measurement alone. Strictly speaking, GR measurements in different patients are not directly comparable since neither of the two variables were kept constant, so it is interesting that clinically relevant information can be derived from them. This is presumably because although there was a wide variation in flow measurements, the mean pressure in most patients, while not being identical, is within a reasonably similar range.

All 5 of the high risk cases, with a pre-papaverine GR >1.7 PRU, had a pre-papaverine IR >1.4 PRU. No technical errors could be identified in any of these cases, and there were no alternative outflow tracts available. This confirms the fact that in the presence of very poor runoff the end result will be early failure, no matter how precise and well judged the surgery may be. The one other case with an IR >1.4 PRU had a GR of 1.33 PRU and fell into the borderline category, and again the outcome was early failure.

These results raise a number of interesting points relating to decision making during femorodistal bypass. The poor outcome of surgery in the group identified as being at high risk with IR measurement provides further weight to the argument that reconstruction should not be attempted in these patients. If surgery is undertaken in spite of these findings, or in the absence of IR measurements, and the

GR is found to be >1.7 PRU, then possible manoeuvres to improve the haemodynamic picture should be considered. The findings from this study, however, suggest that the situation is invariably irretrievable. From a purely logical point of view one could conclude that if nothing can be done to improve the GR then the leg should be amputated there and then. This raises the same ethical issues as amputation on the basis of IR findings, and in addition most vascular surgeons would be extremely reluctant to end several hours demanding surgery on such a pessimistic note. A more realistic option would be to conclude that nothing further could be done and that in the event of early failure the graft should not be re-explored.

It was interesting that the post-papaverine GR was of no benefit in predicting outcome. This was because the falls induced in the group which failed resulted in greater overlap in the higher range, similar to the effect observed with the IR measurements. The effect of papaverine was only transitory, however, with GR returning to resting levels within a few minutes. These findings suggest a possible therapeutic option, since if the resistance fall could be maintained then the graft might be tided over the initial critical period. One agent which has been used on this basis is Iloprost (Schering AG, Berlin) delivered as an intragraft bolus at the end of surgery. This has been shown to improve graft flow for a week compared with a control group (Hickey *et al* 1991). What is not clear, however, is whether or not this effect will improve the outlook for high risk grafts, since GR was not measured in their study.

Completion arteriography

The excellent agreement, with regard to distal runoff, between the pre-bypass on table arteriogram and the subsequent completion arteriogram, confirms the value of the former as a means of siting the distal anastamosis and of the latter as a means of assessing whether or not this situation has been preserved.

The additional function of completion arteriography was in assessment of the distal graft and anastamosis. The potential problem of unligated side branches was

eliminated by mobilisation of the whole vein, and persistent valve cusps in the proximal graft were excluded on the basis of satisfactory haemodynamic assessment. There were no cases in which re-passage of the valvulotome brought about an improvement where the resistance was unfavourable.

It was reassuring that there were only four detectable errors, one of judgement and three of technique. Immediate correction of the technical errors led to a successful outcome in each case. The error in judgement, which entailed siting the anastamosis proximal to a stenosis in order to gain 2 rather than single vessel runoff, is of interest since the lesion was recognised at the time. No action was taken, however, because the graft resistance was considered to be acceptable, although subsequent analysis revealed that the pre-papaverine measurement fell into the borderline group, and the graft ultimately occluded. This case illustrates the point that even in the presence of what might be considered to be a satisfactory haemodynamic result, anatomical lesions which are identified should be corrected, and suggests that both forms of assessment are required for optimal results. The fact that both cases in which the completion arteriogram was unsatisfactory subsequently failed lends further weight to this argument.

The completion arteriogram was a relatively good judge of runoff quality, but was not as reliable as resistance measurement in predicting outcome. This reflects the difficulty of assessing runoff from a morphological investigation and reiterates the fact that arteriography and resistance should be viewed as complimentary.

POSTOPERATIVE ASSESSMENT

Continuous Doppler monitoring

The monitoring system was simple to use and provided good quality data which was of direct relevance to early graft outcome. Using the combination of PI, reflecting peripheral resistance, and TAMV, reflecting volume flow, several different

haemodynamic patterns were identified. The selection of these two parameters was based on the premise that following successful revascularisation there is an expected period of hyperaemic flow, the duration of which is related to the severity of the preoperative ischaemia (Eastcott 1953, Renwick *et al* 1968, Cronenstrand and Ekestrom 1970). One would therefore expect successful cases to exhibit a low PI and a high TAMV, and this was indeed the case in 29 out of 32, with a PI below 2 and a TAMV greater than 10 cm/s being associated with a successful outcome.

The early fall in PI seen in the first few hours (Fig 6.12) indicates that the runoff bed continues to open up during this period. The mediators of this response are unknown but the release of local vasodilatory metabolites is likely to play a significant role. This initial phase, during which the graft is becoming established is an important one and it is crucial that during this period the anticoagulation / thrombosis scale is tipped in favour of the former. With regard to this point high graft flow secondary to low resistance is obviously favourable, but the category of "low flow" grafts which were successful in spite of poor haemodynamics is, at first sight, not so easy to understand. The important point in these cases is that the PI, while being greater than 2 did not rise above 3, and this would seem to indicate a borderline resistance which prevents the establishment of hyperaemic flow, but which nonetheless produces sufficient distal perfusion to reverse tissue ischaemia. The low flow in these 3 cases, with TAMV < 10 cm/s, was not in itself of great concern, since it is known that vein grafts can remain patent in the face of relatively poor flow (Sauvage *et al* 1979). It would appear, however, that in these cases the influence of local factors in the runoff bed in maintaining graft patency is particularly important.

The two distinct patterns associated with early thrombosis, *ie* rapid onset of pulsatile flow and progressive departure from initially favourable flow, were relatively easily distinguished from the patterns seen in successful cases. It is clear that highly pulsatile flow (*Group 1*) or a progression towards pulsatile flow (*Group 2*) are bad prognostic signs. In reality the identification of *Group 1* cases was somewhat

academic since they were all associated with poor runoff identified by both a high prebypass infusion resistance, and high completion resistance. The signal picked up by the probe in such cases was essentially that of a column of blood oscillating within the graft in the face of a thrombosed runoff. This pattern was also demonstrated as the terminal event in one of the *Group 2* cases which was followed to actual thrombosis, and it is reasonable to surmise that it probably occurs as the final sequence in all cases of graft thrombosis.

Of more relevance clinically are those cases in which early haemodynamics are initially acceptable but which progress towards unfavourable patterns, since if the changes are recognised prior to thrombosis intervention to improve matters can be instigated. A similar argument applies to the cases of haemodynamic failure. This situation is slightly different, however, in that one is not dealing with the threat of graft thrombosis, which is a difficult situation to retrieve. The separation between the cases in *Group 3* and the "low flow" grafts was less obvious than the other patterns associated with failure, and the crucial factor was the PI, which was greater than 3.5 in the three cases with a distal anastamosis. This would appear to represent a resistance level which is sufficient to maintain graft patency, presumably by means of retrograde flow, since distal perfusion remains inadequate.

The possibility of intervention upon recognition of unfavourable haemodynamics raises two important points, namely; in which grafts should intervention take place? and what form should it take?

The answer to the first point seems relatively straightforward, since continuous monitoring seems able to reliably identify grafts at risk of early failure, and surely it is these cases that warrant further attention. On closer examination, however, the situation is not so clear cut. It can be argued that there is no point in doing anything for cases in *Group 1* since they are destined to fail whatever, and further action is a waste of resources. It can also be argued that, since there were two cases of early failure in which initial monitoring for 24 hours failed to indicate the subsequent course of events, steps to maximise early patency should be instigated in every case,

with the implication that this would entail overtreatment of the majority. On balance it would seem sensible to adopt a selective approach.

When considering what form of intervention to offer one is faced with the same options discussed earlier in this chapter in relation to patients identified as having a high peripheral resistance, namely formation of a sequential graft, fashioning of a dAVF, and pharmacological manipulation with agents such as Iloprost. The most attractive concept is that of pharmacological manipulation, since in most cases the graft is fashioned to the only available outflow tract and the case for a dAVF remains unproven and unpopular. Assessing the benefit of agents such as Iloprost is very difficult since the actual number of grafts at risk in any series is small, and multicentre studies are required to determine it's role. Furthermore it is important that objective graft assessment is performed so that the effect in high risk grafts can be properly studied. A further role of the continuous monitoring system is that it is ideally placed to study the immediate effect of any such intervention.

An obvious criticism of the system is that the results are analysed retrospectively, and clearly the value of anticipation inherent in any proposed programme of intervention is lost by the delay in data processing. The demonstration that the system is a reliable means of following early graft haemodynamics, however, has prompted work aimed at developing on-line analysis, so that trends in PI and TAMV can be displayed at the bedside. At present the best the system can provide in terms of immediate assessment is an audible Doppler signal, which provides a means of qualitative analysis, albeit crude, to the surgeon with a knowledge of Doppler waveforms. A further refinement would be the addition of a small printer which could supply a read-out of the mean values over each recording period, thus negating the need for any retrospective analysis at all.

Graft surveillance

Although the case for graft screening has never been proven in a prospective randomised fashion, the evidence now available from retrospective and prospective

studies is hard to resist, and a definitive study is now unlikely to be carried out. The fact that 28% of grafts patent at 1 month developed an empirically determined significant stenosis is in keeping with other series, including the retrospective study in this thesis, where the intermediate failure rate was 29%.

It was, therefore, gratifying that treatment of these stenoses resulted in maintenance of patency in all cases at 12 months. It was, however, unfortunate that the single case in which a stenosis led to deterioration was as a result of radiological intervention, although if the lesion had progressed silently and occluded the graft the result may have been even more serious, resulting in amputation, as was the experience in the retrospective study cited above.

Having striven to maximise the success of limb salvage surgery in the first month, it seems that some form of screening programme is a must if patients are to receive the maximum benefit from their surgeons hard graft.

SUMMARY

In spite of the increased efforts aimed particularly at careful patient selection and attention to surgical detail this series highlights the potential problems of an aggressive policy towards femorodistal reconstruction in the severely ischaemic limb.

By far the most significant factor relating to early failure was poor runoff. None of the methods of preoperative assessment used was able to assess the runoff sufficiently well as to predict early outcome. The only investigation which was able to identify this group of patients with any degree of accuracy prior to bypass was measurement of infusion resistance, which is an invasive procedure. The subsequent course in these cases illustrates the point that no matter how good the surgeon may be, inadequate runoff is an insurmountable beast. Early failure in some of the cases of poor runoff clearly involved additional factors, since there were patients in a borderline group who had a successful outcome. The exact nature of these factors is

not clear, but the relative degree of vein trauma, and its consequent effect on early thrombotic factors may be important.

It was gratifying that the number of technical problems was reduced compared with the retrospective series, due presumably to a combination of improved surgical technique and careful intraoperative assessment. The fact that there were still three errors of surgical judgement has two probable causes. The first relates to the case with a runoff stenosis and is an example of the readiness to accept reasonable haemodynamic measurements in the face of an obvious fault, particularly at the end of a 3 or 4 hour procedure when the temptation to close the skin is overwhelming. Unfortunately the temptation must be resisted if the patient is going to benefit from these ardours. This point also highlights the fact that, rather than one test being used in isolation, graft assessment is best achieved by a combination of both morphological and haemodynamic methods. The second factor was probably a determination to use the long saphenous vein in spite of it being narrow in one case, and damaged in the other. Autogenous vein is clearly the graft of choice, but it is not always possible to find an adequate long saphenous vein and other sources of vein must be used, as alluded to in Chapter 2.

The continuous monitor device used for postoperative monitoring represents a period of ongoing research since it is not possible to use the data prospectively. It does, however, represent a means of monitoring the effects of *eg* Iloprost infusions in high risk patients, a role for which it is currently being used.

Maintenance of graft patency after the first month, although outside the scope of this thesis, is clearly desirable and some form of screening is essential in order to detect the fibrous stenoses which represent the principal threat to patency during this period.

Femorodistal bypass, therefore, continues to represent a challenging aspect of vascular surgery with continued room for improvement, before the achievement of maximum benefit for the patient and maximum reward for the surgeon.

FUTURE DEVELOPMENT

There is clearly a need to be able to assess runoff more effectively preoperatively, ideally using a method which is simple to use in order for it to become widely adopted. The techniques available to date are too crude too allow any accurate prediction of outcome, and it may be that some form of metabolic assessment, either of distal limb blood flow or of tissue viability is the way forward.

At present the most only means method of accurately quantifying runoff is intraoperative resistance measurement, but there is a need to develop a simple means of performing this test before it becomes used more widely. The continuous pressure device was deliberately used in this study for this reason, in order to compare it with the more complex infusion method. Its failure to produce any meaningful results was, therefore, very disappointing. The concept behind it is, however, worthy of further exploration, and it may be that a more reliable instrument using constant pressure will become available.

The identification of poor runoff remains a problem in that there is no widely accepted method of creating a more favourable situation. The answer is probably going to be pharmacological rather than surgical, and is somewhat analogous to the frustrations of the early transplant surgeons, who encountered organ rejection in the spite of technically perfect surgery, and who had to wait until Medawar and colleagues pointed out the importance of the immune system before better results could be achieved.

The methods of graft assessment used in this study were relatively straightforward, with resistance being the single best test. The data from the comparative study in Appendix A indicate that the electromagnetic flowmeter used in this study can be replaced with the OpDop (SciMed Ltd, Bristol) flowmeter developed by Beard *et al* in Bristol, with broadly similar results. Angioscopy is being evaluated in a number of centres and appears to be of some value. The equipment is expensive, however, and the endothelial and smooth muscle trauma of

passing the scope and its associated irrigating fluid is unknown.

In the early postoperative period close monitoring, particularly of high risk grafts would seem sensible, but the information from such monitoring needs to be immediately available if any benefit in retrieving failing grafts is to be gained.

APPENDIX A

COMPARISON BETWEEN ELECTROMAGNETIC AND

DOPPLER FLOWMETERS

INTRODUCTION

Some form of assessment to determine technical adequacy on completion of a femorodistal vein graft is generally considered to be mandatory. The modality most commonly employed is completion arteriography, which is particularly well suited to identifying errors in relation to the distal anastamosis (Liebman *et al* 1981, Scarpato *et al* 1981). Arteriography is a morphological investigation, however, and provides only limited information with regard to graft function. This is best assessed by haemodynamic means, by measuring graft blood flow either in isolation (Mannick and Jackson 1966, Terry *et al* 1972) or in combination with pressure measurements to provide resistance (Albrechtsen 1976, Beard *et al* 1989B).

Until recently intraoperative blood flow measurements have always been made with electromagnetic flowmeters (EMF's), which are able to provide accurate readings, but have a number of drawbacks which have prevented widespread use. They are very expensive when compared to their limited clinical application, considerable technical backup is required in order to maintain the equipment in reliable working order, and even with a technician the measurements themselves can be time consuming.

In order to overcome these limitations Beard *et al* (1986C) recently described a Doppler flowmeter specifically developed for blood flow measurement during arterial surgery. In a clinical study the flowmeter was reported to be both accurate

and simple to use (Beard *et al* 1989B). The prototype model has now been developed commercially into a unit (SciMed OpDop 130, SciMed Ltd, Bristol) comprising the flowmeter and a thermal printer on a purpose built trolley (Fig A.1).

The accuracy and practicality of this system was compared with a standard EMF in vitro and then in a group of patients undergoing femorodistal vein bypass.

Fig A.1 The Doppler flowmeter on its purpose built trolley. The thermal printer is seen on the middle shelf. The system is operated either by pushing the arrowed buttons (top) or using the foot switches (bottom).

IN VITRO STUDY

Materials and methods

Flowmeters

EMF measurements were made with a Cliniflow flowmeter (Carolina Medical Electronics, Carolina, USA), using one of a range of cuffed flow probes according to vessel diameter. The most important consideration when using these probes was to ensure a snug fit around the vessel in order to achieve good electrical contact without producing any constriction. Readings from the flowmeter were outputted to a Gould 2202 multichannel chart recorder (Gould Ltd, Hainault, Essex).

The Doppler flowmeter (DF) consisted of 10 MHz continuous wave pencil probe powered by a mean frequency estimator, combined with an analogue system into which the vessel diameter could be inputted. A series of hollow, moulded plastic clips ranging from 3-14 mm were supplied with the system. These were used to hold the vessel and probe constant in relation to each other, with the ultrasound beam subtending an angle of 60° to the graft, thus eliminating potential errors due to uneven insonation. A simple calibration guage was supplied with the DF and this was used to measure the external and internal diameters of the vessel under study so that a clip of appropriate size could be selected. This was then placed around the graft and its lumen filled with sterile ultrasound gel. The Doppler probe was inserted into the back of the clip, carefully ensuring an air-free gel contact between probe and vessel. After being switched on a simple command sequence was commenced during which the vessel measurements were fed in, following which the system calibrated itself automatically. The sequence could be operated either manually, using the push buttons on front of the system, or by using a foot pedal. Once the system was calibrated vessel insonation began, as evidenced by an audible Doppler signal. It was necessary to adjust the volume to within a pre-set range in order for optimal measurement. Once the system was set-up, mean flow was

calculated automatically after analysis of a number of pulse cycles. In addition to an audible signal, the Doppler waveforms and flow measurements were displayed on the small screen on the unit. The screen was frozen after each calculation enabling the option of printing it out before proceeding to further measurements.
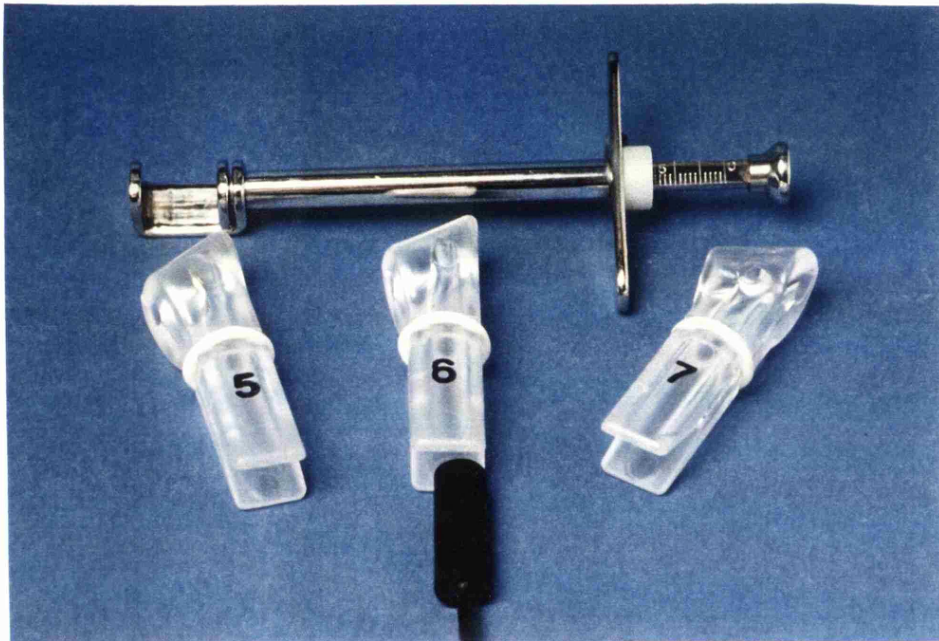
Fig A.2   Components of the Doppler flowmeter system. The simple measuring guage, a selection of clips (the number corresponding to the external diameter of the vessel), and the probe.

Flow circuit

The two flowmeters were compared in a flow circuit powered by a peristaltic pump, at three different flow rates; 54, 114 and 208 ml/min. These were determined by calculating the mean of 10 hand timed runs into a calibrated beaker for each flow rate. The circuit was completed by a length of long saphenous vein harvested from the thigh during varicose vein surgery. Care was taken to ensure that there were no

areas of thickening or marked varicosity in the segment used. After removal, the vein was gently distended with heparinised saline and all tributaries were ligated. During measurements the vein was immersed in a bath of warm saline. Expired whole citrated blood was used in the circuit in order to mimic the clinical situation as closely as possible, particularly with regard to the DF which uses the red cells as reflectors.

In the clinical situation measurements are generally made at a point in the mid to upper graft where the vein is of reasonable calibre, of the order of 5 mm, and flow is likely to be laminar, thus avoiding areas of turbulence. All studies were therefore carried out on the mid portion of the harvested vein.

The probe used for the EMF measurements was selected on the same basis as in the clinical situation, ensuring a snug fit around the vein. In the clinical situation, once the site for flow measurements has been selected the choice of probe is fairly clear, with only one providing a close fit within the chosen segment. In this study only one site was used as outlined above, since the vein was fairly constant in diameter throughout its length.

For the DF the important factor was accurate measurement of the external and internal vein diameters. These were necessary in order to select the appropriate sized plastic clip and to allow the system to calibrate itself. Measurements were made with the simple guage provided with the system, and with a micrometer. It was only possible to input the external diameter in terms of the clip size *ie* in whole millimetres, whereas it was possible to increase the accuracy to one decimal place for the internal diameter. Errors in clip selection were examined by using the two clip sizes nearest to the micrometer determined external diameter for each set of measurements. Initial measurements at the lowest flow rate, however, indicated that the smaller clip resulted in greater inaccuracy, and at the two higher flow rates only the larger clip was used.

For each flowmeter and variable 10 individual measurements were made, the median of these being used in subsequent analysis.

Results

Measurements made with the EMF showed satisfactory reproducibility at all three flow rates but were significantly different from the known flow rates (Table B.1). The mean errors observed were +13.9% at 54 ml/min, +5.3% at 114 ml/min and -9.1% at 208 ml/min, indicating a tendency to overestimate at low flow and underestimate at higher flow.

At the site selected for study the external diameter of the vein was measured at between 5 and 6 mm, and wall thickness at 1 mm with the supplied guage, thus giving an internal diameter of 4 or 5 mm depending on which clip was selected. With the micrometer the external diameter was 5.7 mm and wall thickness was 1.5 mm, giving

Flow rate (ml/min)	54	114	208
Observed	63	126	192
EMF flow	60	115	192
(ml/min)	63	118	188
	60	122	187
	62	125	185
	61	114	190
	60	122	187
	60	117	188
	63	121	190
	63	120	192
Mean flow	61.5	120	189.1
StD	1.43	4	2.47
Mean error	+13.9%	+5.3%	-9.1%
	p=0.0023	p=0.0038	p=0.0024

Table A.1   Reproducibility of the electromagnetic flowmeter at the three flow rates used in vitro, showing mean error between observed and known flow rate. (StD = standard deviation, statistical analysis - Wilcoxon signed rank).

an internal diameter of 4.2 mm. Measurements were made with 5 mm and 6 mm clips at 54 ml/min initially, separate readings being made with the guage and micrometer determined internal diameter.

The DF also demonstrated good reproducibility for all series of measurements, but demonstrated similar errors with an even greater overestimation of low flow and a similar degree of underestimation at the highest flow (Tables B.2, B.3). The observed flow varied greatly according to the size of clip used and the method of (ml/min) vessel measurement. At 54 and 114 ml/min values closest to the known

Known flow (ml/min)		54		
Clip size (mm)	6	6	5	5
Diameter	microm	guage	microm	guage
Observed flow	67	99	89	96
	67	98	87	96
	67	99	84	98
	65	97	86	97
	68	98	85	98
	66	99	84	96
	67	98	89	95
	67	98	88	96
	67	97	87	98
	67	99	86	97
Mean flow	66.8	98.2	86.5	96.7
StD	0.79	0.79	1.84	1.06
Mean error	+23.7%	+81.9%	+60.2%	+79.1%
	p=0.0018	p=0.0022	p=0.0023	p=0.0025

Table A.2 Observed flow with the Doppler flowmeter at known flow of 54 ml/min, demonstrating the effect of different clip size and method used to measure vessel diameter. (StD = standard deviation, analysis - Wilcoxon signed rank test).

flow rates were observed when using the internal diameter as measured by the micrometer rather than the guage provided with the system. At the highest flow rate, however, the errors were similar (Table B.3).

The smallest errors observed with the DF were +23.7% at 54 ml/min, +4.8% at 114 ml/min and -8.75% at 208 ml/min. With the 5 mm clip the lowest flow rate was overestimated by as much as 60-80% depending upon which set of diameter measurements were used. This level of inaccuracy resulted in use of the larger clip only at the two higher flow rates.

Flow rate (ml/min)	114		208	
Clip size (mm)	6	6	6	6
Diameter	microm	guage	microm	guage
Observed	117	162	192	196
DF flow	119	155	185	188
(ml/min)	122	162	182	185
	120	158	188	182
	118	160	186	193
	121	156	190	196
	119	160	190	195
	119	162	192	186
	122	157	184	192
	118	155	182	185
Mean flow	119.5	158.7	187.1	189.8
StD	1.71	2.86	3.84	5.2
Mean error	+4.8%	+39%	-10%	-8.75%
	p=0.0024	p=0.0025	p=0.0025	p=0.0025

Table A.3 Observed flow with the Doppler flowmeter at 114 and 208 ml/min. Measurements were only made with the 6 mm clip, but with two sets of diameter measurement. (StD = standard deviation, analysis - Wilcoxon signed rank test).

Discussion

It is clear from this study that both flowmeters are subject to potentially large errors, especially at the lowest flow rate tested. The flow circuit itself is a potential source of error since it is difficult to construct a pulsatile system which accurately represents the in vivo situation. The selection of physiological flow rates and the use of blood and natural vein were designed to minimise some of the differences. The pulse wave produced by the peristaltic pump consisted of a monophasic peak with a zero baseline and a pulse pressure of 140 mmHg, which is likely to have resulted in uneven sampling over the pulse cycle, particularly at the lowest flow rate, where the inaccuracies were greatest. While this may explain some of the error observed between each set of readings and the known flow rate, however, it does not account for the differences observed between the two flowmeters at a given flow rate, and these were presumably due to true differences between the flowmeters.

The fact that both flowmeters demonstrated good reproducibility indicates that the observed differences were almost certainly due to factors within the flowmeters themselves rather than to technical factors, especially with regard to the EMF. One point which was clear, however, was the importance of accurate diameter measurement with the DF, since the small differences between the guage and micrometer measurements resulted in large differences when converted to flow (Table B.2). The most accurate flow measurements in this study were made with the larger of the two clip sizes using the micrometer derived measurements, and although the study was somewhat limited in extent, it would seem reasonable to extrapolate these findings to the clinical situation. This would involve carrying out flow studies at the widest point in the vein, avoiding areas of potential turbulence, with efforts made to record the internal diameter as accurately as possible, to the nearest half millimetre at least.

When examining the role of flow measurements both as a means of technical assessment and prediction of subsequent function it is the accuracy with which low flow is measured that is of greatest importance. This is because good flow, in excess

of 100 ml/min, is generally indicative of a successful outcome and the significance of any errors is therefore lessened. Grafts with a low flow are at most risk of early failure, be it due to poor runoff or technical problems, and it is clearly important that such cases are recognised so that steps can be taken to improve the situation if possible. It was therefore disappointing to find that both flowmeters overestimated the lowest flow rate in vitro, and clearly this is a problem which should be borne in mind in the clinical situation. Of particular note was the potential inaccuracy of the DF, which resulted in a near doubling of the true flow rate (Table A.2), depending on the clip size and diameter measurements fed into it.

It was reassuring that each flowmeter demonstrated good reproducibility at the lowest flow rate, since even if the observed flow is accepted as being inaccurate it should be so to a pre-determined degree, provided care is taken with probe or clip selection. The same proviso applies to higher flow rates although, as already outlined, the relative importance of inaccuracies is less.

The ultimate test of the relevance of flow measurements is to assess their role in the clinical situation and this was examined in the next section.

CLINICAL STUDY

Patients and methods

Flow and resistance measurements were performed in a series of 21 patients undergoing a total of 22 femorodistal bypass procedures with autogenous vein. On graft completion a suitable segment of the graft was identified as being suitable, and this was measured with the guage provided with the DF. The EMF probe was selected such that a snug fit was achieved adjacent to the selected site (Fig A.3). Flow measurements were made before and after an intragraft injection of 20 mg of papaverine.
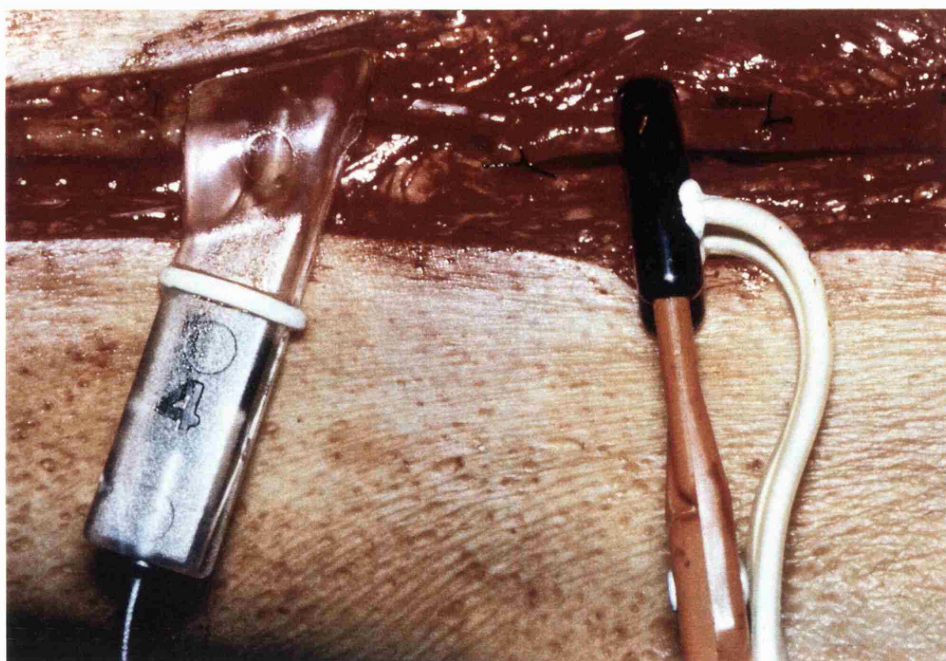
Fig A.3   The Doppler probe (left) and the electromagnetic flowprobe (right) set up
to measure flow on adjacent points of a graft. The Doppler probe can be
seen fitted into the back of the clip.

In order to calculate graft resistance the intragraft pressure was measured by
cannulating the graft either directly or via a tributary with a 19-guage butterfly
needle or venflon (Fig 5.8). In either case the cannula was connected via a
manometer line to a calibrated Gould P23XL isolated pressure transducer. The
output from this was fed simultaneously into the multi-channel recorder used for the
EMF (Fig 5.7), and directly into a port on the DF. Resistance using the EMF was
then calculated by reading the values from the chart at a given point and dividing
mean pressure by mean flow (Fig 6.8). The DF calculated the resistance
automatically by integrating the simultaneously received pressure and flow
waveforms, the value being displayed on the screen (Fig A.4). In each case the
resistance was estimated using the pre- and post-papaverine flow measurements.

CLIP SIZE/ 6.0mm

0   0   49

```
┌─────────────┬───┬──────────────┐
│ Flow 104ml/m│   │              │
│ Vel    9cm/s│   │              │
│ RES  0.98Pru│   │   ᴧ ᴧ  ᴧ  ᴧ  ᴧ│
│ Press102mmHg│   │              │
│┌───────────┐│   │              │
││Print      ││   │──⌒──⌒─⌒─⌒─⌒─│
│└───────────┘│   │              │
└─────────────┴───┴──────────────┘
```

CLIP SIZE/ 6.0mm

0   0   49

```
┌─────────────┬───┬──────────────┐
│ Flow 253ml/m│   │              │
│ Vel   22cm/s│   │ ᴧ ᴧ ᴧ ᴧ ᴧ    │
│ RES  0.34Pru│   │              │
│ Press 88mmHg│   │              │
│┌───────────┐│   │──⌒─⌒─⌒─⌒─⌒──│
││Print      ││   │              │
│└───────────┘│   │              │
└─────────────┴───┴──────────────┘
```
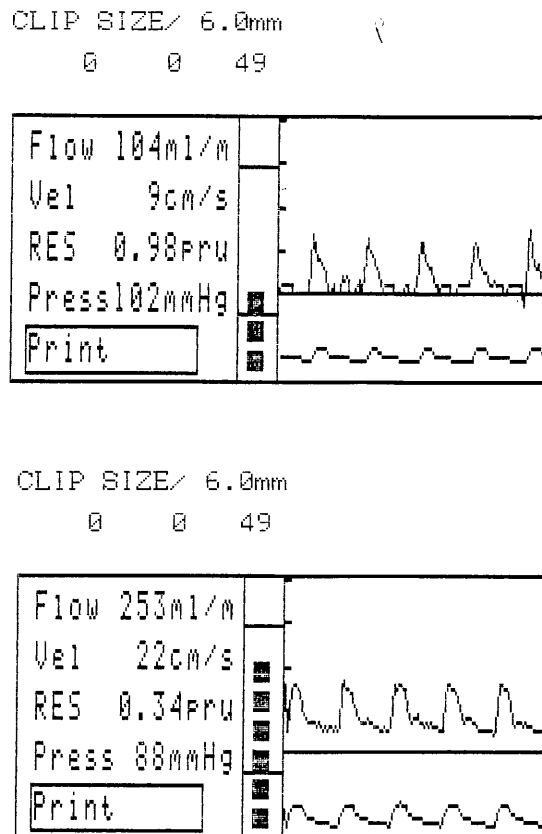
Fig A.4   Printouts from the Doppler flowmeter before (top) and after (bottom) intragraft injection of papaverine. The increase in flow after papaverine is accompanied by a fall in resistance, indicating a good result. Note also the hyperaemic waveform after papaverine (see Fig 5.14).

The results have been expressed as median values and ranges, and comparison between the two flowmeters has been carried out using limits of agreement (Bland and Altman 1986). In addition, the measurements made with the DF have been analysed separately to assess its ability to predict early graft function. The EMF data have been analysed for this purpose in the main body of the thesis (see Chapter 6).

Results

There were no cases of early occlusion but there were three cases of haemodynamic failure, all of which resulted in major amputation.

Accurate graft measurement with the micrometer was not possible in theatre since a sterilisable instrument was not available. Graft measurements were therefore made with the sterilisable guage supplied with the DF. In view of the findings from the in vitro study, however, efforts were made to use as large a clip as possible and to judge vessel thickness to the nearest half millimetre.

Resting graft flow measured with the EMF was 105 ml/min (15-402 ml/min), and with the DF was 118 ml/min (22-324 ml/min) (Table A.4) . The mean difference between the flowmeters (EMF - DF) was -18.9 ml/min, and the limits of agreement ($\pm$2SD) were 78.5 to -116.3 ml/min (Fig A.5). Although the limits for the group as a whole were wide there was better agreement in the low flow range (mean flow < 100 ml/min), where the mean difference was -8.2 ml/min and the limits of agreement were 32 to -48.4 ml/min.

After papaverine EMF flow increased to 204 ml/min (37-450 ml/min), and DF flow increased to 198.5 ml/min (56-403 ml/min) (Table A.4). The mean difference between the two measurements was small at -0.5 ml/min, but the limits of agreement were again very wide at 152.4 to -153.3 ml/min (Fig A.6).

In the majority of cases, 15 out of 22, the DF recorded higher flow than the EMF, a finding in keeping with the in vitro study. On closer inspection, however, the distribution was not entirely as predicted from the flow circuit where the greatest discrepancies were seen at the lowest flow rate, with close agreement being seen at the highest rate. Instead, large discrepancies were seen over the entire flow range. This may reflect the variability of the DF in clinical practice where measurements need to be made with different size clips in different patients, and the controlled environment of the bench study, in which the degree of potential error was indicated, is missing.

GRAFT FLOW (ml/min)

	RESTING		POST-PAPAVERINE	
	EMF	DF	EMF	DF
Successful	193	190	221	254
	108	82	212	102
	125	87	220	110
	45	66	152	90
	60	41	265	80
	97	127	330	403
	245	208	265	200
	92	112	182	200
	102	74	113	74
	81	91	217	217
	138	261	208	270
	210	249	240	321
	87	124	137	197
	140	200	215	256
	135	257	180	283
	138	180	200	249
	110	171	120	194
	402	324	450	347
	35	62	37	70
Failed	33	59	64	86
	54	58	63	65
	15	22	38	56

Table A.4   Resting and post-papaverine graft flow in successful and failed grafts measured with the electromagnetic (EMF) and Doppler (DF) flowmeters.
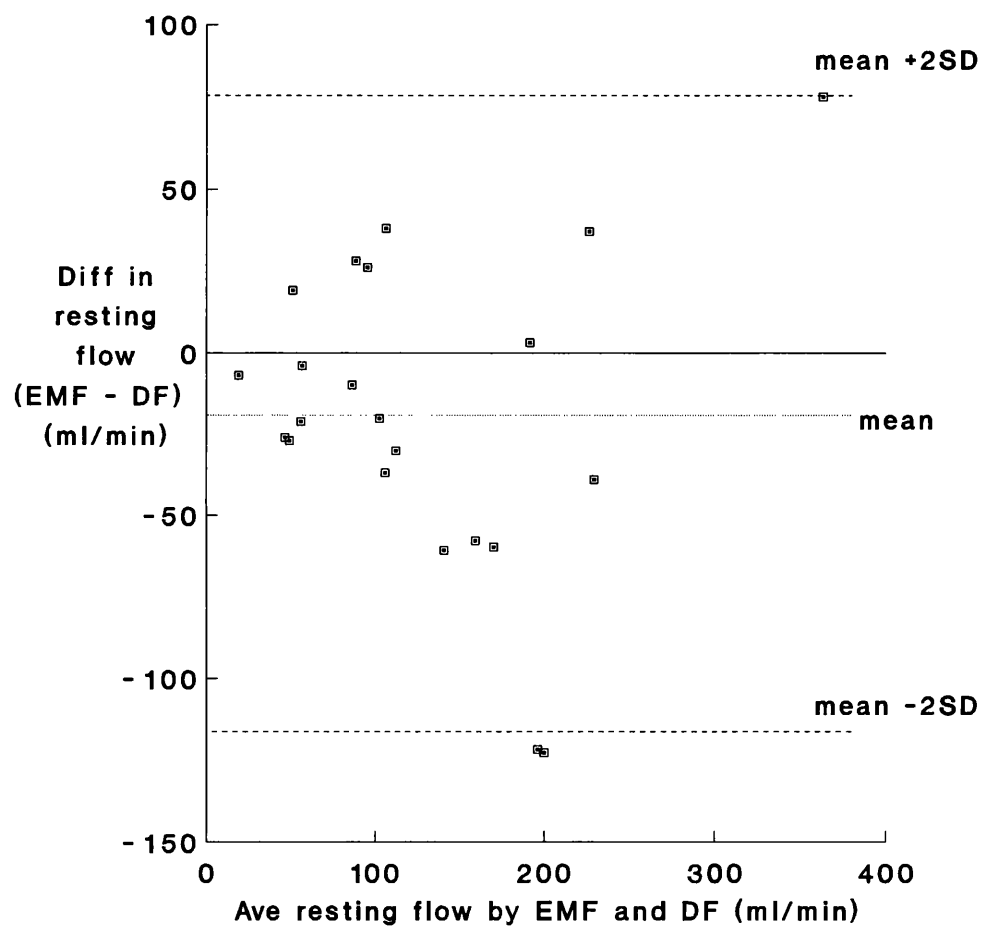
Fig A.5 Limits of agreement for resting graft flow between the two flowmeters.
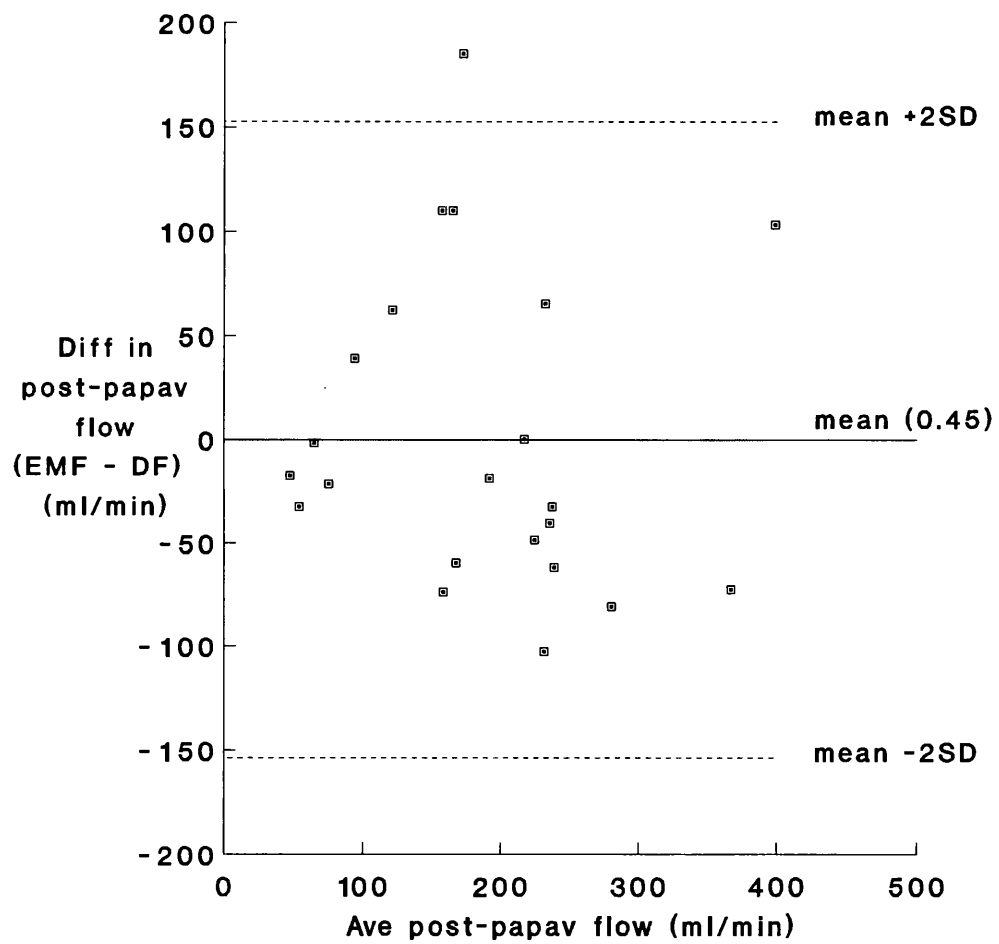
Fig A.6   Limits of agreement for post-papaverine graft flow between the two flowmeters.

Resting graft resistance using the EMF derived flow measurements was 0.92 PRU (0.2 - 4.0 PRU), and with the DF was 0.82 PRU (0.25 - 3.4 PRU) (Table A.5). The mean difference between the two flowmeters was 0.21 PRU, and the limits of agreement were -0.45 to 0.87 PRU (A.7).

After papaverine EMF resistance fell to 0.47 PRU (0.17 - 1.89 PRU), and DF resistance fell similarly to 0.46 PRU (0.22 - 1.43 PRU) (Table A.5). The mean difference between the two sets of measurements was reduced at 0.06 PRU, but the limits of agreement remained wide at -0.52 to 0.64 PRU (Fig A.8).

In keeping with the fact that the DF tended to record higher graft flow, the graft resistance figures were correspondingly lower than those derived from the EMF flow measurements. The greatest discrepancies were seen in grafts with very high resistance, with better agreement seen between grafts with a low mean resistance, particularly before papaverine (Fig A.7).

When the DF data were analysed alone there were highly statistically significant differences between the measurements made in successful and failed grafts for all four categories considered *ie* graft flow pre- and post-papaverine, and graft resistance pre- and post-papaverine (Table A.4). The predictive power of the measurements, however, was hampered by the small numbers.

All 3 failed grafts had a resting flow of <60 ml/min, but a flow of 41 ml/min was recorded in one graft which did not fail, and in 2 other successful cases flows of 62 and 66 ml/min were recorded. Early failure could only be predicted with certainty for flow <40 ml/min, but this only identified one case, with a flow of 22 ml/min. The administration of papaverine improved the things slightly since failure could be predicted with 100% certainty for flow <70 ml/min, a value which

GRAFT RESISTANCE (PRU)

	RESTING		POST-PAPAVERINE	
	EMF	DF	EMF	DF
Successful	0.37	0.41	0.35	0.3
	0.84	0.89	0.39	0.64
	0.86	1.1	0.47	0.81
	1.89	1.12	0.54	0.58
	1.17	1.3	0.24	0.82
	1.11	0.88	0.37	0.23
	0.39	0.47	0.38	0.46
	0.93	0.76	0.45	0.4
	1.08	1.4	0.96	1.4
	1.19	1.03	0.4	0.39
	0.63	0.33	0.41	0.3
	0.4	0.32	0.34	0.24
	1.1	0.74	0.69	0.46
	0.75	0.51	0.46	0.36
	0.77	0.43	0.57	0.3
	0.71	0.53	0.48	0.36
	0.9	0.54	0.73	0.46
	0.2	0.25	0.17	0.22
	1.65	0.9	1.43	0.72
Failed	2.3	1.37	1.2	0.93
	1.7	1.67	1.51	1.43
	4.0	3.4	1.89	1.28

Table A.5 Resting and post-papaverine graft resistance in successful and failed grafts measured with the electromagnetic (EMF) and Doppler (DF) flowmeters.
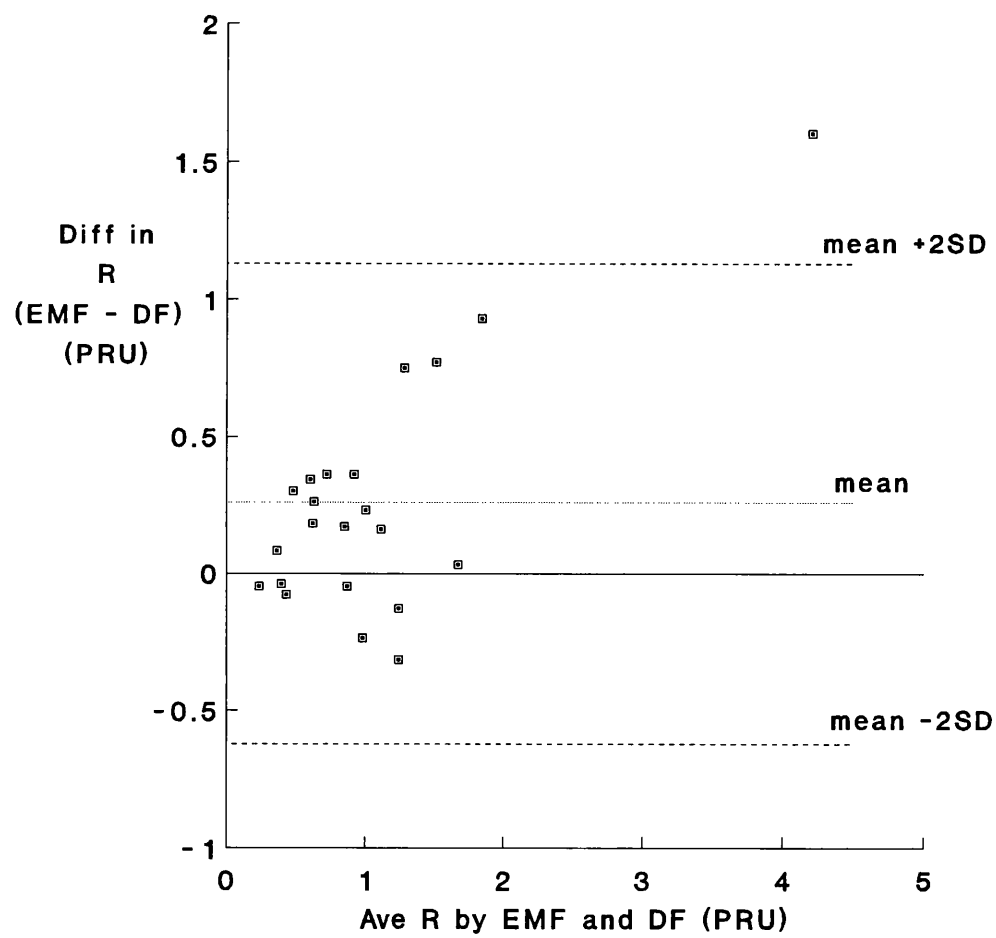
Fig A.7 Limits of agreement for resting graft resistance between the two flowmeters.
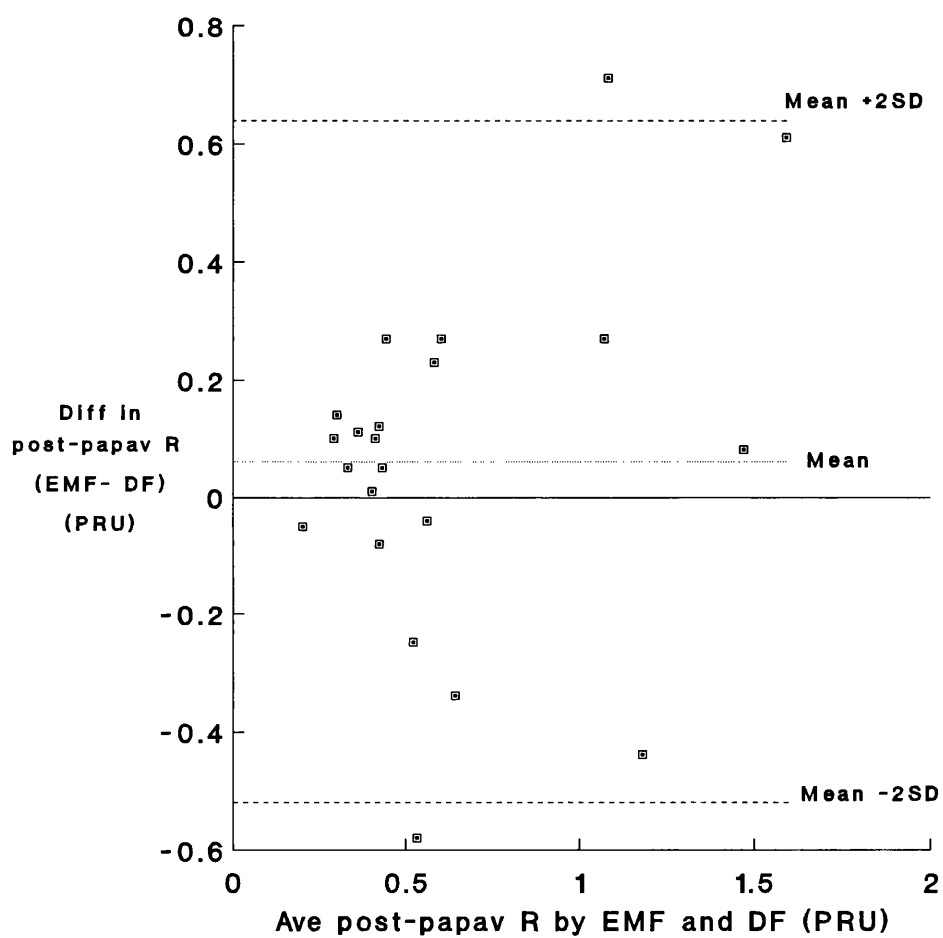
Fig A.8 Limits of agreement for post-papaverine graft resistance between the two flowmeters.

identified 2 out of 3 failures *ie* 66% sensitivity. A cutoff value of <90 ml/min identified all 3 failures but also included 4 successful grafts, and was therefore only 43% predictive.

Resting flow	Success	127 ml/min	(41 - 324 ml/min)
	Failed	58 ml/min	(22 - 59 ml/min)
		p = 0.0056	
Post-papaverine flow	Success	201 ml/min	(70 - 403 ml/min)
	Failed	65 ml/min	(56 - 86 ml/min)
		p = 0.0074	
Resting resistance	Success	0.74 PRU	(0.24 - 1.4 PRU)
	Failed	1.67 PRU	(1.37 - 3.4 PRU)
		p = 0.0043	
Post-papaverine resistance	Success	0.4 PRU	(0.22 - 1.4 PRU)
	Failed	1.28 PRU	(0.93 - 1.43 PRU)
		p = 0.0055	

Table A.6   Comparison of the Doppler flowmeter data in successful and failed grafts (Mann Whitney U test).

Resting graft resistance was a better predictor of early function. A cut off value of 1.5 PRU was 100% predictive of early failure, achieving 66% sensitivity. A lower cut off value of 1.35 PRU identified all 3 early failures, but included one successful case with a resistance of 1.4 PRU and was, therefore, only 75% predictive. The post-papaverine findings were similar, principally because of the same case, in which the resistance remained at 1.4 PRU. The best cut off was achieved at 0.9 PRU, which was 100% sensitive, and 75% predictive of early failure.

Discussion

The results in this group of patients support the findings from the in vitro study that there are potentially large differences in the flow rates recorded by the two flowmeters. This is reflected by the wide limits of agreement between the two for the four categories assessed. The obvious conclusion to be drawn from this is that it is not possible to combine measurements made by either of the systems in a series, and relevant conclusions with regard to early graft function can only be drawn from measurements made with the same flowmeter for all patients.

While this is undoubtedly the case there are also broad similarities which are probably of equal relevance. It is clearly the case that grafts with low flow and high resistance are at high risk of early failure, and both systems are able to identify these patients, albeit with differing sensitivity and specificity. There was in fact better agreement between the two flowmeters in cases of low flow (mean flow < 80 ml/min) than might have been expected following the in vitro study, providing some indication that the artificial nature of the flow circuit may have been partly responsible for the differences observed.

While the data may not, therefore, be directly comparable the message is still the same, with each system identifying cut off values above which early failure is likely. Values which are adopted for use in clinical practice may be derived from local experience with a particular system, but provided care is taken in carrying out flow measurements, particularly with regard to vein measurement when using the DF, then cut off levels determined with a particular system should be interchangeable between different centres.

Neither system was able to separate successful from failed reconstructions completely, but in reality this is unlikely to be possible in view of the number of factors which combine to determine graft outcome. Even with the relatively small numbers in this study, however, the separation achieved with the DF was acceptable, and would presumably be improved by increased numbers.

In terms of its overall performance, therefore, the DF would seem to be a

reasonable replacement for the EMF with regard to intraoperative vein graft assessment. Grafts at risk of early failure are identified by low flow, and the addition of pressure measurement in order to calculate graft resistance is a further refinement. The use of papaverine did not appear to confer better separation, in contrast to the findings of Beard (1987). In view of the fact that grafts may be successful in spite of apparently poor haemodynamics, the main role of identifying these cases is to enable the surgeon to make a decision regarding exploration in the event of early postoperative failure. If the completion resistance is high and nothing further can be done to improve the situation *ie* satisfactory completion arteriogram, no alternative outflow vessels, then there is clearly little point in exploring the graft if it subsequently fails. Conversely, there is clearly a place for exploring a graft which fails early in which the completion measurements were satisfactory. Although this latter scenario was not seen in this smaller study it did occur in the larger group studied in the main body of the thesis.

A surgeon planning to introduce flow and resistance measurements clearly needs to choose between the two instruments, and in this respect the DF would appear to have several clear advantages. The initial outlay is certainly cheaper, even when including the trolley and thermal printer, which must be supplied separately for the EMF. Although the plastic clips are disposable and only recommended for single use, they are relatively cheap. They are supplied in sizes ranging from 3 to 12 mm, but in our experience only the 4 to 7 mm clips are used regularly. Furthermore it is possible to use them on more than one occasion by resterilising them in ethylene oxide or glutaraldehyde. The DF has been designed to be user friendly and this is certainly borne out in clinical use. The steps are easy to follow and can be initiated by the surgeon using the foot pedals, or the push button sequence can be followed by any assistant. This is clearly not the case with the EMF which really requires a competent technician in order to carry out reliable measurements.

A further advantage of the DF is the information supplied in addition to the flow and resistance figures. When flow is being measured the Doppler signal is both

visible and audible. It is reassuring to see and hear a hyperaemic waveform at the end of a long procedure, and this pattern is easily recognised by surgeons with only a minimal understanding of Doppler ultrasound. It is very tempting to put a low flow figure on the EMF down to a machine error but the combination of a low flow and a pulsatile waveform on the OpDop screen are very difficult to ignore.

CONCLUSIONS

The in vitro study certainly introduces a degree of caution into the interpretation of flow measurements in terms of their absolute accuracy, and the comparability of the two instruments, this latter point being emphasised in the clinical study. Experience, however, has shown that in spite of these problems flow and resistance measurements are a valuable means of graft assessment, particularly with regard to predicting early graft outcome.

The EMF certainly appeared to be more reliable at low flow rates in vitro, but in fact the results using either flowmeter were equivalent in the clinical part of the study, and given this fact the DF has a considerable number of advantages to recommend its use over the more traditional instrument.

APPENDIX B - PATIENT DATA

Age	Diab	AP	ABPI	Severity BJS	ECD	Graft	Distal anast
Successful grafts							
67		95	0.68	RP	RP	ISV	Per
51		40	0.24	CI	CI	ISV	TPT
80		40	0.22	CI	CI	RSV	SFA-Per
70		50	0.36	CI	CI	ISV	Per
70		120	0.77	RP	RP	RSV	SFA-Per
77		90	0.56	CI	TN	ISV	Per
72	Y	75	0.44	RP	RP	ISV	SFA-TPT
84		35	0.22	CI	CI	ISV	AT
84	Y	90	0.46	CI	TN	ISV	Per
74		55	0.35	CI	TN	ISV	Per
80		60	0.34	CI	TN	ISV	Per
70	Y	35	0.2	CI	CI	Rev arm	AT
64		70	0.38	CI	TN	ISV	BKPop
81		40	0.19	CI	CI	ISV	Per
79	Y	40	0.23	CI	CI	ISV	SFA-AT
54		80	0.55	RP	RP	RSV	BKPop
82		50	0.29	CI	CI	RSV	Per
74		60	0.4	CI	TN	ISV	Per
81		45	0.23	CI	CI	ISV	Per
85		55	0.29	CI	TN	RSV	Per
80		40	0.23	CI	CI	ISV	Per
77		0	0	CI	CI	ISV	BKPop
77	Y	85	0.53	CI	TN	ISV	AT
66		45	0.38	CI	CI	ISV	Per
69		40	0.28	CI	CI	ISV	BKPop
61		25	0.16	CI	CI	RSV	BKPop
73		60	0.36	CI	TN	ISV	PT
89		40	0.4	CI	CI	ISV	SFA-Per
77		0	0	CI	CI	ISV	TPT
85		30	0.27	CI	CI	ISV	Per
77	Y	30	0.26	CI	CI	ISV	BKPop
65	Y	90	0.64	RP	RP	RSV	SFA-TPT
Failed grafts							
75		70	0.67	CI	TN	ISV	BKPop
74	Y	80	0.61	CI	TN	ISV	AT
59	Y	90	0.5	RP	RP	ISV	TPT
75		60	0.34	CI	TN	ISV	SFA-DP
75		100	0.64	CI	TN	ISV	SFA-DP
70	Y	90	0.69	CI	TN	ISV	BKPop
76	Y	85	0.61	CI	TN	ISV	Per
81	Y	20	0.15	CI	CI	RSV	AT
75	Y	80	0.35	CI	TN	ISV	Per
71	Y	40	0.33	CI	CI	ISV	BKPop

AP = ankle pressure in mmHg, BJS = British Journal of Surgery
ECD = European Concensus Document, RP = rest pain, CI = critical
ischaemia, TN = tissue necrosis, BKPop = below knee popliteal,
Per = peroneal, TPT = tibioperoneal trunk, AT = anterior tibial,
PT = posterior tibial, DP = dorsalis pedis, SFA- = proximal
anastamosis to superficial rather than common femoral artery
ISV = in situ vein, RSV = reversed saphenous vein

PREOPERATIVE ASSESSMENT

SD	Dep Dop		PGR		Arteriogram		
	ves	arch	ves	arch	ves	mod	arch

Successful grafts

SD	ves	arch	ves	arch	ves	mod	arch
3	3	2	3	2	2	3	Y
2	2	2	3	2	3	3	–
1	1	0	1	0	0	0	–
2	3	1	2	0	1	1	–
3	3	2	3	2	3	4	–
2	3	2	2	1	1	2	Y
2	2	2	2	1	2	4	–
2	3	1	3	0	2	3	–
2	3	2	3	1	1	2	–
2	3	2	2	2	1	2	–
3	3	1	3	0	2	3	–
2	2	1	2	1	2	2	Y
3	3	2	3	2	3	4	Y
2	2	0	2	0	2	2	–
3	3	1	2	1	1	1	Y
3	3	1	3	1	3	5	Y
3	2	1	2	1	1	2	Y
2	3	1	3	1	1	2	–
2	2	1	2	1	1	2	Y
2	2	2	2	1	1	2	–
2	3	1	2	1	1	2	Y
0	1	1	1	1	3	4	–
2	2	1	2	1	0	0	–
1	3	0	2	0	1	1	–
3	3	1	3	1	0	0	–
1	3	1	3	2	2	3	Y
3	3	2	3	1	1	1	–
2	2	2	3	0	1	2	–
0	1	1	1	1	0	1	–
2	2	0	2	0	0	0	–
3	3	0	3	0	1	1	–
3	3	2	3	2	3	5	Y

Failed grafts

SD	ves	arch	ves	arch	ves	mod	arch
2	3	1	3	1	1	2	–
2	3	1	3	1	1	1	Y
2	3	2	3	1	2	2	–
3	1	0	3	0	1	1	–
3	3	2	3	2	2	2	Y
2	1	1	3	1	1	2	Y
2	2	2	2	2	1	2	–
1	3	0	3	0	1	1	–
3	2	1	2	1	0	1	–
2	2	0	2	0	1	1	–

SD = standard doppler, Dep Dop = dependant Doppler
ves = No. of patent vessels detected
mod = modified arteriogram score

INTRAOPERATIVE DATA

Inf Res		Graft flow		Graft Res	
Pre	Post	Pre	Post	Pre	Post

Successful grafts

Pre	Post	Pre	Post	Pre	Post
0.95	0.45	77	220	1.32	0.41
0.76	0.72	180	260	0.52	0.34
0.9	0.88	80	108	0.92	0.66
1.03	0.97	120	242	0.89	0.41
1.16	0.8	58	260	1.2	0.25
1.32	1.3	110	120	0.9	0.73
0.5	0.42	193	221	0.37	0.35
0.74	0.68	140	185	0.75	0.48
1.17	0.97	51	82	1.3	0.86
0.68	0.65	140	215	0.75	0.46
1.05	0.95	90	225	1.11	0.4
0.88	0.92	87	82	0.55	0.48
0.46	0.4	285	395	0.29	0.19
0.98	0.9	60	90	1.1	0.73
0.7	0.68	75	110	1.0	0.69
0.96	0.78	72	105	1.22	0.81
1.2	1.11	210	240	0.4	0.35
0.36	0.36	160	195	0.52	0.42
1.35	1.05	70	97	1.21	0.88
1.03	0.92	108	212	0.84	0.39
0.94	0.9	87	137	1.1	0.69
0.62	0.56	210	170	0.26	0.36
0.74	0.76	63	85	1.11	0.88
0.8	0.76	138	200	0.71	0.48
0.54	0.4	400	450	0.2	0.17
0.7	0.68	138	208	0.64	0.41
0.63	0.58	135	180	0.77	0.57
0.46	0.4	62	62	1.16	1.2
1.04	0.92	100	190	1.06	0.53
0.8	0.66	269	390	0.19	0.12
1.25	1.1	35	46	1.66	1.43
1.0	0.7	92	182	1.08	0.96

Failed grafts

Pre	Post	Pre	Post	Pre	Post
0.67	0.45	78	112	1.47	1.04
1.5	1.35	33	64	2.3	1.2
0.92	0.88	50	92	1.3	0.85
>3.0	>3.0	78	85	1.33	1.21
>3.0	>3.0	54	63	1.76	1.51
1.24	0.75	68	175	1.31	0.57
0.72	0.86	260	280	0.28	0.26
2.6	1.08	49	113	2.24	0.88
>4.0	>4.0	28	30	3.18	3.07
>3.0	>3.0	15	38	>4.0	1.89

Inf Res, Graft Res = Infusion and graft resistance
Pre and Post = pre- and post- papaverine
Resistance figures in PRU,   Flow data in ml/min

CONTINUOUS MONITOR DATA

No.	Day	1	2	3	4	5	6	7
Successful grafts								
1	mean TAMV	13.3	15.5	15	16.1	15.4	12.6	13
	mean PI	1.6	1.4	1.4	1.5	1.5	1.6	1.5
2		25.7	31.6	25.7	23.6	13.5	18.6	19.8
		0.9	0.9	0.8	0.9	1.0	1.1	0.9
3		18.6	19.2	17.4	–	–	–	–
		1.3	1.2	1.2	–	–	–	–
4		12.4	13.2	11.6	–	–	–	–
		1.7	1.6	1.8	–	–	–	–
5		13.2	14.4	13.8	12.4	13.6	12.2	–
		1.5	1.3	1.5	1.6	1.5	1.6	–
6		17	15	14.2	23	17.4	17.7	27
		1.0	1.2	1.2	0.8	1.0	1.0	0.8
7		24.6	28.2	27.4	28	25.6	27.3	29
		0.6	0.5	0.5	0.4	0.6	0.5	0.4
8		19.8	21	22.4	19.8	20.4	–	–
		1.1	0.9	0.8	1.0	0.9	–	–
9		11.8	6.8	8.8	–	–	4	–
		1.8	2.4	2.1	–	–	2.6	–
10		23.2	23	26.2	19.2	19.2	16.1	19.0
		0.9	0.9	0.8	1.1	1.1	1.3	1.1
11		18.4	24.5	17.7	14.2	16.4	17.7	17.6
		1.2	0.8	1.3	1.5	1.4	1.3	1.3
12		48	60	36	51	35	42	–
		0.6	0.2	0.7	0.2	0.7	0.6	
13		26.2	24.3	–	–	–	–	–
		0.8	0.8					
14		8.4	9.9	10.2	7.8	8.4	11	9.2
		2.4	2.3	1.9	2.5	2.4	1.8	2.2
15		24.5	23.3	19.5	25.9	14.9	16.2	
		0.8	0.8	1.0	0.7	1.4	1.2	
16		28	24.4	27.2	–	–	–	–
		0.9	1.1	0.9	–	–	–	–
17		24.6	26	25.9	29	28.4	28	25.7
		0.9	0.8	0.8	0.7	0.7	0.7	0.8

cont.

18	38	42.4	37.5	33.2	36.9	41	37
	0.5	0.4	0.5	0.6	0.5	0.4	0.5
19	7.2	10.2	5.6	5.2	4.6	7.1	–
	2.3	2.0	2.5	2.5	2.6	2.3	–
20	13.5	14.6	12.8	11.9	13.6	12.4	12.2
	1.5	1.4	1.6	1.7	1.5	1.6	1.6
21	17.5	22	26	–	–	18	21.4
	1.3	0.8	0.6	–	–	1.3	1.0
22	27	29.2	35	26.7	29.6	32.3	28.7
	0.9	0.8	0.6	0.9	0.8	0.6	0.8
23	23.4	21	24.7	24.6	22.7	21.8	20.9
	0.9	1.0	0.8	0.8	0.9	0.9	1.0
24	21.8	18.8	19.6	–	–	–	–
	1.0	1.2	1.1	–	–	–	–
25	32.2	25.3	23.5	34.6	31.6	28.2	–
	0.6	0.9	1.0	0.5	0.6	0.7	–
26	12.5	13.6	11.8	14.2	–	–	–
	1.6	1.4	1.7	1.2	–	–	–
27	24	38.6	24.2	29.9	22.6	16.8	16.7
	0.9	0.5	0.9	0.7	1.0	1.3	1.3
28	12.2	10.8	12.0	–	–	–	–
	1.7	1.8	1.7	–	–	–	–
29	14.6	13.5	–	–	–	–	–
	1.4	1.5	–	–	–	–	–
30	29.8	27	25.6	24.7	26	28.9	–
	0.9	1.0	1.1	1.2	1.1	0.9	–
31	14.6	12.4	13.6	–	–	–	–
	1.5	1.7	1.6	–	–	–	–
32	15.6	13.4	12.8	15.2	–	–	–
	1.4	1.6	1.7	1.4	–	–	–

Failed grafts

1	16.4	–	–	–	–	–	–
	1.3	–	–	–	–	–	–
2	2.8	3.8	1.6	2	1.7	2.9	4.6
	3.8	3.7	3.9	3.8	3.9	3.8	3.6
3	–	–	–	–	–	–	–
	–	–	–	–	–	–	–
4	0.4						
	10						
4 (a)	0.2						
	12						
5	3.3	4.2	4.8	5.5	4.9	3.0	3.1
	3.8	3.8	3.9	3.6	3.9	4.0	4.0
6	12.2	–	–	–			
		–	–	–			
7	0.9						
	10						
7 (a)	14.2	10.4	9.3	7.2	3.1	2.8	3.1
	1.8	2.1	2.2	2.4	3.2	3.1	3.4
8	6.4	3.2	0.8				
	2.6	3.0	6				
9	0.6						
	8						
9 (a)	4.2	3.6	3.3	2.8	3.1		
	2.4	2.5	2.5	2.6	2.5		
10	9.7	6.7	9.6	9.9	7.4	8.4	4.4
	3.2	3.6	3.5	3.6	3.8	3.9	4.2

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Afoot and light-hearted I take to the open road,
Healthy, free, the world before me,
The long brown path before me leading wherever I choose.
from, Song of the Open Road
Walt Whitman