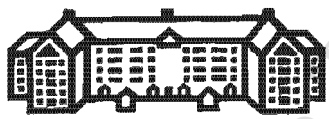
FEMORO-DISTAL BYPASS SURGERY AT GROOTE SCHUUR HOSPITAL: A 4-YEAR RETROSPECTIVE STUDY



Bibombe Patrice Mwipatayi

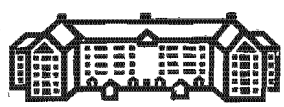
MD (UNIKIN), FCS (SA.)

A research report submitted to the Faculty of Medicine, University of Cape Town, in partial fulfilment of the requirements for the Degree of Master of Medicine in the branch of General Surgery.

Cape Town 2003

FEMORO-DISTAL BYPASS SURGERY AT GROOTE SCHUUR HOSPITAL:

A 4-YEAR RETROSPECTIVE STUDY



BIBOMBE PATRICE MWIPATAYI

DECLARATION

I, Bibombe Patrice Mwipatayi hereby declare that the work on which this thesis is based is my own work (except where acknowledgements indicate otherwise). It is being submitted as partial fulfilment for the degree of Master of Medicine, in the branch of General Surgery, at the University of Cape Town, South Africa. Neither the whole work nor any part thereof has been, or is to be submitted for another degree in this or any other university.

Signature:.....

Date:.....

ACKNOWLEDGEMENTS

I wish to make special mention of the following people, for their patience, support and encouragement throughout the time that I have spent working on this thesis.

My supervisors Dr. Peter Jeffery and Professor D. Kahn for their continued guidance and a source of support, encouragement and wisdom.

Professor E. Immelman for his extraordinary support and contribution throughout the duration of the writing of my thesis.

Dr. Phillip Matley for willingly sharing his considerable knowledge of vascular surgery and for setting the standards.

Dr S. Isaacs who was always willing and available in helping with the statistical analysis.

Dr. Peter Motale, who tirelessly collected the data that I used in this retrospective study.

The laboratory technician Gillian Wheeler and duplex technician Z. Behardien and G. Heuwel of Groote Schuur Hospital, with their assistance.

Michael and Tarquin Wyeth for their expertise with the graphics and printing of this thesis.

To my friends who were a constant source of encouragement and support throughout the whole process.

Finally to my wife, Sandra and my three children: Jose-Marid, Mariah-Theresa and Daniela who had to sacrifice many hours without me, so that I could complete this thesis.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ABI	Ankle Brachial Index
AKA	Above Knee Amputation
BKA	Below Knee Amputation
CLI	Critical Limb Ischaemia
DSA	Digital Subtraction Angiogram
ESRF	End Stage Renal Failure
ETE	End To End
ETS	End To Side
FBC	Full Blood Count
FDB	Femoro-Distal Bypass
GSH	Groote Schuur Hospital
HOCM	Hypertrophic Obstructive Cardiomyopathy
HPCSA	Health Professions Council of South Africa
HUV	Human Umbilical Vein
ICP	Integrated Care Pathways
INR	International Ratio
ISVG	In Situ Vein Graft
LMWH	Low Molecular Weight Heparin
eNOS	endothelial Nitric Oxide Synthesis
NIH	Neo-Intimal Hyperplasia
PGR	Pulse Generator Run-off
PTA	Percutaneous Transluminal Angioplasty

1. INTRODUCTION

The term "critical limb ischemia", while only defined in recent years by international consensus and objective arterial pressure measurements, has been recognized by surgeons since the dawn of reconstructive vascular surgery fifty years ago.

Patients present with increasingly severe and intolerable ischemic rest pain involving a single toe or the entire forefoot. There is usually a preceding history of progressively worsening claudication. Ischemic rest pain is worse at night; it is not relieved by over-the-counter analgesics and eventually dominates the patient's existence. On presentation, these patients frequently exhibit tissue loss, gangrene, ischemic ulceration and forefoot infection. Critical limb ischemia represents the end stage of lower limb atherosclerotic disease, and multi-segmented arterial occlusion is the rule on angiogram.

The incidence of critical limb ischemia in Europe has been estimated at 500 - 1000 per million of the population per annum and carries a cumulative mortality rate of 20% per annum.[1]

A more recent survey in the United Kingdom places the prevalence at 40 per 100 000 of the population per annum (+/- 20 000 patients).[2] In this survey, within one year of their initial presentation, more than 20% of patients will have

undergone major amputation and 10-20% will have died, largely from concomitant cardiac or cerebrovascular disease. Only 56% of patients will survive with both legs intact.

Vascular surgeons have traditionally focused on outcomes such as graft patency and procedural mortality and morbidity. In terms of professional satisfaction, a surgeon who performs a successful revascularisation on a patient with CLI, discharging the patient without rest pain with a patent graft and well healing wounds, classes that patient as a surgical success. Conversely, the inability to perform revascularisation or amputation resulting from early in-hospital graft failure is regarded as a personal failure.

Surgeons are also aware that the last fifteen years have seen a revolution in the management of CLI; a refinement in methods of femoro-distal bypass so often required in those patients, together with the complementary advances in endovascular techniques to obtain optimal inflow viz. balloon angioplasty, subintimal angioplasty and stenting.[3] These perceptions have led many to argue that attempts at revascularisation should be offered to all patients presenting with CLI.[4]

Articles that appear in specialist vascular surgical journals, especially large series, level I randomised trials and meta-analyses, influence vascular surgical practice worldwide. There is possibly the view that, given appropriate surgical expertise, the results achieved in the first world countries of excellence can be achieved

globally. This view is unduly simplistic and not adequately substantiated for a number of reasons.

White, Jones and Rutherford have critically reviewed the variations in the standardized reporting of outcomes, and thus the integrated assessment of results, which was published in the 5th edition of "Rutherford: Vascular Surgery", Chapter 1.[5] The introductory paragraph to this chapter reads:
"The published literature should provide a yardstick against which individual surgical practices and patient outcomes can be measured and serve as a common forum for the comparison of the benefits of different therapeutic approaches. However, unless we use universally accepted standards in reporting the clinical and patient based outcomes of vascular surgical procedures, one could question whether the yardstick is accurate and whether the forum, in fact, provides any commonality in diverse clinical experiences and patient populations. This consideration begs the larger question of whether published reports provide a true measure of vascular therapy and the benefits derived from it."

These authors highlight the fact that a significant proportion of the medical literature contains errors in the application of statistical methods. This was first identified by Glantz.[6] He estimated that between 40% and 60% of samples from British, American and Canadian publications contained significant errors. This has repeatedly been confirmed by other authors.

White, Jones and Rutherford also provide examples of major vascular reconstructive series which strongly influenced vascular practices at the time but which produced widely variable results. Reviewed by means of current day reporting standards these trials either failed to ensure adequate randomization or employed differing reporting standards (although not always stated in the text), resulting in conclusions that were not only misleading, but also erroneous.[5]

The use of actuarial (life-table) analysis was borrowed from the insurance industry and was first applied in medicine to the survival of cancer patients and the role of therapeutic intervention on survival.[7,8] The life-table analysis was widely adopted by vascular surgeons in the 1980s as a measure of outcomes other than mortality, e.g. graft patency.

Classical life-table analysis provides an estimate rather than a mathematical measurement and it may suggest differences that are more apparent than real. There is a better projection of the patency rates when a series is 'front-loaded' with many recent cases. This results in a levelling off of the declining patency curve near the end of the period of observation representing perhaps a handful of patent grafts during this latter period.

In summary the life-table method tends to overestimate the actual patency rate. Patency projections during the first two to three years of graft follow-up are notoriously misleading.

A detailed overview of the merits and demerits of life-table analysis in vascular surgery is provided in the classic paper by Underwood and Charlesworth.[9]

It was largely the enthusiasm and stimulus of Professor Robert Rutherford which led to the Society for Vascular Surgery (SVS) and the North American chapter of the International Society for CardioVascular Surgery (ISCVS), setting up an ad-hoc committee under his chairmanship to address "reporting standards in vascular surgery." The first report of this committee was published in 1986.[10] Subsequently, a revised version was published in 1997.[11]

This committee recognized the Kaplan-Meier survival estimate as possibly being superior to the conventional life-table for the analysis of vascular bypass data. In this publication, the authors define the need for explicit reporting standards in published articles in relation to: associated risk factors, the reporting of deaths and complications, the clinical grading of lower extremity ischaemia, outcome and patency criteria and methods of recording and reporting on patency status. In the case of the latter, the recommended criteria are set out in Table 1.

Table 1. Reporting Criteria of Patency Status[5]

Primary patency	Uninterrupted patency for the period of observation for procedures performed on native inflow/outflow vessels, e.g. percutaneous transluminal angioplasty or bypass graft.
Assisted primary patency	Procedures applied to a failing bypass graft to prevent subsequent occlusion, e.g. PTA or vein patch angioplasty for graft stenoses (neo-intimal hyperplasia).
Secondary patency	Patency achieved after thrombotic graft occlusion by means of thrombectomy or thrombolysis.
Limb salvage	Patients with patent grafts and functional limbs without rest pain or tissue loss, as well as patients with failed grafts who have not reverted to pre-operative rest pain and who retain a painless functional limb.

These recommendations of 1997 are now widely available and should ensure a far greater uniformity and comparability of current and future publications.

Possibly more important than variations in reporting standards is the likelihood that there are significant differences in patient demographics between first world

centres of excellence and highly socialised societies on the one hand, and vascular patients in developing and third world countries on the other. In the cases of the former, better patient education, seeking attention at an earlier stage, a greater proportion of social class 1 and private patients, better patient compliance, and the wide availability of tertiary vascular services together with sophisticated and effective rehabilitation programmes.

Although presently unquantified, these differences may be so great as to render first world reconstructive vascular policies inappropriate in developing countries. There is thus an urgent need for vascular surgeons in developing countries to audit their own outcomes for revascularisation in CLI and their rates and outcomes of primary amputation.

In this regard, quality of life estimates in both groups needs to be established to obtain a balance between available resources and community rehabilitative services. This could allow the establishment of an optimal, affordable and acceptable approach.

2. SETTING

This study was done in a tertiary academic Vascular Unit attached to Groote Schuur Hospital and affiliated to the University of Cape Town. Over the past two decades, vascular surgery has represented the predominant interest of two general surgical units.

With the move from the old to the new Groote Schuur Hospital in 1989, a decision was made by the Department of General Surgery to divide the four general surgical firms along defined sub-specialist lines. At that time each of the four units had access to 40 surgical beds and were allocated seven half-day operating lists per week. A non-invasive Vascular Laboratory supported the Vascular Surgical Unit.

Clinical, research and logistical support for the unit is provided by Vascular Radiology (D.S. angiography and endovascular procedures), cardiology, cardiac surgery (thoraco-abdominal aneurysm repair requiring pump bypass), anaesthetics, neurology (cerebro-vascular ischaemia), hematology, a surgical intensive care unit and the Red Cross War Memorial Children's Hospital.

The Vascular Unit provides a consultative service for our affiliated secondary hospitals: Somerset, Conradie, G.F. Jooste and Victoria hospitals, as well as to greater Cape Town, the Western Province and to areas as far field as the Eastern Cape Province. The Unit runs a multi-disciplinary amputation clinic with

orthopaedic surgeons, orthotists, physiotherapists and occupational therapists, providing a regional service.

Severe and ongoing budgetary restraints imposed on Groote Schuur Hospital since 1994 have impacted negatively on all clinical services. Vascular beds for the period under review have been reduced from 40 to 16 and three half-day operating lists per week.

The total population of the Western Cape Province is estimated at 3 958 000 (census 1996). Apart from the Groote Schuur Vascular Unit the only other tertiary Vascular Unit is situated at Tygerberg Hospital, the teaching hospital of the University of Stellenbosch.

In the period under review (1998 – 2001), the Groote Schuur Vascular Unit staff comprised a Head of Unit and 5 part-time surgeons registered as Vascular Sub-specialists with the Health Professional Council of South Africa. Additional staff comprised a Senior Registrar (Vascular Fellow), two Registrars and two interns.

3. OBJECTIVES OF STUDY

The stimulus for this study arose from the strong impression of the consultant staff of the Vascular Unit that:

- Constraints on bed and theatre availability had resulted in a shift in therapeutic policy since the mid-1990s.
- In the case of patients presenting with CLI, ever-stricter selection criteria were applied for limb salvage resulting in only patients with the best-deemed outcome being offered revascularisation for limb salvage.
- Despite the stringent selection criteria, patients undergoing femoro-distal bypass, in particular, fared badly, even in the short term, when compared to results from first world countries.
- An increasing proportion of patients with C.L.I. were being offered primary amputation rather than revascularisation in this period.

3.1. SPECIFIC OBJECTIVES OF STUDY:

In light of the above, a retrospective study was planned to analyse the demographics and outcome of femoro-distal bypass in patients presenting with defined, critical limb ischaemia, in the period 1998 – 2001 (inclusive). Choice of this period, although it would preclude medium to long-term observation, was decided upon because it coincided with the introduction of a protocol approach to C.L.I.

The objectives in this cohort of patients were:

- To define patient demographics.
- To establish 30-day hospital mortality rates.
- To assess outcome in terms of primary, assisted primary, secondary patency and overall limb salvage.
- To assess, if possible, pre- or post-operative factors that would predict early graft failure.
- To analyse the functional outcome between those patients with patent bypasses and those with failed bypasses.

In addition, this study aimed at analysing the total number of major limb amputations performed by the Vascular Unit in the same 4-year period and, specifically, those that were performed as primary procedures for C.L.I.

The final goal of the study was to compare our results with established international norms and, in this way, try to establish an optimum management pathway for patients presenting with C.L.I. to Groote Schuur Hospital, commensurate with the constraints under which we function.

4. POLICY OF THE GSH VASCULAR UNIT REGARDING C.L.I. (1998 – 2001)

The policy of the Vascular Unit regarding the management of C.L.I. during this period can be broadly summarized as follows:

4.1. INDICATIONS FOR PRIMARY AMPUTATION:

a) Institutionalised, bed-ridden or wheelchair-dependent patients who would not benefit from limb salvage, eg. Dementia, advanced malignant disease and severe medical co-morbidity with adjudged short life expectancy.

b) Patients with severe, established hip and knee contractures.

c) Patients with previous contralateral, major limb amputation, wheelchair bound, who have not achieved a degree of functional rehabilitation.

d) C.L.I. in a functionally useless limb, eg. previous ipsilateral stroke with poor or zero recovery.

e) Patients presenting with C.L.I. with extensive gangrene or tissue loss in whom, even with successful revascularisation, a functionally viable foot is unlikely to be achieved.

f) Patients who are adjudged not to be a candidate for an inflow procedure, a femoro-popliteal bypass or a crural bypass when assessed by a combination of angiography, duplex Doppler and pulse generated runoff studies will not be successful.

4.2. INDICATIONS AND POLICIES FOR REVASCULARISATION:

a) In all patients the intention was to provide optimum hemodynamic inflow to the infra-inguinal vasculature. In elderly patients, with short life expectancy, and those suffering from rest pain but without tissue loss, every effort was made to employ an endovascular procedure; iliac angioplasty with or without stenting, superficial femoral, popliteal or even trifurcation angioplasty for short high grade lesions and, in selected cases, subintimal angioplasty.

b) Aortobifemoral, femorofemoral and, in high-risk patients, axillobifemoral bypass was considered in patients with aorta-iliac disease who are not candidates for an endovascular procedure. In the absence of pedal tissue loss such procedures usually relieve ischemic rest pain.

c) Femoro-popliteal bypass was considered in patients with adequate femoral inflow and superficial femoral artery occlusion presenting with critical ischemic limb and incapacitating short distance claudication. Autogenous vein was the conduit of choice.

d) Femoro-distal bypass was preferred to bypass to the blind popliteal segment in those patient presenting with rest pain and tissue loss where both the SFA and trifurcation were occluded. The dominant crural artery crossing the ankle and communicating with an intact pedal arch was chosen for the distal anastomosis. This vessel was identified by means of pré-operative duplex scanning, angiography, and pulse generated runoff studies and occasionally by on-table angiography. Autogenous vein was the conduit

of choice. In the absence of a suitable vein, a 6.0 mm ringed PTFE graft was employed, together with a distal Miller (or modified Miller) vein cuff. Sequential grafts were avoided and distal arterio-venous fistulae were not constructed.

5. MATERIAL AND METHODS

5.1 STUDY DESIGN:

This is a retrospective study of all patients undergoing femoro-distal (crural) bypass for C.L.I. in the Groote Schuur Vascular Unit between January 1998 and December 2001.

A chart review was performed. Patients were identified from the Vascular Laboratory computer database, copies of operation notes and the operating theatre register. Information was extracted from patients' hospital records as well as by telephonic interviews with the patients or relatives.

5.2 ETHICAL APPROVAL:

Approval for this study was obtained from the University of Cape Town Health Sciences Faculty; Research and Ethics Committee on 9 July 2002, Ref: 244/2002.

5.3 PATIENT DATA AND DEFINITIONS:

Critical limb ischaemia was defined as a patient presenting with ischemic rest pain for more than two weeks, requiring opiate analgesia, with or without tissue loss, and associated with an absolute ankle pressure of less than 50 mmHg or, in diabetics, a toe pressure of less than 30 mmHg.

Segmental Doppler pressures were performed in a standard manner using a 10.0 MH_z continuous wave Doppler probe. Toe pressures were obtained using photo-plethysmography.

Diabetes was diagnosed if the patient was a known diabetic or had a fasting blood glucose exceeding 5-6 mol/l plus glycosuria. Hypercholesterolemia was defined as a fasting serum cholesterol above 5.2 mmol/l or serum L.D.L above 3.4 mmol/l. Lipid screens were not performed routinely on all patients, but on those less than 50 years of age, those with clinical stigmata of hyperlipidaemia or those with a family history. Patients admitting to smoking more than 5 cigarettes per day were classed as current smokers. Hypertension was diagnosed according to WHO criteria, defined as a systolic pressure greater than 160 mmHg or a diastolic pressure greater than 90 mmHg or both.

Demographic data recorded included patient age, gender, atherosclerotic risk factors and cardiovascular co-morbidities. Routine laboratory tests included complete blood counts; hemoglobin, total leukocyte and platelet count, electrolytes, urea and creatinine estimation. The upper level of serum creatinine accepted by our laboratories is 100 mmol/l. All patients were submitted to INR estimation, and patients under the age of 50 were screened for hyperhomocystinaemia with a fasting homocysteine level and response to oral methionine load. Pre-operative assessment included chest radiography and resting electro-cardiography in all patients. Spirometry (FEV1 and FVC) and left ventricular ejection fraction were obtained if clinically justified (effort dyspnoea, orthopnea or signs of cardiac failure).

5.4 COLOUR DUPLEX DOPPLER ASSESSMENT:

Increasingly, during the period under review, pre-operative and pre-angiographic colour duplex Doppler examination of the aorto-iliac and distal vessels was obtained, although it was not routine in all patients.

A dedicated duplex technologist used a Toshiba Sonolayer (model SSH-140A) with a 3.75 mHz curvilinear probe for abdominal arteries and a 7.5 mHz linear array probe for infra-inguinal vessels.

Significant stenosis was defined by identifying localized high peak systolic velocities (PSV). Focal stenosis was defined as follows: an increase of peak systolic velocity of at least 100% (eg. PSV rise from 80-160 cm/s) i.e. a ratio of 1:2 is classed as a +/-50% stenosis; whereas a trebling of PSV (eg PSV rise from 80-240 cm/s) i.e. a ratio of 1:3 is classed as a +/- 70% stenosis.

5.5 ANGIOGRAPHY:

All patients in this series were subjected to angiography. This was performed using a Seldinger technique with the catheter sited in the infrarenal aorta. The equipment used was a Phillips Maximus CM80 with DVI (Digital Vascular Imaging) and a single plane C-arm. Contrast media used was Iopamodil (Omnipaque 300) with an average volume of contrast per examination of 150-200 ml.

When a single flush-run angiogram fails to opacify patent crural arteries a number of techniques to maximize crural arteries imaging have been described. These include multiple contrast runs, angiography after reactive hyperaemia and the use of vasodilators.

Magnetic resonance angiography, which may be superior to contrast angiography in the identification of patent crural arteries, was not available in the period covered by this study.[12]

5.6 ANGIOGRAPHIC SCORE OF PATIENTS WITH CLI:

A single radiologist who was not aware of the surgical procedure performed or the clinical outcome blindly reviewed the angiograms of all patients who underwent femoro-distal bypass in the study period. The system of scoring was that described by Scott et al.[13] The scoring technique is illustrated graphically in Fig 1. The results of the angiographic score were not correlated with the duplex scanning findings in this study.

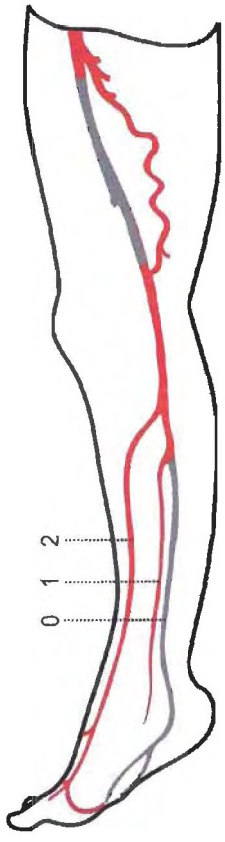


Figure 1: Angiographic Scoring

Two points were given to a widely patent vessel to the ankle (2). One point for a diseased but patent vessel to the ankle (1).
No points for an occluded vessel (0). For a single leg, the scoring range is from 0-6 with 6 representing the best runoff and 0 representing the worst runoff.

5.7. PULSE GENERATED RUNOFF:

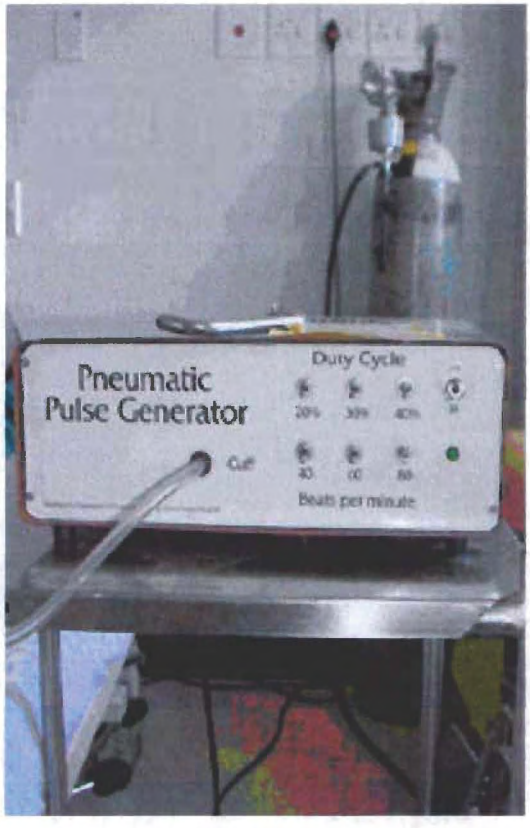
In 1988, Beard and his colleagues in Bristol (England) described this novel yet simple method of identifying crural vessel patency in patients with CLI, especially those patients in whom angiography failed to reveal a suitable crural vessel for femoro-distal bypass and in patients with inaudible Doppler signals at the ankle.[14] The unit is driven by compressed air and allows the inflation of a sphygmomanometer cuff around the upper calf to 300 mmHg and at a variable inflation rate per minute. With the patient supine, the posterior, anterior tibial and peroneal arteries are isolated just above the ankle with a continuous wave Doppler probe (10 MHz). While the system is set to 50 inflations per minute, an audible Doppler signal is sought which coincides with this rate of inflation. The signal is recorded as biphasic, monophasic or absent for each of the three vessels. The pedal arch patency test (Roedersheimer) is easily performed and is classed as patent, incomplete or occluded. This test allows the technologist to determine which crural artery is the most direct feeder of the pedal arch and which possesses the best hemodynamic signal.[15]

The pulse generated runoff equipment employed in this study is illustrated in Fig.2.This equipment was constructed by the Engineering Department of Groote Schuur Hospital.

During the period of the study, all cases where the angiograms failed to demonstrate a patent crural artery were subjected to PGR including

Roedersheimer evaluation of the pedal arch. In addition, patients with more than one crural artery identified by angiography, were subjected to PGR to identify which artery was the most appropriate artery for distal bypass (best signal and direct communication to the pedal arch).

Figure 2. PGR Machine (G.S.H. Vascular Laboratory)



5.8. CHOICE OF BYPASS:

Wherever possible, autogenous vein was utilized for femoro-distal bypass. The decision as to whether this was "reversed" or "in-situ" was left to the consultant surgeon in charge of that individual patient. In the cases of in-situ bypass, valvulotomy was conducted by means of a "Le Maitre" valvulotome and completion on-table angiography was performed in the majority of cases.

5.9. PRE-OPERATIVE VEIN ASSESSMENT (MAPPING):

In all patients with CLI, autogenous vein was the conduit of choice. Pre-operatively all patients are scanned by means of duplex Doppler using a 7.5 MH_z linear array probe (see above) with the patient in the erect position. The ipsilateral long saphenous vein was scanned first and, if suitable, (diameter > 3.5 mm) marked with an indelible pen from ankle to groin, with serial measurements of the diameter.

If no suitable ipsilateral vein was present, the contralateral long saphenous vein was scanned. If no suitable saphenous vein was identified, the arm veins (cephalic) and the short saphenous veins were scanned.

5.10 PHARMACOLOGICAL TREATMENT:

No patient was treated perioperatively with Prostanoids. Most patients were already on low-dose acetylsalicylic acid (150 mg daily) and continued with this post-operatively.

Oral anticoagulation (warfarin) was not used routinely unless indicated for other reasons, usually cardiac.

5.11 FOLLOW UP AND GRAFT SURVEILLANCE:

Patients were followed up in the Outpatients Department and the Vascular Laboratory.

In all patients with an autogenous vein bypass, a formal duplex Doppler surveillance programme was followed post-operatively for two years to identify graft-related problems, particularly graft stenosis. The surveillance programme intervals were as follows: Six weeks, three months, six months, one year and two years post-operatively.

Low flow in the graft or areas of stenosis on duplex Doppler was reported. In these cases a confirmatory angiogram was performed and, if a significant stenosis was confirmed, a decision was made to treat with either balloon angioplasty or surgical vein patch angioplasty.

5.12 MAJOR LIMB AMPUTATIONS FOR CLI:

All patients who underwent major limb amputations (below knee, through knee, above knee and hip disarticulation) during the period under review were identified. The subgroup of those undergoing primary amputation for CLI were identified and analysed for completion of this study, but this did not form part of the primary objective of this study.

5.13 STATISTICAL METHODS:

Patient survival, limb salvage and graft patency (primary, primary assisted and secondary) were assessed by life-table analysis and Kaplan-Meier analysis, using a commercial software package 'Statistica' (version 5) and Epiinfo (version 6). Univariate data analysis of risk factors for graft failure was analysed, comparing discrete variables with Chi-square test and continuous variables with the Mann-Whitney test. Multivariate analysis was done using a Cox proportional hazard model. Data expressed in tables reflects absolute patient numbers or median values for non-parametric data with interquantile ranges (25^{th} to 75^{th} percentile) expressed in parentheses, unless stated otherwise. The one-sided p value of 0.05 was used as the level of significance.

6. RESULTS

Patients included in the study underwent femoro-distal bypass for limb salvage at Groote Schuur Hospital (GSH) from January 1998 to December 2001. Only patients who underwent femoro-distal bypass as defined previously, and whose medical records were available and complete, were included in this study.

During the four years (1998 - 2001), 65 patients underwent femoro-distal bypass. We analysed 57 patients and eight patients were excluded from this study: complete medical records of five patients were not available.

During the same period, 488 amputations were performed at Groote Schuur Hospital by the Vascular Unit, representing 45% of all vascular procedures performed.

6.1 PATIENT CHARACTERISTICS:

The demographics and other relevant data pertaining to the 57 patients are shown in **Table 2.**

The median age of the patients in this study was 62 years (mean 61,1 years) with a male to female ratio of 34 to 23. Thirty-eight patients were mixed race, 13 were white, and six were black.

Twenty-eight patients (49%) were diabetic. The mean hospital stay was 20,9 days with a minimum of seven days and a maximum of 68 days. Five patients (8,8%) died within 30 days of the initial operation. Three died from myocardial infarction

and two from cerebral vascular accidents. Another five patients died within two years of the initial operation, an overall two-year mortality of 19,2%.

Table 2. Demographic characteristic

Parameter	**Result**
Number	57
Sex ratio (M/F)	34/23
Mean age and range (years)	61,1 (27-88)
Race: Mixed race: White: Black: Indian	 38: 13: 6:0
Risk factor: • Smoking • Diabetes • Hypertension • Hyperlipidemia • Coronary artery disease	 36 28 21 6 7
Serum creatinine (umol/l)	96,42 (58-164)

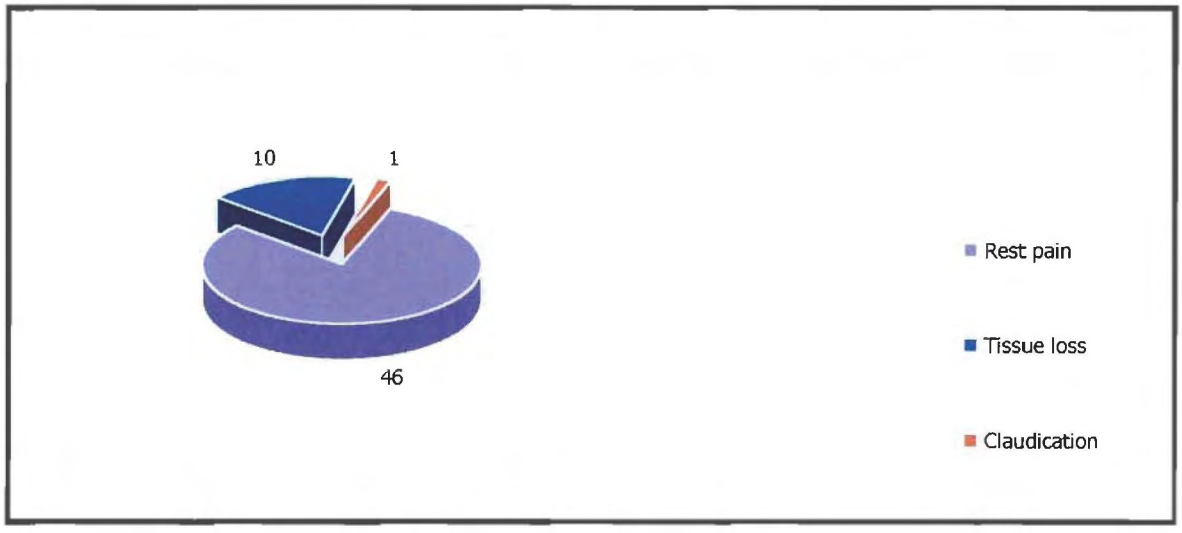
6.2 INDICATIONS FOR SURGERY:

Forty-six patients (80%) presented with rest pain (with or without tissue loss) as shown in **Figure 3.**

There was a subgroup of patients (18%) with tissue loss who had a peripheral neuropathy and didn't have rest pain. They were all diabetic. Those patients had a high incidence of local foot sepsis after revascularisation.

One patient (2%) had less than 20 m incapacitating claudication.

Figure 3. Indications for FDB

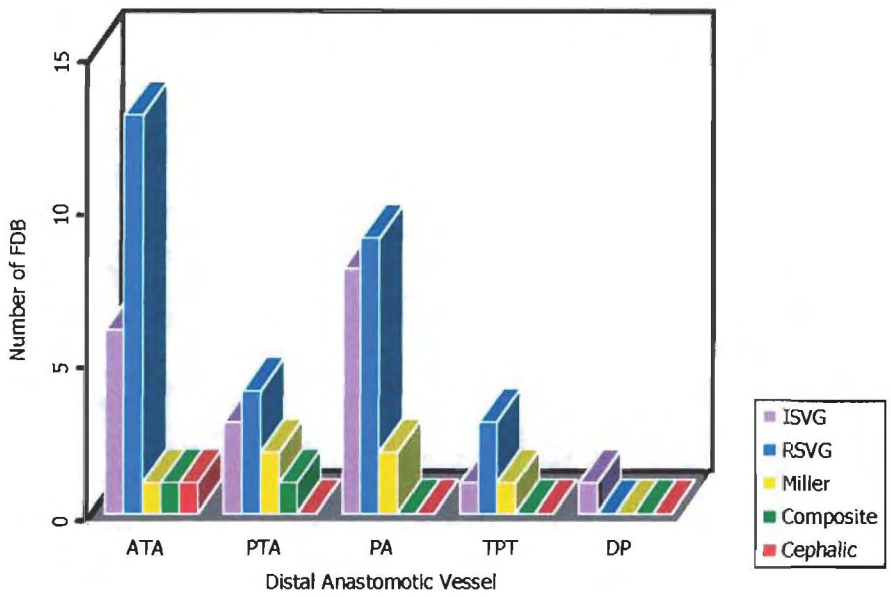


6.3 GRAFT CONDUIT AND DISTAL ANASTOMOTIC SITE:

Using In Situ Vein Graft (ISVG) versus Reversed Saphenous Vein Graft (RSVG) was left to the choice of the individual surgeon. RSVG was used in 29 legs (50,9%) and ISVG in 19 legs (33,3%). There was no statistically significant difference in the graft patency between the two methods (p = 0,39): the two-year cumulative patency was 40% for the RSVG and 39% for the ISVG. Six patients had a 6 mm PTFE graft with a Miller cuff. The peroneal and anterior tibial arteries were mostly used for distal anastomosis, respectively in 19 legs (34,5%) and 22 legs (38,5%)

as represented graphically in Figure 4. Probably, because they are last to be affected by atherosclerotic process.

Figure 4. Type of Graft Conduit and Distal Anastomotic Crural Vessel



6.4 AMPUTATION:

We did analyse all primary amputations performed during the same period for completion of this study, but this did not form part of the primary objective.

A total of 488 major lower limb amputations (ankle and foot amputations excluded) were performed. As stipulated above, only patients who presented with CLI, but with non-reconstructable vessels were analysed: 79 primary amputations were done for non-reconstructable crural vessels, confirmed either by duplex scanning or angiography. The results of this subgroup were compared with the *results of 14 amputations done after failed femoro-crural bypass within 30 days.*

The demographic data of all 79 primary amputations are shown in **Table 3.**

Table 3. Demographic Data

Variable	Value	Standard Deviation
Number of patients	79	
Age (years)	62,5	11,48
Race: Mixed race: White: Black: Indian	48:23:7:1	
Sex (M/F)	51/28	
Smoking	65,8%	
Diabetic	63,4%	
Creatinine (umol/l)	118,1	11, 3
Angiographic score	1,18	0,859

Seventy-nine primary amputations were carried out in 51 male and 28 female patients with a mean age of 62,5 years (standard deviation of 11,48). Forty-eight were mixed race, twenty-three were white and seven were black. Twenty-four patients were diabetic and fifty-two were smokers.

The mean creatinine was 118,1 umol/l with a standard deviation of 11.344. The mean angiographic score was 1,18 (standard deviation of 0.859). Hospital length of stay for all 79 patients averaged 13,1 days with a standard deviation of 8,075.

The demographic data of all 14 amputations performed within 30 days of failed femoro-distal bypass are shown in the Table 5. The mean hospital stay of this

subgroup was 26,9 days, with a standard deviation of 19.340; longer than in the primary amputation group ($P < 0.05$).

Revascularisation prior to amputation did not affect the level of amputation as shown in table 4. The conversion of below knee amputation (BKA) to above knee amputation (AKA) between primary amputation and amputation within 30-days of failed femoro-distal bypass (secondary amputation) was not statistically significant ($P > 0.05$).

Table 4. Type of amputation based on prior revascularisation procedure

Type of Amputations	BKA	AKA	BKA converted to AKA
Primary amputation	35	44	9 (25,7%)
Secondary amputatuion*	6	8	3 (22,2%)

*The 14 patients had an amputation within 30 days after revascularisation.

6.5 FACTORS ASSOCIATED WITH GRAFT FAILURE

Only two factors influenced the outcome of femoro-distal bypass in our unit (Table 5): Local sepsis in the foot and early post-operative ABI (more than 0.85) with a significance level of $P<0.05$.

Diabetes mellitus, sex, age and race had no influence on the outcome.

Using serum creatinine as a parameter of assessing renal function, this was not a factor influencing graft patency (Kruskal-Wallis test, $P=0.16$).

Table 5. Univariate Analysis of Risk Factors in Relation to Graft Failure/Patency (> 1month)

	Early Graft Failure (< 1 month)	Patent Graft (> 1 month)	P value
Patients Number	14	43	-
Age (years)	60	62	-
Sex (M/F)	9/5	25/18	0,89
Smoking	8	32	0,85
Diabetes	9	19	0,49
Creatinine	102,5	90,4	0,12
Hospital stay	26,9	14,9	0,02
Angiogram score	1,16	1,47	0,40
Local sepsis*	4	13	0,01
Graft conduit:			
• ISVG	3	13	
• RSVG	5	22	
• Miller Cuff	4	2	
• Composite	1	1	
• Cephalic	1	0	
Post-op ABI	0,65	0,9	0,01

*Patient with tissue loss and infection at the foot

This study showed that the site of distal anastomosis had no effect on graft patency or limb salvage. Mean hospital stay was statistically different between the two groups (26,9 and 14,9 days respectively).

There was no correlation between the run-off score and early graft patency. The angiographic run-off score failed to predict which grafts would fail.

In the early failure graft group: 5 patients had a score of 0, 8 patients had a score of 1-2 and 1 patient had a score of 3.

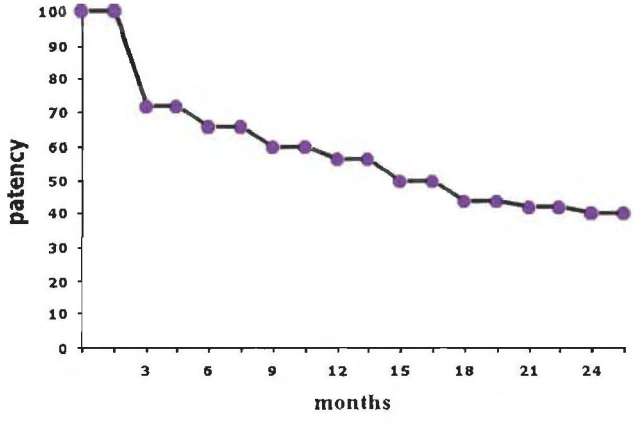
In the group of patient with a patent graft after 1 month, 9 patients had a score of 0, 18 patients had a score of 1-2, 9 patients had a score of 3 and 7 patients had score of 4-6.

6.6 GRAFT PATENCY

At 30 day, the primary patency was 75% with a limb salvage of 75%.

At two years, the cumulative patency and limb salvage rate in this study were 40% and 56% respectively (Figure 5 and Table 6).

Figure 5. Life-table Analysis of Cumulative Patency



*Life table analysis of patency rates of all 57 femorodistal bypass grafts. Y-axis represents the cumulative (%) of graft at risk and the X-axis the time in month. At 24 months, 40% of the 57 femorodistal bypass grafts were at risk.

As mentioned above, the surveillance programme intervals were as follows: six weeks, three months, six months, one year and two years post-operatively. 85% of patients booked for graft surveillance did regularly attend the surveillance programme.

Table 6. Patency and limb salvage for femoro-distal bypass

	Time in month				
	1 month	6 month	12 month	18 month	24 month
Cumulative patency (%)	75	66	56	44	40
Limb salvage rate (%)	75	70	67	62	56

Fourteen grafts failed within 30 days of initial surgery. This resulted in an amputation of the limb. Forty-three grafts were functional after 1 month of initial surgery and they were followed by duplex scanning:

- Eleven grafts required a secondary procedure to be performed to maintain their patency
- Two of the 11(autogenous) grafts were occluded and required thrombectomy and nine grafts had areas of high-grade stenosis with a significant decrease of velocity downstream from the lesion. Those were asymptomatic.
- Six of the 11 grafts stenotic lesions were detected at 18-24 months. The remaining graft stenotic lesions were picked up within 6 months of the revascularisation procedure.
- Six required angioplasty to maintain patency. The stenotic lesions were predominantly along the saphenous vein.
- Three grafts were managed surgically. The stenotic lesions were either at the proximal or distal anastomosis and were not amenable for endovascular interventions.

7. DISCUSSION

The last decade has seen an evolution in the philosophy and practice of infra-inguinal reconstructive surgery for peripheral vascular disease. There has been an aggressive attitude toward the management of those patients. This may have resulted in inappropriate selection of patients for bypasses in many cases, with many patients who would have been better served by a primary amputation, undergoing an ill-judged vascular reconstruction. The results achieved in our series, for both graft patency and limb salvage, are not comparable with most others series in the literature, and it is vital to seek out the factors that might have been responsible for this.

7.1 THE PATIENTS – RISK FACTORS AND SELECTION:

The age and sex distribution of the patients in this study is similar to that described by other authors[16,17] in spite of our small patient numbers. It is generally accepted that age correlates with the extent of atherosclerosis in all areas of the cardiovascular system, specifically the cerebral, medium-sized coronary and tibial arteries, particularly in the elderly.[18] Elderly patients with shorter life expectancy and more extensive atheromatous disease may derive little benefit from vascular reconstruction for limb salvage. However, the study by Chang et al who reviewed the charts of 1723 octogenarians and 2394 septuagenarians who were referred for possible vascular disease between 1978 and 2000, showed:[19]

- Most octogenarians achieved an excellent long-term outcome after infra-inguinal revascularisation.
- Peri-operative survival of octogenarians and septuagenarians was similar.
- Five-year primary and secondary graft patency and limb salvage rate were 74%, 80%, and 86%, respectively.

Ricco et al have shown that age alone does not significantly prejudice graft patency results up to two years after femoro-distal reconstruction.[20] It may, therefore, be unreasonable to withhold infra-inguinal bypass surgery from patients merely on the grounds of advanced age in the absence of other clinical contraindicating factors.

Several studies have found superior patency for bypass grafts in male patients when compared to female patients, and similar findings have been reported in coronary artery bypass surgery.[21] These differences in patency remain unexplained. Watson et al, reported a large, multi-centre, prospective, randomised trial assessing the impact of iloprost on graft patency and the following results were found:[22]

- The patency rate of femoro-distal bypasses was significantly higher in males than females.
- The increased patency in males was probably due to the increased use of prosthetic and composite grafts in female patients, due to poorer vein quality.
- Atherosclerosis appeared to be more advanced in women who needed surgical treatment.

Iloprost is a stable PGI2 analogue; apart from a strong local vasodilatory action, it has an antiplatelet activity that prevents or corrects the activation of platelets and leukocytes as well as their reciprocal interaction.

In our study, we did not find any difference in the patency at one- year between the different sexes.

It is generally accepted that patients with End Stage Renal Failure (ESRF) are not good candidates for infra-inguinal revascularisation, especially if they are diabetic.[23] The vessels are usually heavily calcified contributing to the technical difficulty in this procedure. The life expectancy of patients with ESRF has been extended by renal dialysis and transplantation although the cardiovascular morbidity and mortality rates are high due to the presence of hypertension, hyperlipidemia, and abnormal carbohydrate metabolism. Renal function is usually evaluated by the determination of serum urea and creatinine, more precisely by the determination of creatinine clearance, urine biochemistry and the renal size. In our study, we used serum creatinine to assess the renal function. None of our patients had ESRF, but some had mild renal dysfunction. It is known that patients with mild renal failure have the same outcome after revascularisation as those with normal renal function.[24]

The presence of diabetes mellitus in patients requiring infra-inguinal bypass, mainly to the tibial vessels, has traditionally been thought to prognosticate poorly

with regard to long-term graft patency and limb salvage.[25] This was not found to be the case in our patients nor in those followed-up for longer periods by other authors. Thomas et al reported, in 1988, their analysis of 73 patients who had infra-inguinal bypasses: 23 were diabetics and 50 non-diabetics. They found no differences in amputation rates (21% and 14%) and limb salvage rates (78% and 86%).

Subsequently, Rutherford et al, in their multi-centre dextran-40 trial, found that diabetic patients fared significantly better that non-diabetic patient, presumably because those patients had a lower incidence of smoking and higher use of in-situ grafts.[26] Only the type of graft significantly affected the long-term patency and salvage rate. This will be discussed further on.

Little data has been provided on the role of C-reactive protein in the outcome of lower extremity ischaemia. Kuukasjarvi et al, in 1995, showed that CRP and total leucocyte count were predictive of the outcome of acute leg ischaemia.[27] Subsequently, Upchurch et al showed that serum CRP concentration is higher among diabetic patients with a foot ulcer than in diabetic patients without a foot infection or in non-diabetic control patients.[28] CRP seems, therefore, to be a valuable auxiliary indicator of the operative risk and should be taken into consideration when deciding whether amputation, debridement, or bypass surgery is the treatment of choice.

Rutherford et al did show that tobacco use has an adverse effect on late patency.[29] Smoking did not impact on the one-year patency of femoro-distal bypass in our 57 patients.

In most studies the two factors that have the greatest influence on patency after infra-inguinal bypass, are the graft-type and the level of the distal anastomosis. The facts below are globally accepted:

- With below-knee anastomosis, there is a significant advantage of autogenous vein over polytetrafluoroethylene (PTFE) and Dacron, or human umbilical vein (HUV) grafts by one year and increasingly advantageous thereafter. The preference of vein over PTFE has been establish by randomised trials. Veith et al, in 1986, reported a significant difference in long-term patency between autologous vein (49%) and PTFE (12%), with a limb salvage of 61% and 57% respectively.[30]
- Shah and Leather, from Albany (USA), published their results of more than 1000 femoro-distal bypass over a 10-year period, which showed that there is a potential benefit of 'in situ' over 'reversed vein bypass' [31], but those findings were not confirmed by Harris et al, in 1993. [32] He showed no benefit of 'in situ' over 'reversed vein bypass'.
- No randomised data is available comparing HUV and PTFE, but surgeons are slow to adopt HUV because the grafts are subject to bio-degradation, which is more cumbersome to handle and more expansive than Dacron or PTFE. Many explanations have been proposed for the lower patency rates of PTFE bypass compared with vein:

a) Mismatch in compliance between the relatively stiff prosthetic graft and the native artery
b) The areas of low shear stress at the heel and toe of PTFE graft, as well as on the graft surface, may induce myointimal hyperplasia (MIH).

It has been suggested that a resting ABI after revascularisation of less than 0,85 predicts that the vein graft is at risk of failure. H. Prime et al, in 1992, reported that primary patency rate at two years was 88% for a resting post-operative ABI equal or more than 0.85 and 36% for a resting pot-operative ABI less than 0.85. Most stenoses occurred in the graft not at the anastomoses.[33] In our study, a resting post-operative ABI had a statistically significant influence on the outcome of graft patency ($p<0.05$). We found that a post- operative ABI of more than 0.85 was associated with a graft patency of more than two years.

The finding that only six Black patients were selected for femoro-distal bypass in the 4-year period of the study deserves to be mentioned. Grobelaar described, in 1974, the entity of 'juvenile arteritis in Black South Africans' of which etiology was uncertain: it was previously thought to represent a delayed hypersensitivity reaction to tuberculous infection. Robbs et al showed, in 1985, that atherosclerotic occlusive disease was becoming much more common as primary pathology in Black patients admitted to his unit for reconstructive arterial surgery.[34] Subsequently, there was further description of the association of arterial aneurysmal disease and HIV among patients. The large number of patients in this study requiring femoro-distal bypass for critical ischemic (98%) rather than

intermittent claudication (2%) is a feature in common with previously published reports (McAuley et Williams). This confirms our Unit policy that femoro-distal bypass is indicated for rest pain or tissue loss only.

It has been shown that infra-inguinal bypass surgery can decrease the amputation rate and improve the quality of life of patients with CLI.[35] The outcome of femoro-distal bypass (FDB) is strongly affected by patient selection.

There is a subset of patients who are at high risk for early graft failure and loss of the leg or of life:

- Patients with severe coronary disease, NYHA stage 3 or 4,
- Patients who have had a stroke and who are wheelchair-bound with ischemic leg on the affected side,
- Patients with end stage renal failure requiring long-term dialysis,
- Patients with advanced foot infection, diabetics and patients with raised CRP levels,
- When a suitable autogenous vein is unavailable.[36]

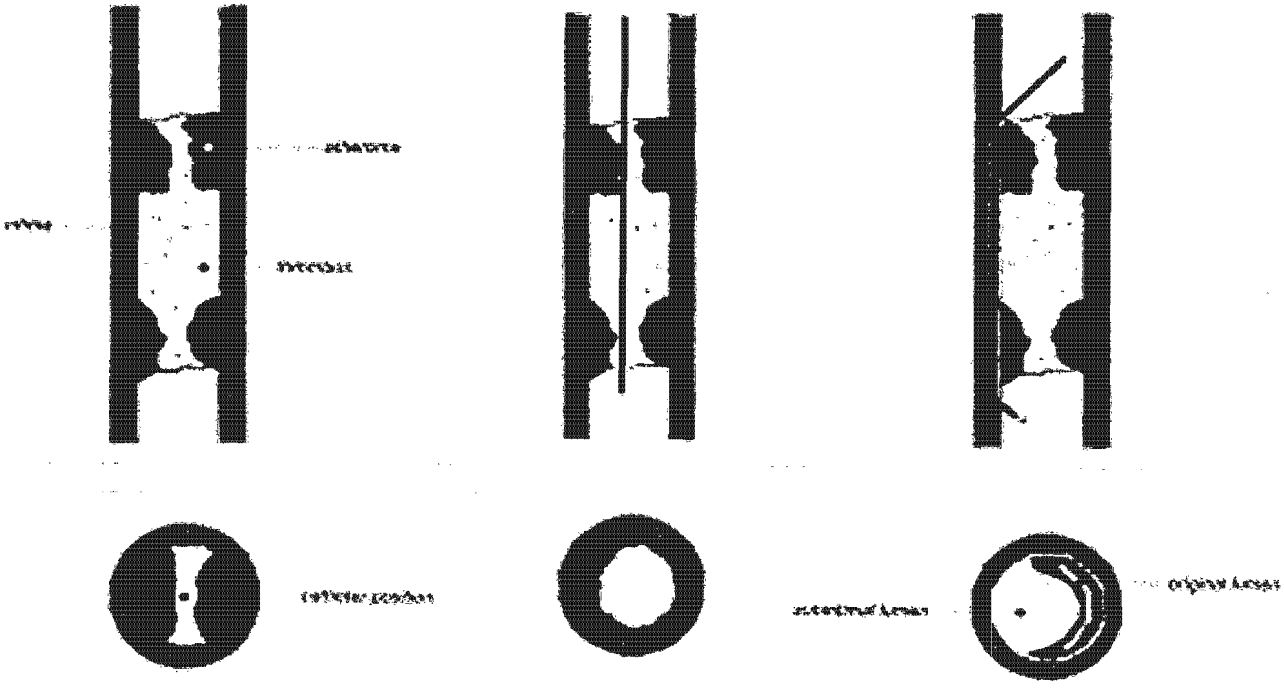
Limb salvage bypass surgery may be contraindicated in patients who fit this subset.

Patients with critical CLI, who are not suitable for surgery, may be considered for an endovascular procedure such as 'conventional' or 'subintimal angioplasty'. (See Figure 7) It has been thought that infra-inguinal angioplasty has a poor outcome because of the small calibre of the crural vessels, a tendency to develop spasm,

and the difficulties of surgical revascularisation if angioplasty should fail. However, technological advances, such as small, strong, low profile balloons, steerable hydrophilic guide wires, and road mapping facilities have facilitated infra-popliteal angioplasty.

Isolated stenotic lesions are easily dealt with by conventional 5F catheters, available in 2.5, 3 and 3.5 mm diameters and a curved tip 0.035, 180 cm long hydrophilic guidewire (Terumo, Tokyo, Japan). Multiple stenotic lesions, particularly in a single runoff vessel, may demand the use of balloon catheters (3.5F) and 0.014 guidewires. Generous use of vasodilators is recommended to prevent or treat arterial spasm such as Papaverine (30 – 60 mg).

Figure 6. **Conventional and Subintimal Angioplasty**



7.2. PRE-OPERATIVE ASSESSMENT-INVESTIGATIONS:

Rest pain, threatened viability of limb and incapacitating claudication remain the primary indications for reconstructive procedures in patients with atherosclerosis affecting the arteries of the lower limb. All investigations specific to the vasculature of the lower limb will help to define the anatomy and extent of the disease, the choice of the distal target artery and the presence of the pedal arch, enabling the surgeon to decide on the feasibility and durability of the proposed reconstruction. In our experience, peripheral angiography has been the mainstay of pre-operative assessment, but recently our practice has been to offer all patients colour duplex arterial mapping pre-operatively.

Conventional angiography is associated with a low but significant local and systemic complication rate.

Digital substraction angiography (DSA) was introduced in 1981 with several advantages, including reduced doses of contrast medium, but its superiority has still to be proven in a randomised trial. Angiography of distal crural vessels may be inadequate in critically ischemic limb due to the fact that there is multilevel disease with alteration of flow hemodynamic. Ricco et al reported no visualization of calf vessels in 20% of pre-operative angiograms and limited visualization in another 20% of patients with critically ischemic limbs.[37]

Recent experience with colour flow duplex imaging, suggests that the accuracy of duplex scanning approaches that of angiography and provides, not only anatomic,

but also hemodynamic information. Moneta et al reported overall sensitivities for predicting distal arterial obstruction of 90% for anterior tibial artery, 90% for posterior tibial artery and 82% for peroneal artery.[38]

Bostrom et al found that in patients undergoing infrainguinal bypass reconstructions, when the site of the distal anastomosis was planned according to duplex scan findings, 98% correlated with pre-bypass angiogram. Duplex scanning correctly evaluated the status of the runoff vessels in 90% of patients undergoing femoro-popliteal and femoro-crural bypass grafting.[39]

Duplex scanning of the infrapopliteal vessels requires ample experience of the vascular technologist. The infragenicular arteries are insonated at a 30-60 degree angle with 5.0 - 7.5 MHz linear array transducers and identified by the presence of a color signal or the vessel wall in the case of an occlusion. The accompanying vein can be used as a road map for each of the arteries if their identification is difficult. The examination can either start at the level of the ankle and follow each tibial artery into its origin from the tibio-peroneal trunk or popliteal artery, or at the level of the knee and follow the crural vessels up to the ankle.

Technical limitations of duplex scanning leading to inaccurate assessment of the inflow and outflow arteries, or non-visualized runoff arteries, should prompt angiographic evaluation.

Magnetic Resonance Angiography (MRA) is becoming widely used. With advances in technology and the improvement of software, MRA has become superior to DSA

in the imaging of infrapopliteal vessels, in critically ischemic limbs, particularly in the diabetic patient.

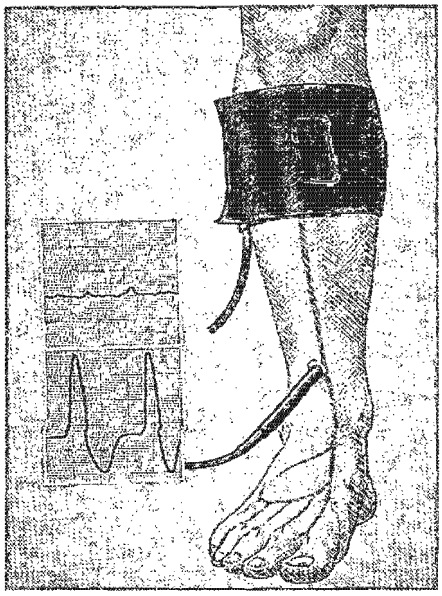
Owen et al, in a series of 25 legs, showed that DSA failed to detect 22% of vessels identified with MRA.[40]

Whilst angiography might only accurately illustrate the anatomy of atheromatous lesions, Doppler measurement of segmental pulse pressures has long been accepted as a means of interpreting the functional effect of arterial stenoses and occlusions. This has been supported by Bell et al, who found that both absolute measurement of ankle pressures and the Doppler derived ankle-brachial pressure index correlates well with both the degree of ischaemia distally and the likelihood of successful reconstruction for atherosclerotic disease.[41] These relationships do not hold for diabetic patients where calcification of medium-sized arteries may produce falsely high-pressure readings.

The success of femoro-distal bypass, as discussed above, will depend on the integrity of the distal Runoff and, particularly, the presence of an intact pedal arch. The determination of the pedal arch is essential and the following modalities are used: Dependant Doppler, PGR/Roedersheimer test, Conventional angiography / DSA, MRA and Intraoperative angiography.

In our study, Pulse generator runoff has been mostly used for assessing the pedal arch with a high sensitivity, as shown by Immelman et al.[42]

Figure 7. PGR Assessment Using Hand-Held Doppler



Scott et al established that PGR is able to adequately determine the status of the pedal arch and that it is an important predictor of both early and late femoro-distal bypass outcome. They found that if the pedal arch was complete, the one-year graft patency was 88% and limb salvage rate 100%; but an occluded pedal arch was associated with a 1-year graft patency and limb salvage rate of 9% and 24%, respectively.[43]

The combination of PGR with the **Roedersheimer** test reduces false negative results. A patent pedal arch, is defined as direct anatomical continuity between the dorsalis pedis, deep plantar, lateral plantar and posterior tibial arteries. The Roedersheimer test (similar to the Allen's test in the hand), determines which tibial vessel communicates with the pedal arch. While listening to the pedal arch signal at the first metatarsal space, the inflow arteries at the malleolar level are alternatively compressed with a finger:

- If only one calf vessel communicates with the pedal arch, compression of that vessel results in obliteration of the pedal arch signal.

- If more than one tibial vessel is in continuity with the arch, compression results in attenuation but not obliteration of the pedal arch signal. The vessel giving the greatest attenuation is defined as the major inflow vessel to the arch and is recommended for the site of the distal anastomosis.

7.3. VASCULAR CONDUIT:

Vascular conduits are divided into:

a) Autologous conduit:
   - Long saphenous vein
   - Short saphenous vein
   - Arm veins
   - Superficial femoral vein

b) Synthetic material:
   - Polytetrafluoroethylene (PTFE)
   - Dacron graft

c) Human Umbilical Vein (HUV)

d) Allografts

There is no debate that autologous veins provide the best result for infrapopliteal reconstruction and is the first choice for all infrainguinal bypass surgery.

In a well designed multi-centre prospective randomised trial, Veith et al, reported a primary patency rate of 29% at three years (12% at four years) for femoro-crural bypass, which was low compared with the 50% primary patency rate observed for vein grafts at three years.[30] They found no difference between randomised vein and PTFE grafts to the popliteal artery (P>0.25). The limb salvage was 61% for vein and 57% for PTFE grafts at four years.

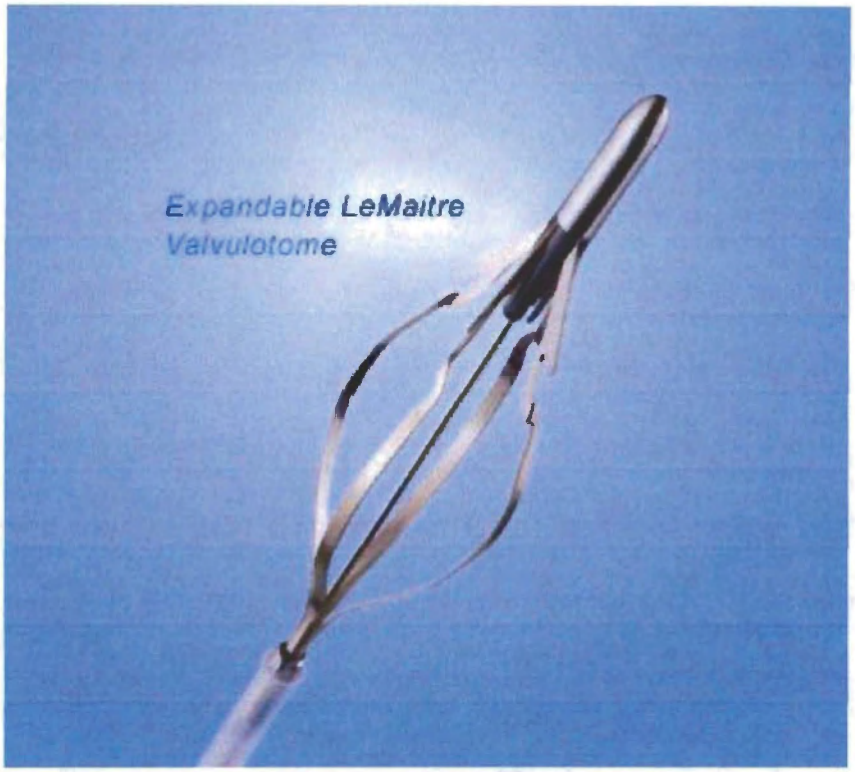
Shah and Leather reviewed the Albany experience with all bypasses to the crural vessels performed during a ten-year period (1981-1991).[31] They performed 1359 infrainguinal bypasses with 3% operative mortality rate. The patency of autogenous vein remained superior to synthetic conduits. The overall cumulative primary patency rate a five years was 68% and secondary patency was 76% for autogenous vein, compared to 33% and 42% for synthetic conduit. The limb salvage at five years was 94% for autogenous vein and 76% for synthetic conduit.

A number of issues remain controversial:

a) <u>Is "In-Situ Vein Graft" superior in infra-inguinal bypass surgery compared to the "Reversed Saphenous Vein Graft"?</u>

The **In-Situ** technique has gained popularity during the last 15 years with the development of safe and reliable methods of valve disruption. The appearance of an expandable, self-centering valvulotome, which is adjustable to vein diameter, has largely superseded the blind valvulotomy technique used previously.

Figure 8. Expandable Valvulotome



The use of angioscopy and duplex ultrasound has simplified the in-situ operation by limiting the number of incisions required. This has been supported by reports that appear to show reduced wound morbidity rates and length of hospital stay.[44] The proponents of 'in-situ' grafting believe that it is superior to reversed vein grafting based on the following theoretical advantages.

- Improved preservation of endothelium by keeping the vasa vasorum.
- Less thrombogenic flow surface.
- Improved fibrinolytic activity.
- Better hemodynamic flow characteristics.

- Better compliance characteristics and diameter match at the anastomosis of artery and venous graft.
- More suitable for graft surveillance because of the subcutaneous location.

Shah and Leather, in their retrospective review as discussed above, reported that the 'in-situ' bypass had a better secondary patency rate of 80% at five years compared to a secondary patency rate of 70% for reversed vein grafts and 30% for synthetic bypasses.

The proponents of the **Reversed Vein Graft** consider this time-honoured technique to be the gold standard for infrainguinal reconstruction. They claim fewer wound complications and fewer interventions to maintain graft patency. They argue that surgeons require more experience with a steep learning curve in order to obtain better results with the in situ technique.[45]

The **Cochrane** review of graft type for femoro-popliteal bypass surgery by Namode N., and Scott RN. analysed two trials comparing 'in situ' and 'reversed saphenous vein grafts' to below-knee popliteal artery. No differences in primary patency (64% versus 62% respectively), secondary patency (65% versus 70%), or survival with intact limb (74% both groups) with five to ten-year follow-up could be demonstrated.[46]

Lawson et al, on behalf of the Dutch BOA Study Group, analysed the patency data on reversed and in situ bypasses collected within the **Dutch BOA Study**, which was a large randomised clinical trial, comparing the efficacy of oral anticoagulation (INR 3.0-4.5) and aspirin (80 mg daily) concluded that: [47]

- The claims for superiority of 'in-situ' grafts over reversed grafts for femoro-popliteal and femoro-crural bypass surgery are unjustified. It is not the Holy Grail that some proponents would like people to believe.
- They observed no statistically significant differences in terms of assisted primary patency, secondary patency and limb salvage. The study shows that primary patency in femoro-popliteal and femoro-crural bypass surgery was in favour of reversed bypass grafting.
- The risk of occlusion or secondary intervention was greater for the 'in situ' bypass.

b) <u>What should be the alternative conduit in the absence of an adequate ipsi-lateral long saphenous vein?</u>

Long saphenous vein is the preferred conduit for infrainguinal revascularisation. However, up to 40% of patients seen with critically ischemic limb do not possess a usable ipsilateral long saphenous vein. The alternative conduits may be generally divided into:

- Autogenous group: contralateral long saphenous vein, arm's veins (cephalic, short saphenous and basilic veins).
- Prosthetic conduit with or without adjunctive measures.

- Composite grafts.
- Arterial allografts.

Since the report by Kakkar, in 1969, who demonstrated in cadavers that the tensile strength of the cephalic vein was adequate for the purpose of arterial replacement, there have been few clinical trials of infra-inguinal bypass using arm veins.[48] Frequently, however, the length of conduit required cannot be achieved by using a single segment of alternative vein, and two or more segments must be spliced together. There has been concern that the performance of a veno-venostomy may lead to the development of intimal hyperplasia and vein graft failure.

The early results of a prospective randomised trial of spliced vein versus polytetrafluoroethylene graft with a distal vein cuff for limb-threatening ischaemia by Shah DM, Chang BB et al[49] are:

- Both modalities produce acceptable limb salvage rates; at two years, namely 85% and 94% for the PTFE and spliced groups respectively.
- The two-year primary patency rates were 50% and 44% for PTFE and spliced vein group. Secondary patency rate at two years were 52% and 86% respectively.
- Despite a better patency rate of the spliced vein compared to PTFE grafts, spliced vein grafts often require revision or reoperation for wound complications.

Holzenbein et al studied retrospectively their results of 224 patients, with a total of 250 arm vein grafts, reporting a one year cumulative secondary patency of 76,9% and limb salvage of 88 %.[50] Most authors have reported that arm vein conduit is superior to composite prosthetic-autogenous grafts in lower extremity revascularisation. But the use of adjunctive measures with prosthetic material has improved the overall patency rate with a better limb salvage of PTFE graft to the tibial vessels. However, these are still lower than with autogenous conduits.
The arterial all graft is not widely used because of mid- and long-term degradation, despite their biomechanical properties being similar to normal arteries. It is widely used in France where a retrospective study on the results of infragenicular arterial allograft for limb salvage was conducted in three academic departments of vascular surgery (CHU Nord-St-Etienne, CHU Nord-Grenoble, CHU Timone-Marseille) between 1991 and 1997. They performed 165 infragenicular bypasses and the findings were as follows:

- Five patients died in the postoperative phase. There were 30 postoperative failures, of which 28 were bypass occlusions. The reasons for occlusion were: bad runoff (n=16), technical mistake (n=3), stenosis of the graft (n=1), poor inflow (n=1), sudden termination of anticoagulant medication (n=1), and unknown (n=6). 14 bypasses were revised within a month.
- Primary and secondary patency was respectively 48.7% and 59.8% at one year; 16.1% and 25.9% at five years. The limb salvage rate at one year and five years were 83.6% and 74,2%.

- They concluded that early results were excellent but late results were poor and comparable with other techniques in similar clinical situations.[51]

c) What is the role of distal anastomotic cuffs and patches?

The interposition of vein at the distal anastomosis has been incorporated into the surgical repertoire in an attempt to minimize myointimal hyperplasia with acceptable overall patency and limb salvage rates. In addition, other techniques such as distal arteriovenous anastomosis and precuff PTFE have been used in combination with vein cuff technique.

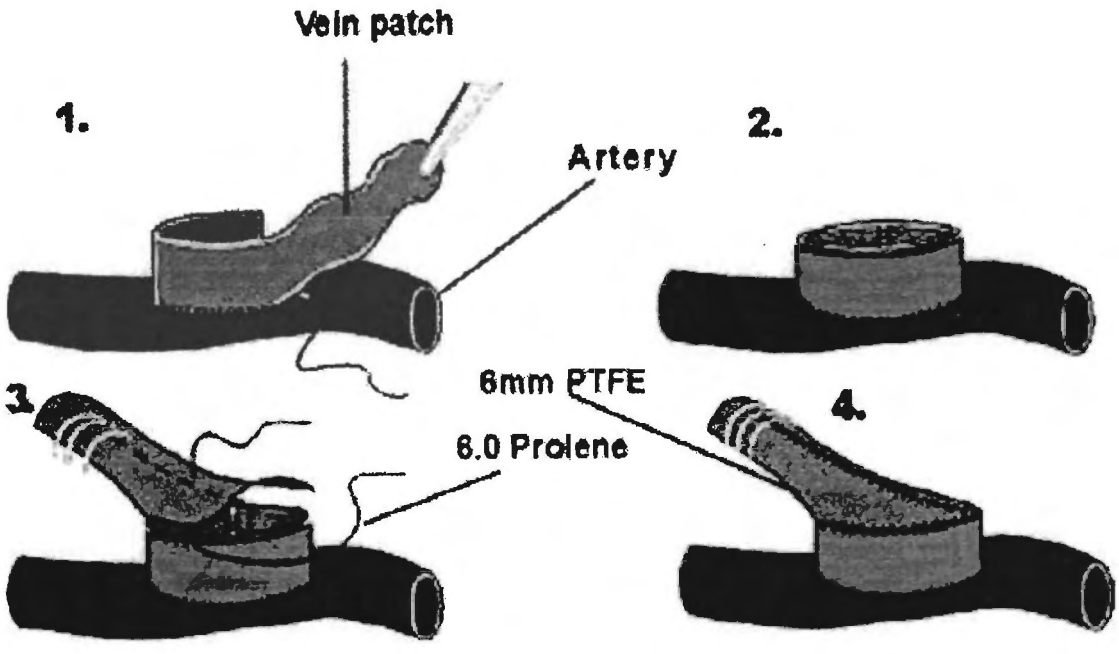
Most centres have not achieved a five-years overall patency rate of more than 50% by using these anastomotic modifications. The report by Mamode and Scott did not show any difference when comparing PTFE grafts with or without a vein cuff in above-knee grafts. However, primary patency below-knee was higher with a PTFE plus vein cuff bypass (52% versus 29%, p=0.03) at two years.[46]

MILLER CUFF

Siegman described, in 1979, the first venous cuff, which was adopted by Miller a few years later. Recently, Stonebridge and Ruckley, in a prospective randomised trial showed that the Miller cuff does not improve the patency of above-knee femoro-popliteal grafts, but it does improve the patency of below-knee femoro-popliteal and femoro-crural bypasses.[52]

A recent publication by Fisher and Harris on the influence of geometry on anastomotic flow patterns has shown that the optimisation of Miller cuff dimensions do optimise wall shear stress and inhibit myointimal hyperplasic: the cuff dimensions were 13mm long and 8-11mm high. In order to reproduce these specific configurations, a standardized pre-cuff PTFE graft has been developed.[53]

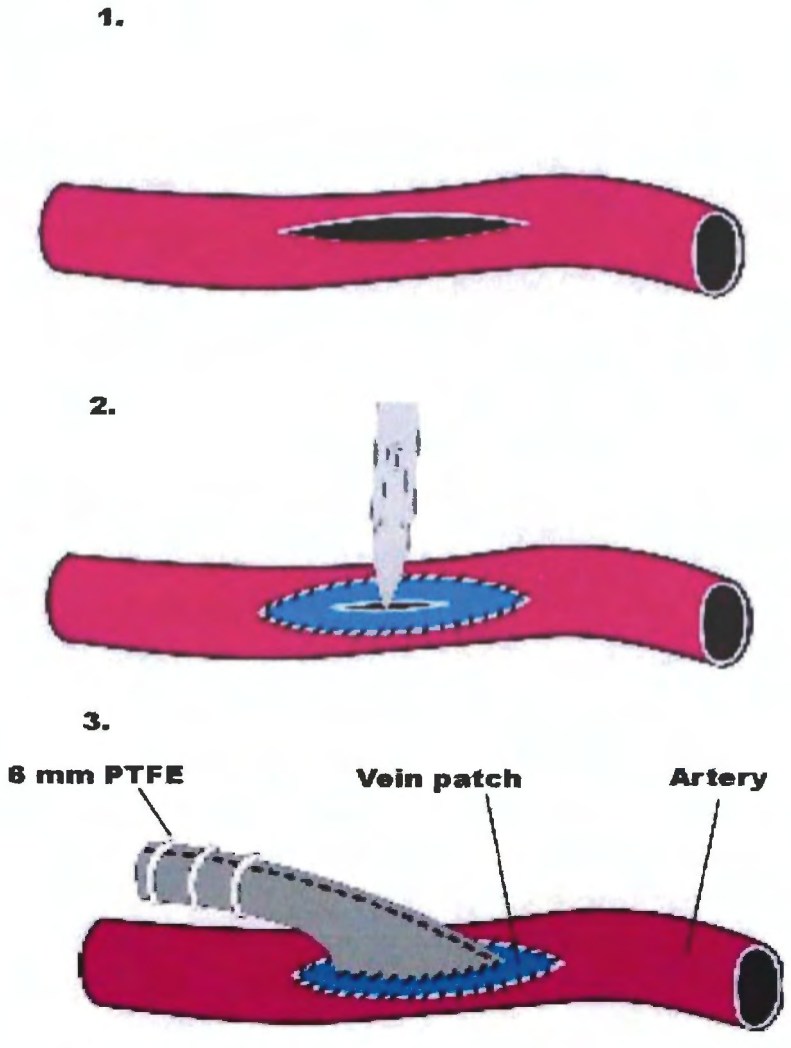
Figure 9. Showing the different steps in the construction of the Miller cuff.



OTHERS ANASTOMOTIC TECHNIQUES

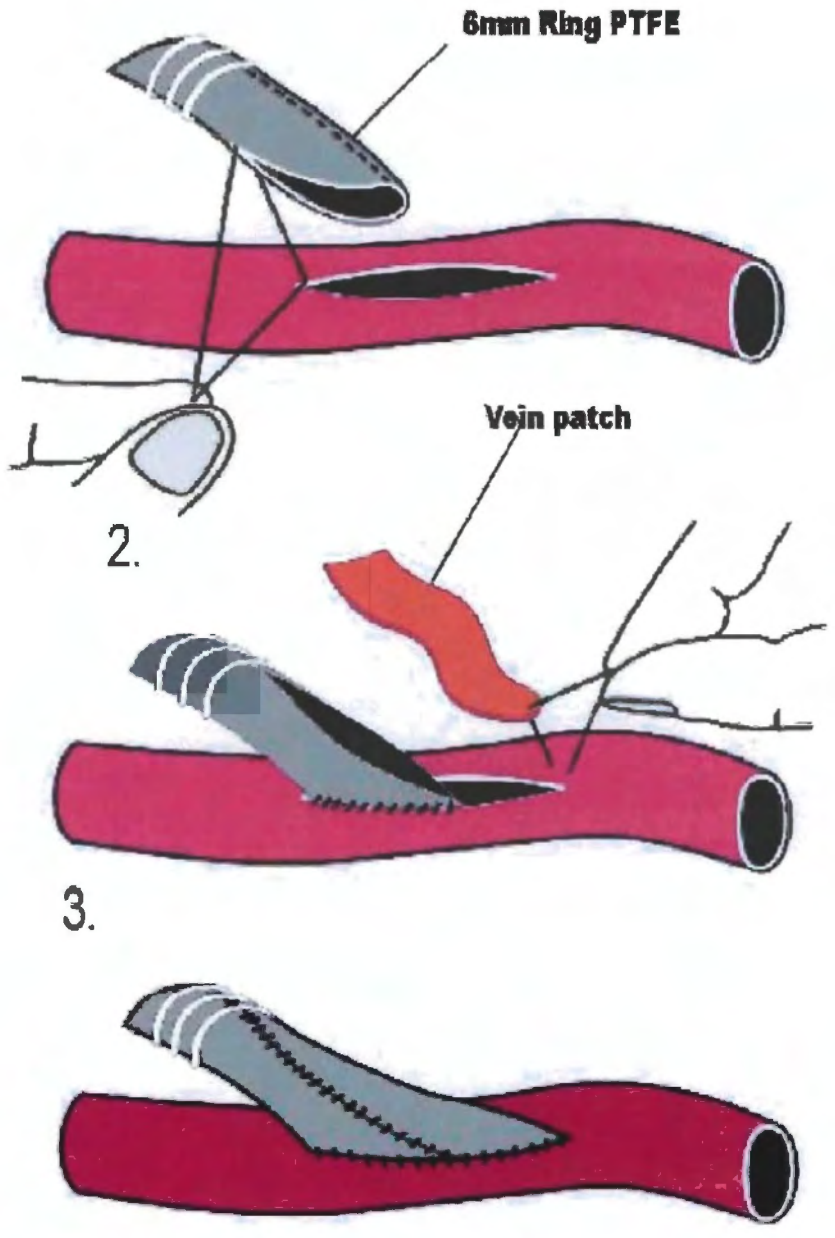
i) Linton Patch

Figure 10. Showing the different steps in the construction of the Linton patch



ii) Taylor Patch

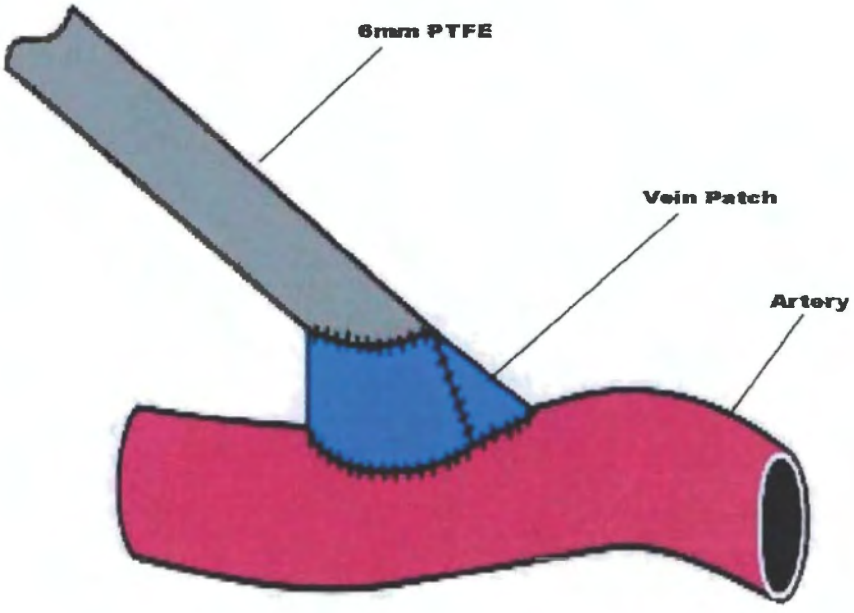
Figure 11. Showing the different steps in the construction of the Taylor patch



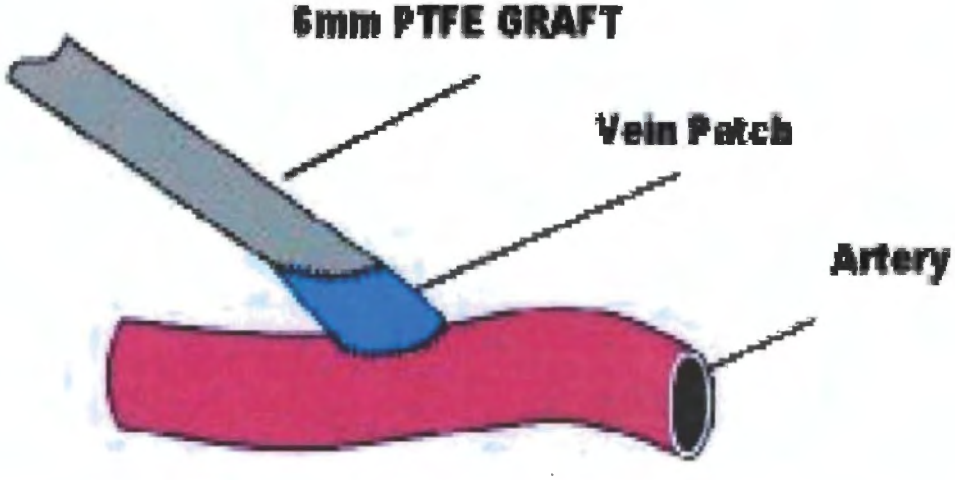
iii) St Mary's Boot and Karacagil's Cuff

Figure 12. Showing St Mary's Boot and Karacagil's Cuff

(a) St Mary's Boot



(b) Karacagill's Cuff



7.4 TECHNIQUE OF FEMORO-DISTAL BYPASS:

Several options are available for restoring arterial continuity, but I will describe the reversed saphenous vein graft that is the standard with which all other infrainguinal techniques must be compared.

a) Preoperative evaluation and anesthetic techniques:

Peripheral vascular disease patients have a high incidence of coronary artery disease and pulmonary disease (most of them are smokers or diabetic).

An appropriate work-up is required:

- Full blood count, serum viscosity and INR, PTT
- Renal function
- ECG, lung function test, chest X-ray.

The anesthetic technique used is a combination of spinal and epidural using local anesthetic agents (eg. macaine 0.5%) which provide better operative conditions: avoidance of exposure to airway and pulmonary morbidity and ablation of the surgical stress response.

The epidural catheter is left in situ for overnight pain control in a high care unit.

b) Surgical technique:

Prior to the surgery, vein assessment and mapping is performed by means of duplex scanning. To reduce surgical time, a two-team approach is recommended.

The operation begins with exposure of the saphenous vein from groin to knee by

one team. The harvest incision is placed directly over the vein to avoid development of flap necrosis. During the harvesting, the vein must be kept moist; grasping with forceps avoided, silastic loops are preferable and the vein should be gently irrigated with heparanized papaverine solution to open tributaries that were missed for ligation with silk sutures.

The inflow artery is exposed through a femoral groin incision: common femoral, profunda femoris and superficial femoral artery are completely freed; avoiding injury to the common femoral vein, femoral nerve and lymphatics.
The site of the distal anastomosis is chosen and the vessel exposed. Heparin is administered and the proximal anastomosis is constructed with a 6-0 running polypropylene suture. The distal anastomosis is completed in a similar fashion with a 7-0 running polypropylene suture. Flow is restored, and hemostasis is secured, with or without protamine reversal of the heparin effect. It is essential to perform a completion angiogram to detect any technical problem. After the adequacy of the hemodynamic result has been established, the wounds are closed with running subcutaneous absorbable sutures or skin staples.

7.5 ADJUVANT MEDICAL THERAPY:

Opinions are divided concerning the best medical therapy in peripheral bypass surgery with the aim to improve both early and late graft patency.

Different pharmacological agents have been used:

a) **Rheomacrodex (dextran-40)**

- Dextran has the ability to inhibit factor VIII activity, increase clot lysability, and decrease the aggregation of platelets in response to collagen.
- Side effects include acute renal failure, fluid overload leading to congestive heart failure, thrombocytopenia, and anaphylaxis
- Dosage and methods of administration of dextran have not been well standardized. Various investigators have given patients 500 to 1000 ml during each 24-hour period for times ranging from one to five days. It is given either by intermittent rapid bolus or by continuous infusion.

Robert B. Rutherford, as a pioneer of the use of dextran as adjuvant therapy, published a prospective randomised trial comparing dextran and placebo in difficult distal bypass grafts: He only entered vein grafts if they had poor runoff or terminated in crural arteries.[26] The thrombosis rate for both control and dextran-40 patients was identical and only 2,6%. In the PTFE or umbilical vein grafts, the one-week thrombosis rate for controls was 36% compared with only 12% for

those receiving dextran-40. They concluded that dextran-40 is beneficial in any scenario in which the risk of early thrombosis is high, mostly in grafts to the tibial or peroneal vessels.

In 1998, Katz and Kohl published the results of a prospective, randomised study of 244 patients in which they found that the administration of dextran-40 did not increase the early patency of autogenous infrainguinal bypass grafts.[54] There was no significant difference between the group of patients who received dextran and those who did not receive it, with respect to rate of early occlusion, death, or 30-day patency.

b) Antiplatelet agents

The most studied agent for the maintenance of vascular patency in peripheral bypass grafts is **aspirin.** A meta-analysis review by B. Girolami et al, of all English-language studies published from 1976 to 1997, included 32 studies, in which aspirin (alone or in combination with dipyridamole) was used in 16 publications, concluded that there was enough evidence to suggest that 100-300 mg aspirin daily with dipyrimadole should be prescribed to patients with peripheral arterial disease who undergo revascularisation, since they both improve patency and probably prolong survival.[55] But all these studies were randomised and most were double blind. There was a tendency for smaller studies and those with shorter follow-up to be more positive for aspirin use. This may be related to the predominance of prosthetic grafts in the smaller and shorter studies.

Jean-Pierre Becquemin conducted, from 1989 to 1992, a multi-centre, double blind trial looking at the effect of **ticlopidine** on the long-term patency of saphenous vein bypass grafts in the legs. He found that ticlopidine significantly improved the long-term patency of saphenous vein bypass grafts in the legs.[56] A total of 243 patients with femoro-popliteal or femoro-tibial saphenous were randomly assigned to receive either ticlopidine, 250 mg twice daily, or matching placebo for two years. They found after two years that:

- 66,4% patients with a patent graft were alive in the ticlopidine group, as compared with 51,2% in the placebo group, with 95% confidence interval for the two groups.
- The two-year cumulative patency rate was 82% in the ticlopidine group and 63% in the placebo group (p=0.002)
- There was no significant difference between groups in overall mortality or major ischemic events.

A multi-centre, three-year prospective study, in 1990, by Shionoya et al analysed the effect of ticlopidine on graft patency following infrainguinal reconstruction and showed treatment benefit only in a subgroup of patients with hyperlipidemia.[57]

c) Oral anticoagulants

Five studies have been published, but none was double blind and placebo controlled. The study by Sarac TP et al demonstrated a significant long-term

benefit when warfarin was added to aspirin in the treatment of high-risk vein grafts such as those with poor run-off or poor quality vein.[58]

A Swedish study failed to find any significant differences in graft patency (46% with coumarin versus 42% for controls), limb salvage or patient survival.[59]

There is a need for a double blind, placebo-controlled study to justify the use of oral anticoagulants for the maintenance of patency in routine vein bypass procedures. However, despite the lack of evidence, many vascular surgeons use warfarin after infrainguinal bypass.

d) Low molecular weight heparin

Low molecular weight heparin (LMWH) is well established as the conventional prophylactic and therapeutic drug for venous and coronary thrombosis. Its use in arterial thrombosis has not been well studied. During the past ten years, interest in the use of LMWH has increased. Recently, three trials have been published:

- A small comparative trial of enoxaparin with placebo did not show any difference in graft occlusions at 30 days, but the overall failure rate was low, despite the majority of grafts being below-knee prosthetic grafts.[60]
- An open, randomised, multicentre trial compared dalteparin sodium with aspirin and dipyrimadole in 200 patients undergoing femoro-popliteal bypass. Prosthetic material was mostly used (74%) and 69% of patients had an above-knee anastomosis. They reported a significant absolute difference in primary patency of 15% in favour of LMHW at 12 months, mostly for patients with

severe ischemic symptoms (36%) rather than those with claudication only (5%).[61]

- A second randomised trial compared enoxaparin with unfractionated heparin (UFH), 68% of patients had vein grafts placed. Patients were followed up for only 30 days. The patency rate with LMWH was 89% versus 76% with UFH with an absolute difference of 13% in the number of occlusions.[62]

7.6 GRAFT FAILURE-ETIOLOGY AND PREVENTION:

Surgical revascularisation using autologous saphenous vein remains standard for care for patients with critical ischemic limb. But those grafts are at risk of failure. Approximately 10-15% of grafts fail within the first month after insertion, and this is most commonly due to a technical error or poor patient selection, ie. failing to correct a severe proximal or distal arterial lesion.[63]

Technical errors include poorly constructed suture lines, restricting the flow, intimal flaps, twisted grafts, inappropriate placement and tunnelling, intra-operative overestimation of flow rate, branch ligature placement, missed valves or arterio-venous fistula.

Intermediate failure occurs from one month to eighteen months and is mainly due to stricture development within the vein graft or just beyond the distal anastomosis, and accounts for up to 80% of failures within five years after operation. Those strictures are the result of **myointimal hyperplasia (see below)**, the proliferative response of smooth muscle cells in the vessel wall.

Late graft failure, which accounts for 2-3% annually, is commonly due to the progression of atherosclerosis in the native vessels. It is known that outflow (popliteal or crural vessels) atherosclerosis frequently progresses faster than the inflow (aorto-iliac segment) disease, which leads to an increase of outflow resistance predisposing to graft thrombosis.

7.6.1 NEO-INTIMAL HYPERPLASIA- PATHOPHYSIOLOGY

Saphenous vein has been the conduit of choice for over 50 years since Kunlin's publication in 1949, despite the widespread use of prosthetic grafts. However, long-term success of bypass is limited either by progressive thickening of the vein graft wall from intimal hyperplasia or either by superimposition of atherosclerotic process resulting in symptom recurrence. Neo-intimal hyperplasia (NIH) remains a problem with a huge economic impact on health care resources and serious effects on the individual. NIH involves migration and proliferation of Vascular Smooth Muscle Cells (VSMC) through the internal elastic lamina resulting in medial thickening.

The hyperplastic intima constitutes:

- 60-80 % VSMC
- 20-40% epithelial cells, macrophages, lymphocytes.[64]

The etiology of neo-intimal hyperplasia is complex and multifactorial and the precise initiating stimuli has not been fully defined but it appears to be the

response of VSMC to a combination of physical, cellular and humoral factors accompanied by dysfunctional endothelium regulation.

It occurs at different sites along the vein:

1) Neo-intimal anastomotic stenosis is promoted by:

a) Variations in anastomotic construction.

There is evidence that graft geometry influences the development of neo-intimal hyperplasia:

End-to-Side (ETS) anastomoses develop more neo-intimal hyperplasia than End-to-End anastomoses (ETE). However, an ETS distal anastomosis is usually necessary to maintain antegrade and retrograde flow.[65]

Different measures can be taken to decrease the incidence of neo-intimal hyperplasia in ETS anastomosis:[66]

- Optimal diameter ratio for graft to native vessel is **1,6 - 2 to 1** as demonstrated by numerical simulation models.
- Lengthening of the anastomosis reduces shear stress on the floor of the arterial wall but not the flow disturbances at the heel and toe. This could still induce VSMC migration and proliferation. The optimal dimensions are **4 mm diameter** at the arterial side and **7mm diameter** at the venous side.
- Lower angle (20^0) produces less flow disturbance and a lower range of shear stress variation than higher angle.
- Compliance mismatch explained the high incidence of NIH in prosthetic graft.

b) Turbulent flow and Deformation stress.

After implantation, the vein is exposed to:

- Immediate increase in flow
- Longitudinal wall stress
- Circumferential deformation and pulsatile stress.

2) Neo-intimal hyperplasia along the graft is related to:

a) Vein quality:

The intrinsic quality of vein (size less than 2,5 mm, multiples valves, multiples tributaries, varicosities and wall abnormalities) is predictive of poor outcome.

b) Vein handling:

Procedures involved in preparing veins for bypass graft (dissection, distension of the vein and storage) may result in:

- Physical damage to the vein graft.
- Denudation of the endothelium.
- Adventitial denudation and occlusion.

All the above contribute to the promotion of neo-intimal hyperplasia.

The adventitia contains microvessels that form the vasa vasorum, responsible for providing oxygen and nutrients to the walls of vessels. It also contains fibroblasts, macrophages and unmyelinated nerves. It has been suggested that myofibroblast from the adventitia are the Progenitors of neo-intimal hyperplasia, which may progress and result in atherosclerotic changes in the wall.[67]

c) Pre-existing abnormalities.

7.6.2 NEO-INTIMAL HYPERPLASIA – PREVENTION AND MANAGEMENT

1. Harvesting technique:

- **Conventional technique:**

The under mentioned steps below are to be followed for reversed vein graft harvesting and preparation:

(1) Mark the skin overlying the vein before the operation, with the patient standing,

(2) Infiltration of papaverine solution (0,12 mg/ml) subcutaneously along the tract of the vein before skin incision;

(3) Perivenous injection and adventitial irrigation with papaverine solution after exposure and at intervals during dissection of the vein;

(4) Use of atraumatic dissection technique;

(5) Ligation of tributaries 2 - 3 mm from the vein wall;

(6) Irrigation and gradual distension of the graft with a solution of heparinized colloid or autologous whole blood containing papaverine, at body temperature, to a pressure of 100 mmHg;

(7) Storage, while distended, in cold (4 degree), heparinized colloid solution containing papaverine; and

(8) Reimplantation by atraumatic technique.

The use of this harvesting technique should avoid damage to the normal endothelium when the vein graft has been reversed but doesn't guarantee his functional status.

- **No touch technique – "Souza technique"**

This technique was described by Souza in 1996.[68] The vein is harvested together with a cushion of surrounding tissue. There is no need for mechanical distension. The remaining perivascular tissue may act like an external stent to reduce the effects of pulsatile pressure, altered flow rates and shear stress that the arterialised vein is subjected to. There is preservation of endothelial NO synthase (e NOS) and the NOS within the intact adventitia that contribute to improve graft patency.

2. Anastomotic technique.

Basic surgical procedure should be followed with dexterity to achieve the desired result.

7.7 GRAFT SURVEILLANCE

It is known that intervening in a failing but still functioning graft before its occlusion greatly improves the patency rates and most importantly, preserves the limb. Reports provide evidence that strictures impose a three to six-fold risk of graft occlusion if left untreated.[69] According to a publication in the early 1990s by Wolfe and Taylor, limb loss has to be prevented in only 2% of patients for a

duplex scanning surveillance programme including six examinations in a year, to be cost-effective.[70]

Therefore, identification of failing grafts prior to their occlusion seems logical and periodic surveillance of infra-inguinal grafts has become a common policy.
The ideal method for surveillance should be non-invasive, universally feasible and applicable, reproducible, simple, quick and easy to perform, inexpensive, able to detect lesions and their progression within both the graft and the native vessels, and mostly highly sensitive and specific.
The surveillance programme should consists of:

a) Clinical evaluation:

The appearance of symptoms, pulse palpation, development of bruits, segmental Doppler pressure measurements and pulse volume recordings.
Cohen et al in 1986, however, found that the combination of symptoms and clinical examination was both insensitive and inaccurate.[71] Subsequently, Scott et al, in 1987, published a study on the accuracy of pulse palpation and their findings were that many limbs had palpable distal pulses despite a failing graft. In addition, pulse palpation is notoriously unreliable.[72]

b) Periodic measurement of resting and post-exercise ankle brachial indices.

This is a simple, cheap, quick and reproducible test. It is proposed that a decrease of 0,15 or more in the resting ankle brachial index is usually associated with a

failing graft. A postoperative increase of less than 0,4 may be an indicator for early failure, and early resting ABI less than 0,85 as a predictor of late failure. Persistently low ABI is considered a sign of significant inflow or outflow disease.[73] The ABI has been found to be of limited value in identifying graft stenosis, especially in diabetic patients with stiffened and incompressible distal vessels and in 'in situ' vein distal grafts with small calibre vessels and low flow.[74]

c) Duplex scanning of the entire length of the graft, with measurement of the systolic velocities and the velocity ratios across all identified lesions.

Peak systolic velocity usually measured in the midgraft portion, has been proposed by Bandyk et al. as indicating a failing graft when it is less than 45 cm/s.[75] Subsequently, 10 years later, they suggested that a PSV greater than 150-180 cm/s was an indication for an angiogram.[76]

A.D. Giannouks et al. suggested a V2/V1 ratio to be the most reliable parameter (V2: peak systolic velocity at the site of maximal stenosis, V1 within 2cm upstream).

A V2/V1 >2.0 characterises a stenosis greater than 50% in diameter reduction.[77]

d) Surveillance should be performed in the immediate post-operative period and at regular intervals for at least 2 years.

There are only two randomised controlled trials with respect to duplex-based vein graft surveillance:

- The first was by Lindell et al in 1995.[78] One hundred and fifty-six grafts, both vein and prosthetic, were randomised to duplex or non-duplex surveillance. Primary-assisted graft patency rates were shown to be better in the duplex group, but the effect upon limbs was not reported. Nevertheless, the trial did demonstrate, in a randomised manner for the first time that graft surveillance has a positive effect upon patency rates.
- The second randomised trial was that reported by Ihlberg et al in 1998.[79] One hundred and eighty-five patients were recruited and randomised to clinical examination and ABPI measurement with or without duplex scanning. Primary-assisted and secondary patency and limb salvage rates were better in the group randomised not to receive duplex graft surveillance, though not significantly so. This study failed to show any benefit for routine duplex-based graft surveillance.

There is, however, enough level 2 evidence to support the benefit of vein graft surveillance.

Mills et al, in 2001, found a substantial body of evidence that duplex vein graft surveillance is clinically useful, cost-effective and associated with an improvement of limb salvage by 10 to 15%.[80] The initial duplex scanning is done when patient is discharged, then again, at six weeks and at three, six, nine, twelve, eighteen and twenty-four month periods post-operatively, as well the clinical assessment of the patient with ABP indices.

The **Vein Graft Surveillance Trial** funded by the British Heart Foundation, which is under way in the U.K., may give some clarity to these issues. It is a prospective trial that randomises patients with patent infrainguinal vein grafts at hospital discharge into either duplex or clinical surveillance groups. All patients will be followed up on for 18 months.

Graft patency, amputation rate, quality of life and cost are the main outcome measures.[81]

7.8 REVASCULARISATION VERSUS AMPUTATION

It is accepted that infrainguinal bypass does improve the quality of life in atherosclerotic patients.[82,83] However, Stoney has suggested that the rewards of femoro-distal for limb salvage seldom justify the risk involved and that primary amputation constitutes an option in rehabilitation of patients with critically ischemic limbs.[84] Whether to revascularise or amputate is a difficult decision faced frequently by all vascular surgeons. While trying to find solution to these questions, one must consider the quality of life and cost-effectiveness as well the details of graft patency rates, complication rates, rehabilitation rates, and long-term outcomes.

The complexity of the issue hinges on the absence of objective criteria with which to identify which patients would be best served by primary amputation rather than reconstruction.

7.8.1 INDICATIONS FOR PRIMARY AMPUTATION

Indications for primary amputation are summarized as follows:

a) Absolute Indications:

- Nonambulatory patients with no transfer capability.
- Limited cognitive capability.
- Patients with ipsilateral paralysis.
- A complete absence of reconstructible vessels.

b) Relative Indications:

- A patient with an expected survival of less than one year.
- Life-threatening sepsis.
- No autogenous vein available for a distal bypass site
- A surgeon not skilled in distal bypass technique.
- A hind foot ulcer requiring free flap, and no donor vessel available.

7.8.2 COMPARATIVE MORBIDITY AND MORTALITY

Three major recent series are listed in the table below (Table 7.)

Table 6. Comparative Morbidity and Mortality: Studies Review

Author (Year)	Procedure	No. Patients	Mortality (%)	Long-Term Survival
Bunt (1991)	→ Age < 70 Revascularization Amputation	183 212	2.2 1.5 (NSS)	
	→ Age > 70 Revascularization Amputation	119 253	8.0 1.5 (p<.01)	84% at 1 year 50% at 1 year
Schina (1992)	Revascularisation Amputation	211 122	2 4 (NSS)	
Plecha's Cleveland Metropolitain Registry	→ Age > 75 Revascularisation Amputation	38 62	6.7 14.7 (p<.01)	
	→ Age < 75 Revascularization Amputation	55 77	2.2 9.8 (p<.01)	

Blunt et al. did analyse the long-term survival at one year and found that patients who underwent revascularisation had a better survival rate than those who underwent primary amputation, but perioperative mortality was worse in the revascularisation group (not statistically significant), and this was particularly so with increasing age.[85]

In all the studies above, amputation in the elderly patient had a better outcome if done before tissue loss led to frank sepsis. The comparative morbidity and

mortality of elective revascularisation and primary amputation were roughly equivalent.

Robbs et al in 1984 showed that, where feasible, infrainguinal bypass would restore independent gait much more quickly than primary amputation, although graft failure may minimize this disadvantage.[86]

It should be noted that there is a school of thought that believes that previous femoro-distal bypass surgery will adversely affect the level of amputation, which would have a negative outcome in rehabilitation of the patients.[87] However T.A. Cook et al, in 1992, reviewed data on patients presenting to their unit with lower limb-threatening ischaemia between September 1984 and December 1990. 330 patients underwent either femoro-popliteal or femoro-distal reconstructive surgery and 281 patients underwent 316 primary amputation. They found that the level of amputation was the same in both groups: The below-knee amputation to above-knee amputation ratio (BKA/AKA) was 1.0 in the primary amputation group to 0.91 in the secondary amputation group.[88]

7.8.3 COST-BENEFIT RATIO COMPARISON

Studies have been done analysing the cost of revascularisation versus primary and secondary amputation:

- Gupta (1982): 289 patients underwent either femoro-popliteal (166) or femoro-distal (123) reconstruction, whereas 24 underwent primary amputation.[89] The average hospital stay in the revascularisation group was 50 days at a cost of

$26,194 while the primary amputation group had an average hospital stay of 60 days, at a cost of $27,225.

- The secondary amputation group (after failed bypass procedure) had a hospital stay of 78 days and at a higher cost (US$ 42,107). He concluded that primary amputation was cheaper, being associated with a shorter hospital stay.
- H. Myrhe (1996) estimated an in-hospital stay and cost of a successful bypass procedure to be about US$ 5700, that of primary amputation US$ 13,000 and that of amputation after failed bypass US$ 25,000.[90]

Analysis of these series leads to conclusions below:

- A successful bypass procedure is cost effective and psychologically better accepted than amputation.
- A failed bypass procedure or complications of either revascularisation or amputation markedly increase the costs.
- Patients who do not require any subsequent prosthesis, amputation is less costly and probably the better option.

8. CONCLUSION

The management of Critical limb ischaemia is a major part of the workload in our unit with most patients undergoing primary amputation. The results for graft patency and limb salvage are not comparable to that obtained by Shah et al from the Albany school. An attempt has been made to identify those factors that correlate with both graft and limb survival, as well the escalation of amputation. Factors that influenced the outcome of femoro-distal bypass were local foot sepsis and post-operative ABI ($p < 0.05$). Furthermore, the poor outcome can be attributed to the financial constraints that had an impact on our theatre waiting list. We find that most of the lesions detected during graft surveillance occurred after 18 months. Graft surveillance programmes should probably continue beyond 18 months.

Other factors studies such as diabetes mellitus, age, sex, race and angiographic scoring had no significant influence on the graft patency rate. It is important to emphasize that autogenous graft still remains the first choice and this study has shown that despite the small number of prosthetic grafts used with adjuvant measures, the poor outcome with non-autogenous material.

In this study there was a male predominance with 60% being male, but among the early amputation group ten patients (58,8%) were female. This difference was not statistically significant. Other reported series in the literature also reported a similar observation but was not able to prove the negative influence on the limb salvage rate.

In this study, Coloureds made up 66% of the population study. This may justify the high incidence of cardiovascular disease in the Coloureds compared to the indigent black population, and they constitute a far larger portion of the population in the Western Cape. The median age (61 years) in our population was younger than that reported in the literature.

The concept of atherosclerosis as malignant disease is not an overstatement. It is now accepted that reconstructive arterial surgery does improve the quality of life of the patients but does not have any impact on the natural history of the cardiovascular and cerebrovascular disease, which accounts for a five-year mortality of up to 50%.[83] In our study, the mortality at 30-days post surgery and the overall two years mortality were respectively 8,8% and 19,2%. Those results were similar to those reported by most authors.

The issue of functional outcome after a successful infra-inguinal reconstruction could not be established in this study. However, the hospital stay after failed bypass was prolonged with a mean of 27 days in this study.

The 2-year cumulative patency rate was 40% with limb salvage rate of 56%, which discrepancy as explained above is due to a subsequent revision procedure to salvage and maintain an intact limb. But all patients with early graft failure (less than a month) underwent an amputation in our study. This suggests that aggressive management for late graft failure (more than a month) is worthwhile in selected patients.

Fourteen patients had an amputation within 30 days of the bypass surgery, and only four patients were eventually fitted with a prosthetic leg. To date, only two use their prosthetic leg. These findings confirm that most amputee patients will remain wheelchair-bound or still use a walking frame and crutches. The level of amputation was not influenced by previous bypass procedure and the conversion rate from below-knee to above-knee was similar between the group of primary and secondary amputee patients.

Critical limb ischaemia was previously considered a primary indication for bypass surgery and endovascular procedures were indicated only for patients at high risk for surgery or if autogenous bypass material was not available. But recent studies have shown a trend towards more utilization of percutaneous transluminal angioplasty with an overall cumulative patient survival and limb salvage rates respectively of 82% and 89% at one year, and 45% and 87% at five years.[91]

9. FUTURE PERSPECTIVES

This retrospective study should be considered as the cornerstone for a prospective study that will address others aspects that have not as yet been explored fully: functional outcome after amputation (primary or secondary) and femoro-distal bypass, the impact of socio-economic situation of the patients on the outcome of infra-inguinal bypass, and long term patency rates.

It is vital to establish an Integrated Care Pathways (ICP), representing a multidisciplinary approach to clinical patient care.

I would like to propose the ICP as follows:

a) Patients are referred by a general practioner to our Outpatient/Vascular Laboratory as soon as the symptoms have begun.

b) Assessment of the patients by the vascular consultant, clinical nurse and social worker.

c) Symptoms of critical ischemic limb are established as well the socio-economic circumstances of the patients.

d) Assessment of the patient by vascular laboratory nurse to establish the ischemic etiology by non-invasive investigations: Hand held Doppler.

e) Assessment of the co-morbidity and risk factors:

- Patients with non-salvageable legs, patients that cannot tolerate a lengthy surgical procedure, patients with fixed flexion deformity of the limb or limited life expectancy, or patients in whom revascularisation cannot be considered,

should be offered primary amputation or palliative care. These patients require social workers, occupational therapists, physiotherapists and psychologists to plan the management of post-amputation in the ward and at home.

- Patients with a potentially salvageable limb and with no gross contraindication to anaesthesia should undergo a duplex scan with vein assessment and mapping, and evaluation of the pedal arch (using pulse generator run-off equipment). These patients should have a full preparation for an angiogram: rheology, clotting profile, renal function study and consent for the angiogram as well for any infrainguinal to be followed if necessary. An angiogram is appropriate for these patients. Any lesion suitable for angioplasty should be addressed at the time of the angiogram. Failing this, a femoro-distal bypass should be planned, together with post-operative physiotherapy support.

f) The discharge planning should start from the first day of admission: it is important to define the patient's social circumstances, his ability to perform daily activities and the level of family support.

The importance of adjuvant medical therapy following revascularisation should be explained to the patients as well the complications and duration. Family members should be present at each of those interviews. The risk of adverse effects from warfarin and the need for INR monitoring should be emphasized if patients have been anti-coagulated. The issue of graft surveillance should be discussed with the patients, emphasizing the prolonged period of follow-up that is demanded.

The only way ICP can be applied is by conducting a pilot study to assess its efficacy to improve the working efficiency and the quality of service given to the patient.

10. REFERENCES

1. Wolfe JHN. Defining the outcome of critical ischaemia. A one-year prospective study. Br J Surg 1986; 73:321-328.

2. The Vascular Surgical Society of Great Britain and Ireland: management and outcome. Report of a national survey. Eur J Vasc Endovasc Surg 1995; 10: 108-113.

3. Robinson J and Beard JD. Management of critical limb ischaemia: quality of life issues. The evidence for vascular surgery. Ed: Earnshaw JJ and Murie JA. 1999: 67-71.

4. Humphreys WV, Evans F, Watkins G, Williams T. Critical limb ischemia in patients over 80 years of age: options in a district general hospital. Br J Surg 1995; 82: 1361-1363.

5. White JV, Jones DN and Rutherford RB. Integrated assessment of results: Standardised reporting of outcomes and the computerized vascular registry. Rutherford: Vascular Surgery, 5th Ed; 2000: 20-37.

6. Glantz SA. Principles of Biostatistics. New York. Mc Graw Hill. 1981: 7-10.

7. Peto R, Pike MC, Armitage P et al. Design and analysis of randomised trials requiring prolonged observations of each patient. Part I: Introduction and design. Br J Cancer 1976; 34: 585.

8. Peto R, Pike MC, Armitage P et al. Design and analysis of randomised trials requiring prolonged observations of each patient: Part II, analysis and examples. Br J Cancer 1977; 35: 1.

9. Underwood CG and Charlesworth D. Uses and abuses of life table analysis in vascular surgery. Br J Surg 1984; 71: 495.

10. Rutherford RB, Flanigan DP, Gupta SK et al. Suggested standards for reporting dealing with lesser extremity ischemia. J Vasc Surg 1986; 4: 80.

11. Rutherford RB, Baker JD, Ernst C et al. Recommended standards for reports dealing with lesser extremity ischemia: Revised version. J Vasc Surg 1997; 26: 517.

12. Owen RS, Carpenter JP, Baum RA, et al. Magnetic resonance imaging of angiographically occult runoff vessels in peripheral arterial occlusive disease. N Engl J Med 326 : 1577,1992.

13. Scott DJA, Hunt G, Beard JD, Hartnell GG, Horrocks M. Arteriogram scoring systems and pulse generated runoff in the assessment of patients with critical ischaemia for femoro-distal bypass. Br J Surg 1989; 76: 1202-1206.

14. Beard JD, Scott DJA, Evans JM, Skidmore and Horrocks M. Br J Surg 1998; 75: 361-363.

15. Roedersheimer LR, Feins R, Green RM. Doppler evaluation of pedal arch. Am J Surg 1981; 41: 601-604.

16. Sayers RD, Thompson MM, London NJM et al. Selection of patients with critical limb ischemia for femoro-distal vein bypass. Eur J Vasc Surg 1993; 7: 291-297.

17. Tordoir JHM, Van der Plas JPL, Jacobs MJHM, Kitslaar PJEHM. Factors determining the outcome of crural and pedal revascularisation for critical limb ischemia. Eur J Vasc Surg 1993; 7: 82-86.

18. Criqui MH et al: the epidemiology of peripheral arterial disease: importance of Identifying the population at risk. Vasc Med 1997; 2: 221-6.

19. Chang JB, Stein TA. Infrainguinal revascularisation in octogenarians and septuagenarians. Journal of vascular surgery 2001; 34: 133-8.

20. Ricco JB, Flinn WR, Mc Daniel MD, Yao JST, Bergan JJ. Objective analysis of factors contributing to failure of tibial bypass grafts. World J. Surg 1983; 7: 347-352.

21. Chong AK, Chu KM, Wong M. The influence of gender difference on the outcomes of infrainguinal bypass for critical limb ischemia in Chinese patients. Eur J Vasc.Endovasc. Surg. 2002; 23: 134-139.

22. Watson HR, Schroeder TV, Simms MH et al. Association of sex with patency of femoro-distal bypass grafts. Eur J Vasc. Endovasc. Surg. 2000; 20: 61-66.

23. Peltonen S, Biancari F, Lindgren L et al. Outcome of infra-inguinal bypass surgery for critical leg ischemia in patients with chronic renal failure. Eur J Vasc Enndovasc Surg 1998; 15: 122-127.

24. Harrington EB, Harrington ME, Schanzer H, Haimov M. End-stage renal disease: Is infrainguinal limb revascularisation justified? J. Vasc. Surg. 1990; 12:691-696.

25. Hakaim AG, Gordon JK, Scott TE. Early outcome of in situ femoro-tibial reconstruction among patients with diabetes alone versus diabetes and end-stage renal failure: analysis of 83 limbs. J Vasc Surg 1998; 27: 1049-1055.

26. Rutherford RB, Jones DN, Bergentz S, et al : The efficacy of dextran-40 in preventing early ostoperative thrombosis following difficult lower extremity bypass. J Vasc Surg 1 : 765, 1984.

27. Kuukasjarvi P, Salenius JP, Riekkinen H. Prognostic value of preoperative c-reactive protein concentration and white cell count in acute extremity ischaemia. Eur J Surg 1995; 16: 335-339.

28. Upchurch GR, Keagy BA, Johnson G. An acute phase reaction in diabetic patients with foot ulcers. Cardiovasc Surg 1997; 5: 32-36.

29. Rutherford RB, Darrell NJ, Bergentz SE, Moore ES, Shah DJ, Yano T. Factors affecting the patency of infrainguinal bypass. J Vasc Surg. 1988; 8: 236-246.

30. Veith FJ, Gupta SK, Ascer E et al.. Six-year prospective multicenter randomised comparison of autologous saphenous vein and expanded PTFE grafts in infrainguinal arterial constructions. J Vasc Surg 1986; 3:104-114.

31. Shah DM, Paty PSK, Leather RP, Chang BB, Darling III RC, Feustel PJ. Optimal outcome after tibial artery bypass. Surgery, Gynaecology and Obstetrics 1993; 177: 283-288.

32. Harris PL, Veith FJ, Shanik GD, Moore DJ. Prospective randomised comparison of in situ and reversed infrapopliteal vein grafts. Br J Surg 1993; 80: 173-176.

33. Prime HT, Mayers KA, Matthews PG, Zeng G. Early post-operative ankle pressure indices help predict late patency rates after femoro-distal vein bypass grafting. J Cardiovasc Surg 1992; 33: 426-431.

34. Robbs JV. Atherosclerotic peripheral arterial disease in blacks- an established problem. SA Med J 1985; 67: 797-802.

35. Pedersen AE, Olsen BB, Krasik M et al. Halving the number of leg amputations: The influence of infrapopliteal bypass. Eur J Vasc. Surg.1994; 8:26-30.

36. Taylor LM, Haimre D, Dalman RI, Porter JM. Limb salvage versus amputation for critical limb. Arch Surg 1991; 126: 1251-1258.

37. Ricco JB, Pearce WH, Yao JST et al: The use of operative pre-bypass arteriography and Doppler ultrasound recordings to select patients for extended femoro-distal bypass. Ann Surg 1983; 198: 646.

38. Moneta GL, Yeager RA, et al: Accuracy of lower extremity arterial duplex mapping. J Vasc Surg 1992; 15: 275.

39. Bostrom A, Karacagil S et al. Duplex scanning as the sole preoperative imaging method for infrainguinal arterial surgery. Eur J Vasc Endovasc Surg. 2002; 23:140-145.

40. Owen RS, Carpenter JP et al. Magnetic resonance angiography of peripheral runoff vessels. J Vasc Surg 1993; 17: 1136-1137.

41. Bell PRF, Charlesworth D, De Palma RG et al. The definition of critical ischemia of a limb. The report of a working party of the International Vascular Symposium. Br J Surg 1982; 68 (suppl): 52.

42. Immelman EJ and Louwrens HD. Pre-operative assessment of the pedal arch using pulse generated run-off. Current surgery 1995; 52: 438-440.

43. Scott DJ, Horrocks EH, Kinsella D, Horrocks M. Pre-operative assessment of the pedal arch using pulse generated runoff and subsequent femoro-distal and subsequentfemoro-distal outcome. Eur J Vasc Surg 1994; 8: 20-25.

44. Rosenthal D, Arous EJ, Friedman SG, Ingegno MD, Johnson BI et al. Endovascular-assissted versus conventional in situ saphenous vein bypass grafting: cumulative patency, limb salvage, and cost results in a 39-month multicenter study. J Vasc Surg 2000; 31: 60-68.

45. Mills JL, Taylor SM. Results of infrainguinal revascularisation with reversed vein conduits: a modern control series. Ann Vasc Surg. 1991; 5: 156-162.

46. Mamode N, Scott RN. Graft type for femoro-popliteal bypass surgery (Cochraine Review). Issue 1,2002.

47. Lawson JA, Tangelder MJD, Algra A et Eikelboom BC (on behalf of the Dutch BOA group). The myth of the in situ graft: Superiority in infrainguinal bypass surgery? Eur J Vasc Endovasc Surg 1999 ;18: 149-157.

48. Brochado-Neto FC, Albers M, Pereira CAB et al. Prospective comparison of arm Veins and greater saphenous veins as infrageniculate bypass grafts. Eur J Vasc Endovasc Surg. 2001; 22: 146-151.

49. Kreienberg PB, Darling RC 3rd, Chang BB, Champagne BJ, Paty PS, Roddy SP, Lloyd WE, Ozsvath KJ, Shah DM. Early results of a prospective randomised trial of spliced vein versus polytetrafluoroethylene graft with a distal vein cuff for limb-threatened ischemia. J Vasc Surg. 2002 Feb ; 35(2) : 299-306.

50. Holzenbein TJ, Pomposelli FB et al. Results of a policy with arms veins used as the first alternative to an unavailable ipsilateral greater saphenous vein for infrainguinal bypass. J. Vasc. Surg.1996; 23(1): 130-140.

51. Albertini JN, Barral X, Branchereau A, Favre JP, Guidicelli H, Magne JL, Magnan PE. Long-term results of arterial allograft below-knee bypass grafts for limb salvage: A retrospective multicenter study. J Vasc Surg 2000 Mar; 31(3): 426-435.

52. Stonebridge PA, Prescott RJ, Ruckley CV. Randomised trial comparing infrainguinal polytetrafluoroethylene bypass grafting with or without vein interposition cuff at the distal anastomosis. J Vasc Surg 1997; 26: 543-550.

53. Fisher RK, How TV, Carpenter T, Brennan JA, Harris PL. Optimising Miller cuff dimensions. The influence of geometry on anastomotic flow patterns. Eur J Vasc Endovasc Surg 2001; 21: 251-260.

54. Katz SG, Kohl RD. Does dextran 40 improve the early patency of autogenous infrainguinal bypass grafts? J Vasc Surg 1998; 28: 23-26.

55. Girolami B, Bernardi E, Prins MH et al. Antiplatelet therapy and other interventions after revascularisation procedures in patients with peripheral arterial disease: a meta-analysis. Eur J Vasc Endovasc Surg 2000; 19: 370-380.

56. Becquemin JP. Effect of ticlopidine on the long-term patency of saphenous vein bypass graft in the legs. NEJM 1997; 337: 1726-1731.

57. Shionoya S, Sakurai T, Ueyama T, Kusakawa M, Sakaguchi S, Tsuchioka H *et al.* Effect of ticlopidine on graft patency following arterial reconstructive surgery in the lower extremity: A multicenter, three- year prospective study. J Vasc Surg 1990; 24: 541-7.

58. Sarac TP, Huber TS, Back MR et al. Warfarin improves the outcome of infrainguinal vein bypass grafting at high risk for failure. J Vasc Surg 1998; 28: 446-457.

59. Arfidsson B, Lundgren F, Drott C, Schersten T, Lundholm K. Influence of coumarin treatment on patency and limb salvage after arterial reconstructive surgery. Am J Surg 1990; 159: 556-60.

60. McMillan WD, McCarthy WJ, Lin SJ, Pearce WH, Yao JST. Perioperative low molecular weight heparin for infragenculate bypass. J Vasc Surg 1997; 25: 796-802.

61. Edmondson RA, Cohen AT, Das SK, Wagner MB, Kakkar VV. Low-molecular weight heparin versus aspirin and dipyridamole after femoro-popliteal bypass grafting. Lancet 1994; 344: 914-18.

62. Samama CM, Gigou F, Ill P. Low-molecular-weight heparin versus unfractionated heparin in femoro-distal reconstructive surgery: a multicenter open randomised study. Enoaxt Study Group. Ann Vasc Surg 1995; 9(Suppl): S45-53.

63. Miller A, Jepsen SJ, Stonebridge PA *et al.* New angioscopic findings in graft failure after infrainguinal bypass. Arch Surg 1990; 125: 749-755.

64. Kraiss LW, Clowes AW. Response of the arterial wall to injury and intimal hyperplasia. In: Sidaway AN, Sumpio BE, DePalma RG, Armonk NY, eds. The basic Science of Vascular Disease. Futura Publishing Company Inc., 1997; 289-317.

65. Sottiurai VS, Sue SL, Feinberg EL et al. Distal anastomotic intimal hyperplasia: Biogenesis and etiology. Eur J Vasc Surg 1988; 2: 245-256.

66. Lemson MS, Tordoir JHM, Daemen MJAP and Kitslaar PJEH. Intimal hyperplasia Vascular grafts. Eur J Vasc Endovasc Surg 2000; 19: 336-350.

67. Wilson YG, Davies AH, Southgate K et al. Vein quality influences neointimal hyperplasia in an organ culture model of human saphenous vein. Eur J Vasc Endovasc Surg 1997; 13: 557-562.

68. Souza D. A new no-touch preparation technique. Technical notes. Scand J Thorac Cardiovasc Surg 1996; 30: 41-44.

69. Mills JL, Fujitani RM, Taylor SM. The characteristics and anatomic distribution of lesions that cause reversed vein graft failure: A five-year prospective study. J Vasc Surg 1993; 17: 195-206.

70. Taylor PR, Wolfe JHN, Tyrrell MR, Mansfield AO et al. Graft stenosis: Justification for 1-year surveillance. Br J Surg 1990; 77: 1125-1128.

71. Cohen JR, Mannick JA, Cough NP, Whitemore AD. Recognition and management of impending vein graft failure. Importance for long-term patency. Arch Surg 1986; 121: 758-759.

72. Scott DF, Myers KA, Devine TJ et al. Palpation of the femoral and popliteal pulses: A study of the accuracy as assessed by agreement between multiple observers. Eur J Vasc Surg 1987; 1: 245-249.

73. Corson JD, Johnson WC, Locerfo FW et al. Prognostic value in vein bypass grafts of the lower extremity. Arch Surg 1978; 113: 932-935.

74. Wolfe JHN, Lea Thomas M et al. Early diagnosis of femoro-distal graft stenosis. Br J Surg 1987; 74: 268-270.

75. Bandyk DF, Cato RF, Towne JB. A low velocity predicts failure of femoro-popliteal Femoro-tibial bypass grafts. Surgery 1985; 98: 799-809.

76. Bandyk DF, Mills JL, Gahtan V, Esses GE. Intraoperative duplex scanning of reconstructions: Fate of repaired and unrepaired defects. J Vasc Surg 1994; 20: 426-433.

77. Buth J, Disselhoff B, Sommeling C, Stam L. Colour-flow duplex criteria for grading stenosis in infrainguinal vein grafts. J Vasc Surg 1991; 14: 716-728.

78. Lundell A, Lindblad B, Bergquist D, Hansen R. Femoro-popliteal-crural graft patency is improved by an intensive surveillance: a prospective randomised study. J Vasc Surg 1995; 21: 19-27.

79. Ihlberg L, Luther M, Tierala E, Lepantalo M. The utility of duplex scanning in infrainguinal vein graft surveillance: results from a randomised controlled study. Eur J Vasc Endovasc Surg 1998; 16: 19-27.

80. Mills JL, Wixon CL, James DC, Devine J, Westerband A, Hughes JD. The natural history of intermediate and critical vein graft stenosis: recommendations for continued surveillance or repair. J Vasc Surg 2001; 33: 273-278.

81. Kirby PL, Brady AR, Thompson SG, Torgerson D and Davies AH. The Vein Graft Surveillance Trial(VGST). Eur J Vasc Endovasc Surg 1999; 18: 469-474.

82. Thompson MM, Sayers RD, Reid A et al. Quality of life following infragenicular bypass and lower limb amputation. Eur J Vasc Surg 1995; 9: 310-313.

83. Chetter IC, Spark JL, Scott DJA et al. Prospective analysis of quality of life in patients following infrainguinal reconstruction for chronic critical ischemia. Br J Surg 1998; 85: 951-955

84. Stoney RJ: Ultimate salvage for the patient with limb-threatening ischaemia. Am J Surg 1978; 136: 228.

85. Bunt TJ, Malone JM. Amputation or revascularisation in the more than 70 years old. Am. Surg 1994; 60: 349-352.

86. Robbs JV, Human RR, Rajaruthnam P. Bypass versus primary major amputation in patients with femoro-popliteal distal disease and a threatened limb. SAMJ 1984; 66: 809-812.

87. Evans WE, Hayes JP, Vermillion BD. Effect of failed distal reconstruction on the level of amputation. Am J Surg 1990; 160: 217-220.

88. Cook TA, Davies AH, Horrocks M and Baird RN. Amputation level is not adversely affected by previous femoro-distal bypass surgery. Eur J Vasc Surg 1992; 6: 599-601.

89. Gupta SK, Veith FJ, Samsom RH et al: Cost analysis of operations for infrainguinal arteriosclerosis. Circulation 1982; 66(suppl 2); II-9.

90. Myrhe H, Fosby B, Witsoe E et al. Cost-effectiveness of therapeutic options for critical limb ischemia. Critical ischaemia 1996; 6: 37-41.

91. Nasr MK, McCarthy RJ, Hardman J, Chalmers A and Horrocks M. The increasing role of percutaneous transluminal angioplasty in the primary management of critical limb ischemia. Eur J Vasc Endovasc Surg 2002; 23: 398-403.