

**The influence of diabetes mellitus on early  
outcome following vascular surgical  
interventions.**

**Dr Thanyani Victor Mulaudzi**

**Submitted in fulfillment of the requirements for the degree of MMed in  
the Department of General Surgery.**

**As the candidate's supervisor I agree to the submission of this dissertation**

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**Supervisor: Professor JV Robbs**

*Plagiarism*

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**Dedicated to my family for their endless support.**

**Publication**

1. Mulaudzi TV, Robbs JV , Paruk N, Pillay B, Madiba TE, Govindsamy V. The influence of diabetes on short-term outcome following a prosthetic above the knee femoro-popliteal bypass. *Cardiovasc J Afr*, May/June 2009, 20(3):170-172.  
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## **CHAPTER 1**

### **ABSTRACT**

#### **Objective**

To assess the influence of diabetes mellitus on early morbidity and mortality following open vascular surgical interventions.

#### **Methods**

Clinical data on patients subjected to open vascular surgical procedures over a 5 year period at the Durban Metropolitan Vascular Service was culled from a prospectively maintained computerized database.

They were divided according to the type of surgical procedure performed. These were open abdominal aortic surgery, peripheral bypass surgery, lower extremity major amputation and carotid endarterectomy. They were further subdivided into 2 groups, diabetic and non-diabetic.

#### **Results**

1104 charts were analysed. There were no significant differences in demographics and risk factors between the two groups.

273 patients had open abdominal aortic surgery. 217 (79%) were non-diabetic. Diabetic patients had significantly higher incidence of myocardial infarction ( $p=0.00001$ ) (6 of 6

patients), graft sepsis ( $p=0.000001$ ) (7 of 7 patients) and mortality rate ( $p=0.0335$ ) (5 of 10 patients).

337 patients had peripheral bypass procedures. 204 (60%) of these were non-diabetic. There was a high prevalence of smokers among non-diabetics and of hypertension among diabetics. Diabetic patients had a preponderance of graft infection ( $p=0.0015$ ) (15 of 20 patients) and cardiovascular complications ( $p=0.0072$ ) (7 of 8 patients).

230 patients had lower extremity major amputations, 81 (35%) were diabetic and 149 (65%) non-diabetic. Myocardial infarction and death (6 of 8 patients each) were significantly higher among diabetics ( $p =0.04$ ).

264 patients had carotid endarterectomy, 170 (64%) being non-diabetic. The surgical outcome was similar between the two groups.

## **Conclusions**

This is retrospective study and as such it has some its limitations. Not all patients might have been included in the study and some of the information might have been lost. The numbers in this study are large and these limitations would appear not to have influenced the outcome of this study.

This study has shown that diabetes mellitus had diverse influence on the early outcome following different vascular surgical procedures.

Diabetes mellitus significantly increased the incidence of graft sepsis among those who had aorto-bifemoral bypass and peripheral bypass procedures.

The incidence of peri-operative cardiovascular morbidity was significantly increased among diabetics who had peripheral bypass procedures, open abdominal aortic surgery and lower extremity major amputations.

Diabetes mellitus had no influence on the surgical outcome following carotid endarterectomy.

## **CHAPTER 2**

### **INTRODUCTION**

There is little information in the literature on the influence of diabetes mellitus (DM) on early outcome following vascular surgical intervention, despite the fact that in recent decades there has been a significant increase in the incidence of DM and it is estimated that globally the number of people with DM is 220 million and expected to reach 300 million by 2025<sup>1</sup>.

The complications of DM are often irreversible and can affect multiple organs. These complications are responsible for the excess morbidity and mortality associated with DM. DM is an independent risk factor for atherosclerosis and is a leading cause of lower limb amputation<sup>2</sup>. The majority of patients with DM die from cardiovascular disease, which is a leading cause of death among diabetics in western countries<sup>2-6</sup>

The vascular complications of DM may be microvascular, presenting with neuropathy, retinopathy and nephropathy. Complications may also be macrovascular presenting with peripheral arterial disease, cerebrovascular disease and coronary heart disease.

Patients may have diabetic cardiomyopathy presenting with congestive cardiac failure<sup>4</sup>.

One of the major issues for diabetics is the presence of silent myocardial ischaemia, manifesting with myocardial ischaemia by objective testing in the absence of angina. Its

prevalence ranges from 0.5 to 9% in population based studies but is estimated to be even higher among diabetics due to neuropathy affecting cardiac afferent nerves<sup>7-10</sup>. This becomes a problem with pre-operative cardiac assessment for non cardiac vascular surgical procedures when only symptomatic patients are referred for cardiac investigation. The significance of this is that a number of patients with significant coronary artery disease are not properly assessed<sup>6 11-13</sup>.

There is evidence from some studies that patients with DM have an increased incidence of complications after vascular surgical intervention<sup>6 11-16</sup>. This has been reported to be mainly after aortic aneurysm repair and peripheral bypass surgery<sup>6 11-13</sup>. It is believed that there is an increase in the perioperative incidence of myocardial infarction and mortality. The outcome following carotid endarterectomy in diabetic patients is less clear as studies have reported conflicting results, other studies reporting poor outcome among diabetics and others reporting similar outcome to those that do not have DM<sup>14-19</sup>.

The relationship between DM and vascular disease is now well established. The influence of DM on early outcome following vascular surgical interventions has been reported for some vascular surgery and with conflicting results in others.

This study was undertaken to assess the influence of DM on early outcome following diverse vascular surgical procedures.

## **CHAPTER 3**

### **PATIENTS AND METHODS.**

Clinical data on patients managed with open surgical intervention in the Durban Metropolitan Vascular Services, Department of Surgery, Nelson R Mandela School of Medicine between 01 January 2001 and 31 December 2005 were culled from a prospectively maintained computerized database.

Only patients who were managed for non traumatic vascular disease were included in the study.

This study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu Natal.

One thousand one hundred and four (1104) charts were analyzed. These were divided into those that had DM and those that were non diabetic. Patients who were known to be Diabetic were referred to us on treatment. All other patients were evaluated for DM through blood tests and treated accordingly.

These patients were further subdivided according to the type of surgical procedure that was performed.

Operations studied were:

- Abdominal aortic surgical procedures.
- Peripheral bypass procedures.
- Major lower limb amputation.
- Carotid endarterectomy.

Information that was extracted and analysed was:

- Patient demographics
  - Age
  - Gender
  - Race
- Diagnosis
- Presenting symptoms
- Risk factors for vascular disease:
  - Diabetes mellitus (this was not divided according to types of DM)
  - Hypertension
  - Cigarette smoking (included current smokers and ex-smokers)
  - Hyperlipidaemia
- Co-morbidities:
  - Ischaemic heart disease
  - Chronic obstructive airways disease
- Surgical procedures:

- Surgical complications (graft sepsis was defined as infection that involved the graft and wound sepsis as tissue infection where the graft is not involved)

The analysis was limited to a thirty day morbidity and mortality. Patients with diabetes mellitus were analyzed separately from those that were non-diabetic.

Statistical analysis was made using the Fishers exact test (two tailed) to determine the significance of differences in proportions of the diabetics and non-diabetics. A p-value of  $<0.05$  was regarded as significant.

#### **Abdominal aortic surgery:**

Surgery involving the aorta was either for aneurysmal or occlusive disease.

For those patients with abdominal aortic aneurysm the indications for surgery were an aneurysm diameter of more than 5.5cm, symptomatic aneurysm and those aneurysms with an expansion rate of more than 5 mm within six months.

Indications for surgical intervention in patients with occlusive aorto-iliac disease were critical limb ischaemia or disabling claudication.

Patients for aortic surgery were assessed for fitness for a major surgical procedure. These patients had cardiac assessment with electro cardiography and an echocardiogram. They also had a chest X-ray, pulmonary function test and a creatinine clearance test.



All these patients had blood analyzed for full blood count, liver function test, urea and electrolytes, blood glucose, lipid profile and coagulation studies.

Patients included in this study had open aortic surgical intervention and a prosthetic graft was used. This was done under general anaesthesia. Prophylactic intravenous antibiotics (Ceftriaxon and vancomycin) and peri-operative heparin anticoagulation were given to all patients.

Post operatively they were all admitted into an intensive care unit.

**Peripheral bypass surgery:**

Peripheral bypass surgery constituted either an above knee femoro-popliteal bypass or an extra anatomical femoro-femoral bypass. Prosthetic grafts were used in both procedures. Patients who had peripheral bypass surgery did not have the same extensive pre-operative assessment as that of aortic surgical interventions. Only those patients with symptomatic ischaemic heart disease had extensive cardiac assessment. Patients with chronic pulmonary disease were selected for pulmonary function tests.

All these patients had peripheral bypass surgery under regional anaesthesia. Intravenous prophylactic antibiotics and peri-operative heparin anticoagulation were given to all patients.

**Major amputation:**

This included patients who had amputation performed below or above the knee level. Indications for major amputations included critical limb ischaemia, but with vascular disease that was not amenable to reconstruction. Another group of patients offered major amputation were those who had failed revascularization procedures. Tissue oxygen tension (TcPO<sub>2</sub>) was used to evaluate the level of ablation. This utilized the operation site to chest wall ratio. A ratio of more than 0.55 for those without DM and more than 0.6 for diabetic patients were used as indicators for level of ablation.

Patients without sepsis were offered primary limb ablation (closure of muscles, fascia and skin). Those with a focus of sepsis were offered staged procedures with a guillotine amputation first and later a secondary procedure to revise the stump once sepsis was eradicated.

These patients were given prophylactic antibiotics and deep vein thrombosis prophylactics with low molecular weight heparin.

**Carotid endarterectomy:**

Indications for carotid endarterectomy (CEA) in symptomatic patients were internal carotid artery (ICA) stenosis of equal or more than 50% or those with a thrombus within the ICA.

In those who were asymptomatic the indication for surgery was a degree of stenosis of equal to or more than 70%.

The degree of stenosis was assessed using duplex ultrasound. Digital subtraction angiogram was done only in those with unsatisfactory duplex report, suggestion of aortic arch disease or those with a suggestion of an occluded ICA on duplex.

CEA was done under general anaesthesia or local cervical block anaesthesia. There were no criteria for choosing either form of anaesthesia other than individual surgeon preference.

Those patients that had CEA under local anaesthesia had an intraluminal shunt inserted only if they developed a neurological deficit on carotid artery clamping.

For those that had CEA under general anaesthesia a shunt was inserted when a mean stump pressure of less than 50mmHg was found.

Closure of the carotid arteriotomy was either a primary closure or with a prosthetic Dacron patch. The decision to close with a patch was that of the surgeon when the ICA was less than 5mm in diameter or those that had a revision CEA.

Patients who had CEA were given intra-operative intravenous heparin and post operative low molecular weight heparin. They were all managed in an intensive care unit after the surgery.

## **CHAPTER 4**

### **4. RESULTS**

#### **4.A: OPEN ABDOMINAL AORTIC SURGERY**

Two hundred and seventy three records of patient who had an open abdominal aortic surgical intervention were analyzed (table 4A:I). Fifty six (21%) were diabetic and 217 (79%) non-diabetic.

The overall age range was 27 to 82 years, a median of 60.7 years. The age range for those who were diabetic was 48 to 71 years (median = 61.6 years) and for non-diabetics 27 to 82 years (median = 60.3 years).

One hundred and ninety two (70%) patients were males. Of these patients, 33 (17%) were diabetic and 159 (83%) non-diabetic. Of 81 (30%) females, 23 (28%) were diabetic and 58 (72%) non-diabetic.

One hundred and fifty three (56%) were white, of whom 35 (23%) were diabetic and 118 (77%) non-diabetic. Of the 78 (29%) Africans with 15 (19%) were diabetic and 63 (81%) non-diabetic. Thirty six (13%) patients were Indian, of whom 4 (11%) were diabetic and 32 (89%) non-diabetic. Six (2%) were of mixed race, two diabetic and four non-diabetic.

Table 4A.I:

Patient demographics with aortic disease.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>
<b>TOTAL</b>	<b>273</b>	<b>56 (21)</b>	<b>217 (79)</b>
Age range (years)	27- 82	48-71	27-77
Age median (years)	61	62	60
Females	81 (30)	23 (28)	58 (72)
Males	192 (70)	33 (17)	159 (83)
Race			
whites	153 (56)	35 (23)	118 (77)
Africans	78 (29)	15 (19)	63 (81)
Indians	36 (13)	4 (11)	32 (89)
Mixed races	6 (2)	2 (33)	4 (67)

DM: Diabetes Mellitus

Aortic surgery was performed for aneurysmal disease (Figure I) or aorto-iliac disease (Figure II).

One hundred and forty eight patients had surgery for abdominal aortic aneurysm (Table 4A:II). 23% had DM and 77% were non-diabetic. The majority of these patients had asymptomatic disease. The clinical presentation in terms of symptoms and signs for those with aortic disease did not differ significantly between the two groups ( $p=0.6836$ )(Table 4A:II).

One hundred and twenty five patients had aorto-bifemoral bypass for aorto-iliac occlusive disease (Table 4A:II). 18% were diabetic and 82% non-diabetic. There were significantly more non-diabetic patients that presented with rest pain ( $p=0.0392$ ). Tissue loss (ulceration or gangrene) was significantly more common among diabetics ( $p=0.0009$ ).

Disabling claudication was the least common presenting symptom. There was no significant difference in clinical presentation when diabetics were compared with non diabetics ( $p=0.2230$ ).

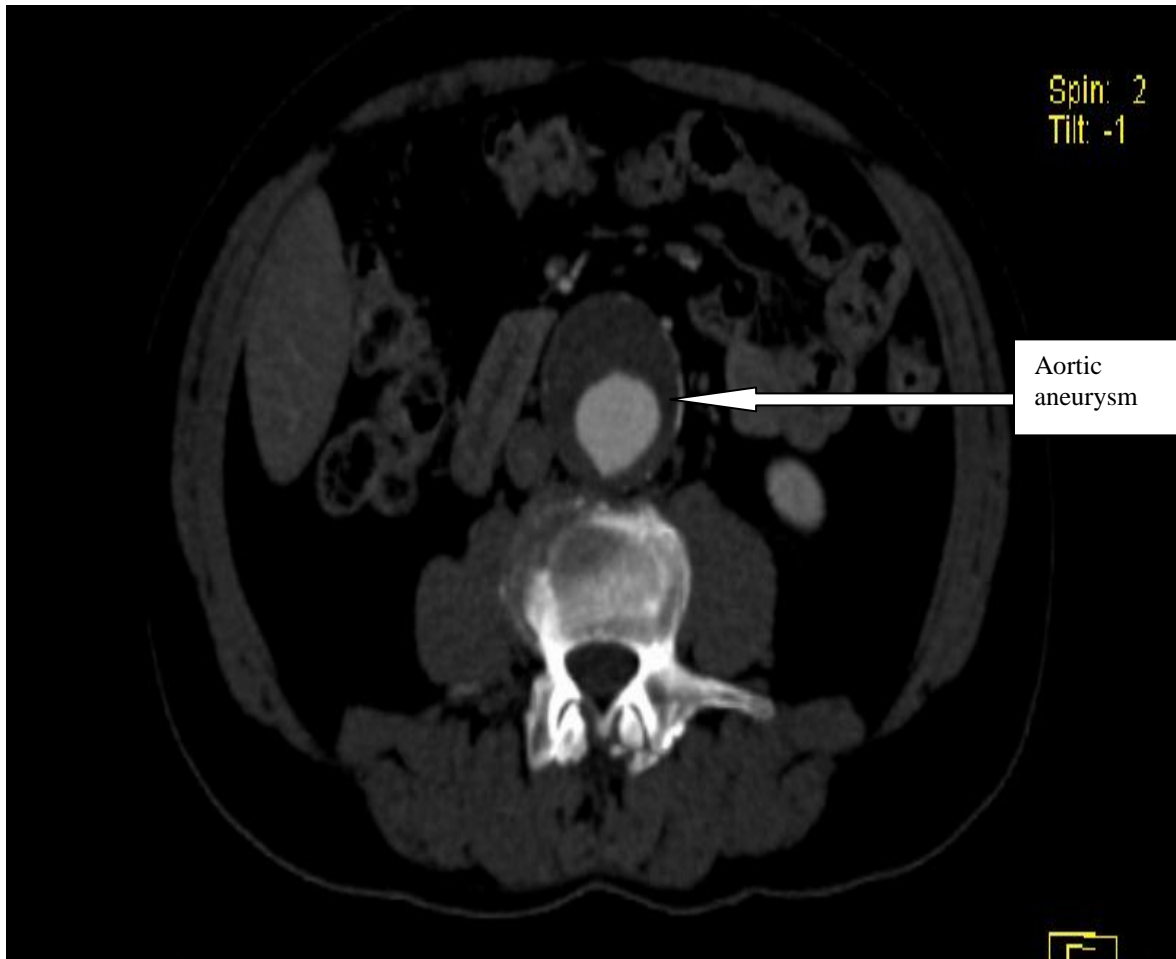
Table 4A.II:

Clinical presentation of patients with aortic disease.

	<b>TOTAL</b>	<b>DM (%)</b>	<b>NON- DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>273</b>	<b>56 (21)</b>	<b>217 (79)</b>	
<b>Aneurysm</b>	<b>148</b>	<b>34 (23)</b>	<b>114 (77)</b>	
asymptomatic	98 (66)	24 (24)	74 (76)	0.6836
Backache	50 (34)	10 (20)	40 (80)	0.6836
<b>Occlusive</b>	<b>125</b>	<b>22 (18)</b>	<b>103 (82)</b>	
Claudication	26 (21)	2 (8)	24 (92)	0,2230
Tissue loss	49 (39)	16 (33)	33 (67)	0,0009
Rest pain	50 (40)	4 (8)	46 (92)	0,0392

DM: Diabetes Mellitus, P-value: Fisher exact test

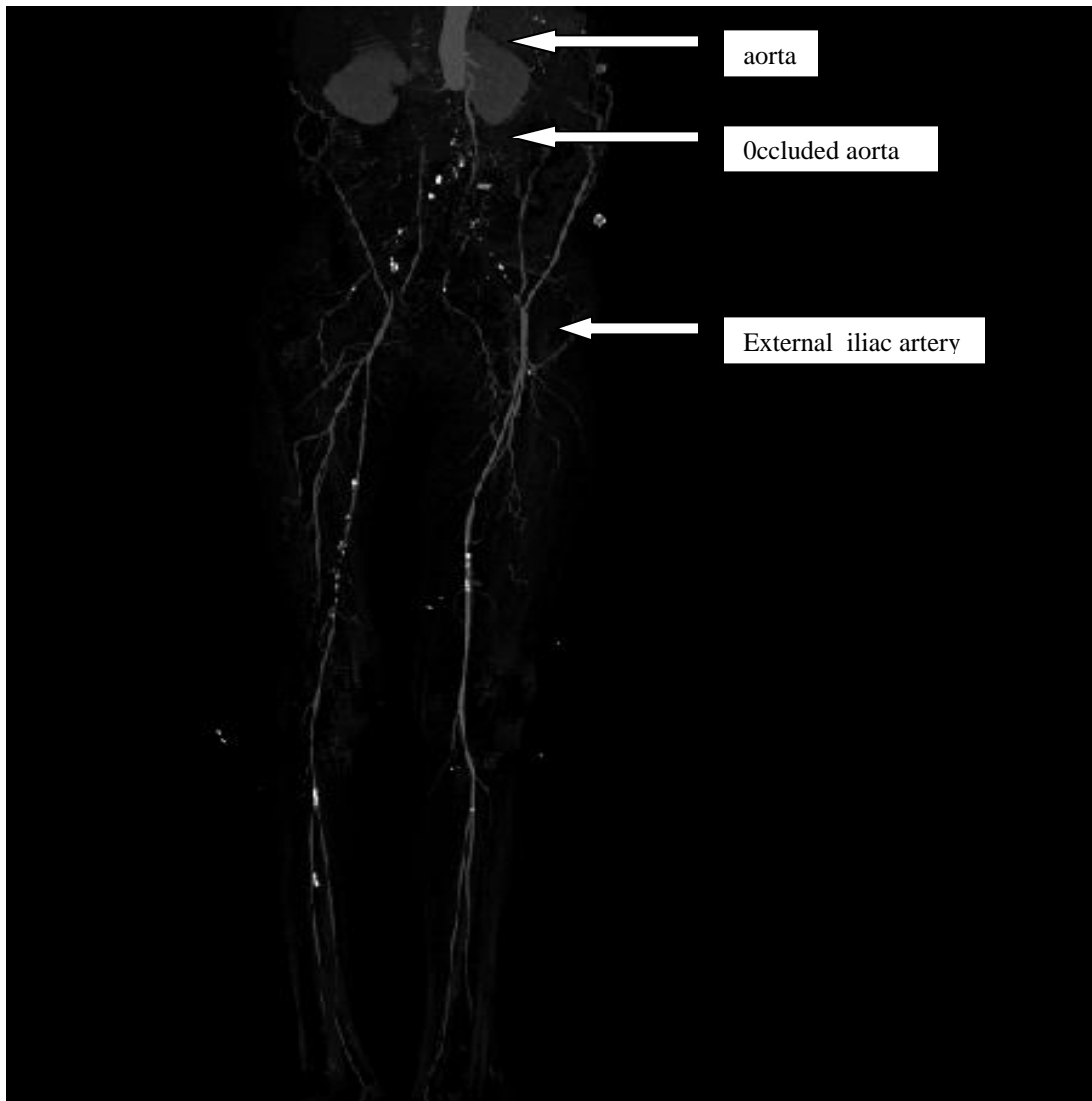
Figure I. Abdominal aortic aneurysm



CTA showing an abdominal aortic aneurysm that was managed with open aneurysm repair



Figure II. Aorto-iliac disease.



CTA of aorto-iliac disease with occluded infra-renal aorta with pickup at external iliac arteries. This was managed with an aorto-bifemoral bypass

**Risk factors: (Table 4A:III):**

Cigarette smoking (82%) was the most common risk factor for atherosclerotic disease.

The prevalence of cigarette smoking was not significantly different between the two groups ( $p=0.8916$ ).

The second most common risk factor was hypertension (39%) also with no significant differences between the two groups ( $p=0.5891$ ).

The incidence of hyperlipidaemia was only 4% with no differences between the two groups.

The incidence of ischaemic heart disease (IHD) was 18% and it was significantly more prevalent among diabetics ( $p<0.00001$ ).

Chronic obstructive airways disease (COAD) was present in 9% of patients with no significant differences between the two groups.

Table 4A:III

Risk factors for atherosclerosis and co morbidities of patients with aortic disease.

	<b>TOTAL</b>	<b>DM (%)</b>	<b>NON- DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>273</b>	<b>56 (21)</b>	<b>217 (79)</b>	
Cigarette Smoking	225 (82)	46 (20)	179 (80)	0.8916
Hypertension	106 (39)	24 (23)	82 (77)	0.5891
hyperlipidaemia	10 (4)	1 (10)	9 (90)	0.6600
COAD	25 (9)	3 (12)	22 (88)	0.3975
IHD	50 (18)	27 (54)	23 (46)	0.000001
HIV	2 (0,7)	0	2 (100)	0.8747
PTB	2 (0,7)	0	2 (100)	0.8747
Thrombocytosis	1 (0,4)	0	1 (100)	0.4644

DM: diabetes mellitus, COAD: chronic obstructive airways disease, IHD: ischaemic heart

disease, HIV: Human Immunodeficiency Virus, PTB: pulmonary tuberculosis, P-value: Fisher

exact test

**Post operative systemic complications (Table 4A.IV)**

Myocardial infarction (MI) post open abdominal aortic surgery was significantly more common ( $p=0.00001$ ) among diabetics than non-diabetics. MI was confirmed by elevated cardiac enzymes.

There were no significant differences between the two groups with the other systemic complications. The ICU stay was also not significantly different.

The overall mortality rate was 4%. Five diabetic patients died from an MI. Three non-diabetic patients complicated with congestive cardiac failure (CCF) and two with multiple organ dysfunction syndrome (MODS), they did not respond to therapy and died.

There were significantly more diabetic patients who died following aortic surgical procedures ( $p=0.0335$ ) than non-diabetics.

Table 4A.IV.

Systemic early morbidity and mortality following open aortic surgery.

	<b>TOTAL</b>	<b>DM (%)</b>	<b>NON- DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>273</b>	<b>56 (21)</b>	<b>217 (79)</b>	
MI	6 (2)	6 (100)	0	0.00001
CCF	6 (2)	2 (33)	4 (66)	0.7831
pneumonia	2 (0.7)	0	2 (100)	0.8747
ARDS	2 (0.7)	0	2 (100)	0.8747
MODS	2 (0.7)	0	2 (100)	0.8747
ICU stay (days)	4.08	4.32	3.84	0.2546
Death	10 (4)	5 (50)	5 (50)	0.0335

DM: diabetes mellitus, MI: myocardial infarction, MODS: multiple organ dysfunction syndrome,

ARDS: adult respiratory dysfunction syndrome, ICU: intensive care unit,

P-value: Fisher exact test

**Post operative local complications (Table 4A.V)**

Aorto-bifemoral bypass (AFBG) involved dissections of the groin area whereas aortic aneurysm repair was an intra-abdominal operation. The local post operative complications were analysed separately for these two aortic procedures.

For the AFBG graft sepsis was statistical significantly more common among diabetic patients (Table 4A.IV). There were no significant differences in the incidence of wound infection and graft thrombosis among the two groups.

One hundred and forty eight patients had aortic aneurysm repair. Sixteen (11%) patients, 7 (44%) diabetics and 9 (56%) non diabetics had superficial wound sepsis but with no significant difference between the two groups ( $p=0.0755$ ). There was no graft sepsis and thrombosis among those that had aortic aneurysm repair.

Table 4A.V

Early local complications following aortic surgery

	<b>TOTAL</b> (%)+	<b>DM (%)</b>	<b>NON-DM</b> (%)	<b>P-VALUE</b>
<b>Early local complications following an aorto-bifemoral bypass surgery</b>				
<b>TOTAL</b>	<b>125</b>	<b>22 (18)</b>	<b>103 (82)</b>	
Wound sepsis	7 (6)	2 (29)	5 (71)	0.9830
Graft sepsis	7 (6)	7 (100)	0	0.000001
Graft thrombosis	2 (2)	1 (50)	1 (50)	0.7018
<b>Early local complications following aortic aneurysm repair</b>				
<b>TOTAL</b>	<b>148</b>	<b>34 (23)</b>	<b>114 (77)</b>	
Wound sepsis	16 (11)	7 (44)	9 (56)	0.0755

#### **4.B PERIPHERAL BYPASS PROCEDURES**

Three hundred and thirty seven patients had peripheral bypass procedures (Table 4.B:I). One hundred and thirty three (40%) had diabetes mellitus and 204 (60%) were non-diabetic.

The peripheral bypass procedures performed were femoro-femoral cross-over bypass in 120 patients for uni-iliac occlusive disease (Figure III) and femoro-popliteal bypass in 217 patients for femoro-popliteal disease (Figure IV).

The overall age range was 34 to 80 years with a median of 63 years (Table 4.B:I). The median age for those with DM was of 62 years and 60 years for the non-diabetics.

Ninety eight (29%) patients were females, 53 of them diabetic and 45 non-diabetic. Males were in the majority (71%). Eighty male patients were diabetic and 159 non-diabetic.

The majority of patients (43%) were of Indian descent (Table 4B:I). There were significantly more Indian patients with DM ( $p < 0.0001$ ). African patients comprised 37% White patients and those of mixed races comprised 18% and 2% respectively



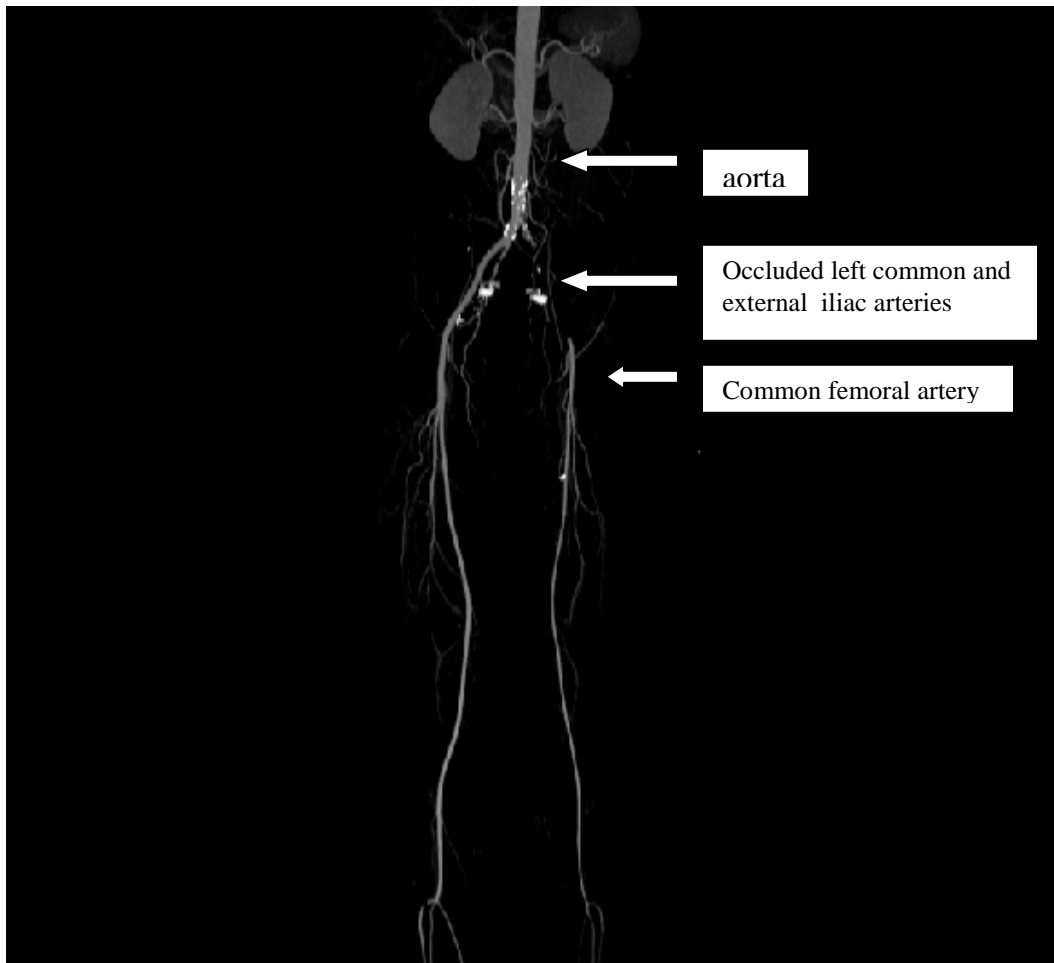
Table 4.B:I.

Demography of patients who had peripheral bypass procedures

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>
<b>TOTAL</b>	337	133 (40)	204 (60)
Age range (years)	34-80	45-76	34-80
Age median (years)	63	64	60
Female	98 (29)	53(54)	45 (46)
Male	239 (71)	80 (33)	159 (67)
<b>Race</b>			
Indian	146 (43)	84 (58)	62 (42)
African	124 (37)	31 (25)	93 (75)
White	62 (18)	16 (26)	46 (74)
Mixed race	5 (2)	2 (40)	3 (60)

DM: Diabetes mellitus

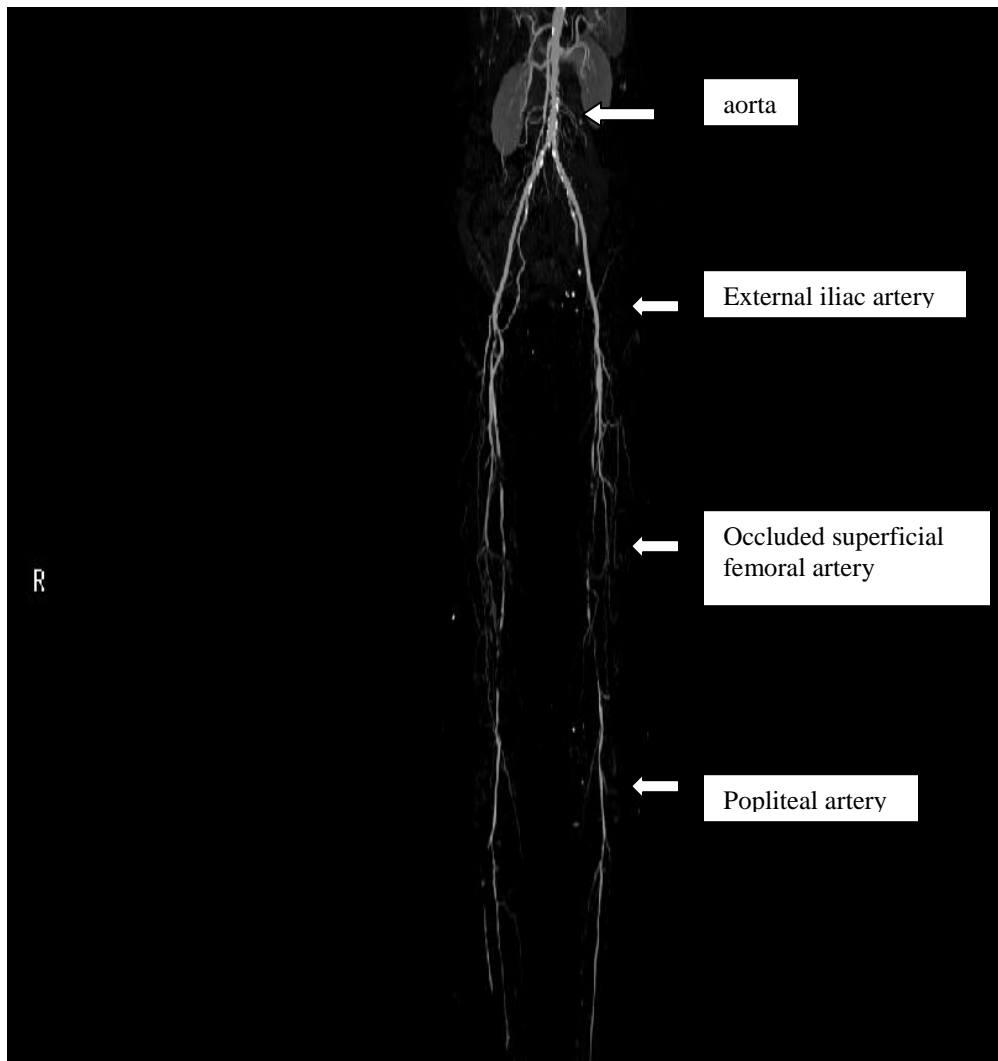
Figure III. Uni-iliac disease.



CTA showing uni-iliac disease with occluded left common and external iliac arteries.

Patient managed with right to left femoro-femoral crossover bypass.

Figure IV. Femoro-popliteal disease



CTA showing femoro-popliteal disease: occluded superficial femoral arteries with pickup at the popliteal arteries. This patient had an above knee femoro-popliteal bypass

The majority of patients (44%) presented with tissue loss (Table 4B.II). This includes ulceration or gangrene. There was no significant difference in the incidence of tissue loss between the diabetics and non-diabetics ( $p=0.2164$ ).

Rest pain was the second most common presenting symptom (35%), with disabling claudication a presenting symptom in 21%. The differences between the two groups were not significant.

Table 4.B:II.

Clinical presentation of patients who had peripheral bypass surgery.

	<b>TOTAL</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	337	133 (40)	204 (60)	
Tissue loss	147 (44)	64 (44)	83 (56)	0.2164
Rest pain	118 (35)	48 (41)	70 (59)	0.8279
Disabling claudication	72 (21)	21 (29)	51 (71)	0.0600

DM: Diabetes mellitus, p-value: Fisher exact test

Cigarette smoking (80%) was the most common risk factor for atherosclerosis in patients who had peripheral bypass surgery. There were significantly more smokers among non-diabetics ( $p < 0.0001$ ).

Hypertension (40%) was the second most common risk factor (Table 4B.III).

Hypertension was statistically significantly more common in those patients with DM ( $p = 0.0013$ ).

Only 4% of patients had hyperlipidaemia but there was no statistically significant difference between the two groups ( $p = 0.1757$ ).

17% of patients had symptomatic IHD at presentation. The difference between the two groups was not significant (0.0990).

The presence of other co-morbidities like COAD, HIV, chronic renal failure and lung cancer was rare. There was no significant difference between the two groups except for lung carcinoma (Table 4B.III).

Table 4.B:III.

Risk factors for atherosclerosis and co morbidities of patients who had peripheral bypass surgery.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON- DM (%)</b>	<b>P value</b>
<b>TOTAL</b>	<b>337</b>	<b>133 (40)</b>	<b>204 (60)</b>	
Cigarette smoking	269 (80)	68 (25)	173 (75)	0.0000
Hypertension	128 (40)	65 (51)	63 (49)	0.0013
Hyperlipidaemia	14 (4)	8 (57)	6 (43)	0.1757
IHD	56 (17)	28 (50)	28 (50)	0.0990
COAD	9 (2)	1(11)	8 (89)	0.0939
HIV	4 (1)	0	4 (100)	0.1563
Renal failure	1 (0,3)	0	1 (100)	1.0000
lung carcinoma	4 (1)	4 (100)	0	0.0236

DM: diabetes mellitus, COAD: chronic obstructive airways disease, IHD: ischaemic heart disease, CABG: Coronary artery bypass graft, HIV: Human Immunodeficiency Virus, P-value: Fisher exact test

**Results (Table 4B.IV)**

Deep wound sepsis with graft infection was significantly more common among patients with DM ( $p=0.0015$ ). The incidence of graft sepsis was 6% (Table 4B.IV).

Only five of the 20 patients who complicated with graft sepsis had presented with tissue loss. The difference in the incidence of graft sepsis among those who presented with or without tissue loss was not significant ( $p=0.1046$ ).

Five (2%) patients had graft thrombosis (Table 4B.IV). There was no significant difference in the incidence of graft sepsis between those with DM and those without ( $p=0.4092$ ).

Cardiovascular complications (2%) were the most common systemic complications (Table 4B.IV). Of these 8 patients, 7 had myocardial infarction (MI) and 2 complicated with stroke. The difference in the incidence of cardiovascular complications between the 2 groups was significant ( $p=0.0072$ ). All with cardiovascular complications were Indian patients and had presented with critical limb ischaemia. These patients had presented with asymptomatic coronary artery disease.

Other systemic complications, acute renal failure and septicaemia were not common and with no significant differences between the two groups.

The mortality rate was 1%. Four patients had DM, two died from MI, one after a stroke and the other from acute renal failure. Two patients did not have DM, one died from an MI and the other from septicaemia. The difference in the mortality rate between those with DM and those without was not significant ( $p=0.2176$ ).



Table4.B:IV.

Thirty day morbidity and mortality following peripheral bypass surgery.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON- DM (%)</b>	<b>P value</b>
<b>TOTAL</b>	<b>337</b>	<b>133 (40)</b>	<b>204 (60)</b>	
Graft sepsis	20 (6)	15 (75)	5 (25)	0.0015
Graft thrombosis	5 (2)	1 (20)	4 (80)	0.4092
Cardiovascular complications	8 (2)	7 (88)	1(12)	0.0072
ARF	2 (0,6)	1(50)	1 (50)	1.0000
Septicaemia	1 (0,3)	0	1 (100)	1.0000
death	6 (1)	4 (67)	2 (33)	0.2176

DM: diabetes mellitus, ARF: acute renal failure, P-value: Fisher exact test

#### **4.C. LOWER EXTREMITY MAJOR AMPUTATION**

Two hundred and thirty patients were managed with major amputations (table 4C.I). One hundred and eight had an above knee amputation (figure V) and 50 a below knee amputation (figure VI). 81 (35%) patients had DM and 149 (65%) were non-diabetic.

The overall age range was 27 to 86 years, the median of 62 years. The age range for diabetic patients was 27 to 84 years with the median of 59 years. For those who did not have DM the age range was 27 to 86 years with the median of 63 years.

Sixty four (29%) patients were females, 25 of them being diabetic and 39 non-diabetic.

One hundred and sixty six (72%) were male. 56 were diabetic and 110 non-diabetic.

African patients were in the majority. Of the 103 (45%) African patients, 29 were diabetic and 74 non-diabetic.

Eighty nine (39%) patients were Indian with 41 being diabetic and 48 non-diabetic.

Thirty eight (17%) were white, 11 had DM and 27 were non-diabetic.

Table 4C.I:

Demographics of patients who had lower extremity major amputation.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>
<b>TOTAL</b>	<b>230</b>	<b>81 (35)</b>	<b>149 (65)</b>
Age range (years)	27 - 86	27 - 84	27 - 86
Age median (years)	62	60	63
Females	64 (28)	25 (39)	39 (61)
Males	166 (72)	56 (34)	110 (66)
<b>Race</b>			
Africans	103 (45)	29 (28)	74 (72)
Indians	89 (39)	41 (46)	48 (54)
whites	38 (17)	11(29)	27 (71)

DM: diabetes mellitus

Two hundred and two (88%) patients presented with chronic arterial occlusive disease at different levels (table 4C.II). 72 of whom were diabetic and 130 non-diabetic. This was not statistically significant ( $p=0.8789$ ). The levels of disease for chronic arterial occlusion were aorto-iliac, femoro-popliteal and tibio-peroneal disease.

Twenty eight (12%) patients presented with acute arterial occlusion. Nine patients had DM and nineteen were non-diabetic ( $p=0.8789$ ).

Symptomatic popliteal artery aneurysm not amenable to reconstruction due to poor run-off was present in five diabetic patients. This difference in the two groups was statistical significant ( $p=0.0095$ ).

Gangrene was present in 151 (66%) patients with 59 being diabetic and 92 non-diabetic ( $p=0.1218$ ).

Thirty two (14%) patients had an ulcer on presentation, eight of these were diabetic and 24 non-diabetic ( $p=0.2693$ ).

Thirty seven (16%) patients presented with intractable rest pain with disease that was not amenable to revascularization. Fourteen patients had DM and 33 were non-diabetic ( $p=0.4832$ ).

Thirteen patients had amputation following a failed femoro-popliteal bypass surgery, 4 diabetic and 9 non-diabetics.

Two diabetic patients had amputation following a failed thromboembolectomy for acute arterial occlusion.

Table 4C.II:

Clinical presentation and level of disease of patients who had major amputation.

	<b>TOTAL</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>230</b>	<b>81 (35)</b>	<b>149 (65)</b>	
Chronic presentation	202	72	130	0.8789
Acute presentation	28	9	19	0.8789
<b>Presentation:</b>				
Rest pain	37	14	33	0.4823
Gangrene	151	59	92	0.1218
ulcer	32	8	24	0.2693
<b>Diagnosis:</b>				
Femoro-popliteal disease	155	58	97	0.3910
Aorto-iliac disease	67	15	52	0.0139
Tibio-peroneal disease	3	3	0	0.0790
Popliteal aneurysm	5	5	0	0.0095

DM: diabetes mellitus, P-value: Fisher exact test

There was statistically significant ( $p=0.0104$ ) more patients with hypertension among diabetics (table 4C.III). A total of 103(44.8%) patients were hypertensive. Forty six patients had DM and 57 non-diabetic.

Hundred and forty seven (63.9%) patients were cigarette smokers, 49 were diabetic and 98 non-diabetic. This was not statistically significant ( $p=0.5141$ ).

Only four (2%) patients had hyperlipidaemia. One of these patients was diabetic and three non-diabetic ( $p=0.9232$ ).

Symptomatic ischaemic heart disease was present in 23 (10%) patients. The difference in the two groups was not statistically significant ( $p=0.2694$ ), 11 diabetic and 12 non-diabetic.

There was statistically significant more ( $p=0.0424$ ) patients with COAD among those who did not have DM. Twenty six (11.3%) patients had COAD, of these 4 were diabetic and 22 non-diabetic.

Fifteen (7%) patients had congestive cardiac failure at presentation, 6 were diabetic and 9 non-diabetic ( $p=0.9032$ ).

Table 4C.III:

Risk factors for atherosclerosis and co morbidities of patients who had major amputation.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>230</b>	<b>81 (35)</b>	<b>149 (65)</b>	
Cigarette smoking	147 (64)	49 (33)	98 (67)	0.5141
Hypertension	103 (45)	46 (45)	57 (55)	0.0104
Hyperlipidaemia	4 (2)	1 (25)	3 (75)	0.9232
IHD	23 (10)	11 (48)	12 (52)	0.2694
COAD	26 (11)	4 (15)	22 (85)	0.0424
CCF	15 (7)	6 (40)	9 (60)	0.9032

DM: diabetes mellitus, IHD: ischaemic heart disease, COAD: chronic obstructive airways

disease, CCF: congestive cardiac failure, P-value: Fisher exact test



Fifty (22%) patients had a below knee amputation, 22 of whom were diabetic and 28 non-diabetic (Table 4C.IV).

One hundred and eighty (78%) patients were offered above knee amputation, 59 diabetic and 121 non-diabetics. The difference between those that had DM and the non-diabetic was not statistically significant ( $p=0.1928$ ).

Table 4C.IV:

Level of amputation offered.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>230</b>	<b>81 (35)</b>	<b>149 (65)</b>	
BKA	50 (22)	22 (44)	28 (56)	0.1928
AKA	180 (78)	59 (33)	121 (67)	0.1928

BKA: below knee amputation, AKA: above knee amputation, P-value: Fisher exact test

**Results (Table 4C.V)**

The stump sepsis rate was 11% (27 patients). Fourteen of the patients had DM and 13 were non-diabetic. This difference was not statistically significant ( $p=0.0869$ ).

Table 4C.V.

Eight (4%) patients complicated with myocardial infarction. Six of whom were diabetic and two non-diabetic. There were statistically significantly more diabetic patients who complicated with myocardial infarction ( $p=0.0433$ ) than non-diabetics.

The mortality rate was 4% (8 patients). Six patients who died had DM and two were non-diabetic. This difference was statistically significant ( $p=0.0433$ ). All patients died following myocardial infarction.

Table 4C.V:

Early morbidity and mortality following major amputation.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>230</b>	<b>81 (35)</b>	<b>149 (65)</b>	
Stump sepsis	27 (11)	14 (52)	13 (48)	0.0433).0869
MI	8 (4)	6 (75)	2 (25)	0.0433
Death	8 (4)	6 (75)	2 (25)	0.0433

DM: diabetes mellitus, MI: myocardial infarction, P-value: Fisher exact test

#### **4.D CAROTID ENDARTERECTOMY**

Two hundred and sixty four patient records of patients who had carotid endarterectomy for internal carotid artery stenosis (figure VII) were analyzed (table 4D.I). Ninety four (36%) of these patients had DM and 179 (64%) did not have DM. The overall age range was 37 to 89 years with a median age of 62 years.

In those that were diabetic the age range was 37 to 89 years with a median of 59 years.

Patients who did not have DM had an age range of 39 to 87 years and the median was 62 years.

One hundred and fifteen (42%) patients were females. Of the female patients 42 were diabetic and 73 non-diabetic.

Male patients were in the majority constituting 56% (149 patients) of the total cohort, 52 were diabetic and 97 non-diabetic.

One hundred and forty eight (56%) patients were Indian, of whom 77 were diabetic and 71 non-diabetic.

Ninety four (36%) patients were white, 13 of whom were diabetic and 81 non-diabetic.

Twelve (5%) patients were of mixed race, one being diabetic and 11 non-diabetic.

Ten (4%) patients were African, three of them had DM and seven non-diabetic.

Figure VII. Internal carotid artery stenosis.



Digital subtraction angiogram of a patient with symptomatic right internal carotid artery stenosis.

Table 4D.I:

Demographics of patients with extra cranial cerebro vascular disease.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>
<b>TOTAL</b>	<b>264</b>	<b>94 (36)</b>	<b>170 (64)</b>
Age range (years)	37 - 89	37 - 89	39 - 87
Age median (years)	61	59	63
Females	115 (46)	42 (37)	73 (63)
Males	149 (56)	52 (35)	97 (65)
<b>Race</b>			
Indians	148 (56)	77 (52)	71 (48)
Whites	94 (36)	13 (14)	81 (86)
Mixed Race	12 (5)	1 (8)	11 (92)
Africans	10 (4)	3 (30)	7 (70)

DM: diabetes mellitus

Of the 264 patients, 188 (71%) had symptomatic disease, of these 63 were diabetic and 125 non-diabetic (table 4D.II). This was not statistically significant ( $p=0.3289$ ).

Eighty three (44%) patients presented with a transient ischaemic attack, of these 23 were diabetic and 60 non-diabetic. This was not statistically significant ( $p=0.0938$ ).

One hundred and five (56%) patients presented with a stroke, of whom 40 were diabetic and 65 non-diabetic ( $p=0.5788$ ). All these patients could still function independently.

Other symptoms were speech deficit in 31 (17%) patients, five of them diabetic and 26 non-diabetic.

Twenty eight (15%) patients had transient visual loss, nine of these patients were diabetic and 19 non-diabetic.

Fifteen (8%) patients who were non-diabetic had syncopal attacks.

Asymptomatic patients with internal carotid artery stenosis of more than 70% were offered carotid endarterectomy. 76 (29%) patients had surgery for asymptomatic disease.

Thirty one of them were diabetic and 45 non-diabetic.



Table 4D.II:

Clinical presentation of patients with extra cranial cerebro vascular disease

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>264</b>	<b>94 (36)</b>	<b>170 (64)</b>	
Asymptomatic	76 (29)	31 (41)	45 (59)	0.3289
Symptomatic	188 (71)	63 (34)	125 (66)	0.3289
TIA	83 (44)	23 (28)	60 (72)	0.0938
Stroke	105 (56)	40 (38)	65 (62)	0.5788
<b>Associated symptoms</b>				
speech	31 (17)	5 (16)	26 (84)	
visual	28 (15)	9 (32)	19 (68)	
syncope	15 (8)	0	15 (100)	

DM: diabetes mellitus, TIA: transient ischaemic attack, P-value: Fisher exact test

There was a significantly higher number of patients with hypertension among those with DM ( $p=0.0161$ ). A total of 173 (66%) patients were hypertensive, of whom 71 were diabetic and 102 non-diabetic. (Table 4D.III)

One hundred and sixty-six (63%) patients were cigarette smokers. There was no statistically significant difference between the two groups ( $p=0.3375$ ). Fifty five patients were diabetic and 111 non-diabetic.

Twenty five (10%) had associated symptomatic ischaemic heart disease, of these 10 were diabetic and 15 non-diabetic. This difference was not statistically significant ( $p=0.7928$ ).

Only eight (3%) patients who did not have DM had confirmed hyperlipidaemia, but this did not have statistical significance ( $p=0.0782$ ).

A non-diabetic patient had COAD and the other who was diabetic had non-end-stage chronic renal failure ( $p=0.7633$ ).

Table 4D.III:

Risk factors for atherosclerosis and co morbidities of patients with extra cranial cerebrovascular disease.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>264</b>	<b>94 (36)</b>	<b>170 (64)</b>	
Hypertension	173 (66)	71 (41)	102 (59)	0.0161
Cigarette smoking	166 (63)	55 (33)	111 (67)	0.3374
Hyperlipidaemia	8 (3)	0	8 (100)	0.0782
IHD	25 (10)	10 (40)	15 (60)	0.7928
COAD	1 (0,4%)	0	1 (100)	0.7633
Renal failure	1 (0,4%)	1 (100)	0	0.7633

DM: diabetes mellitus, COAD: chronic obstructive airways disease, IHD: ischaemic heart disease, HIV: Human Immunodeficiency Virus, P-value: Fisher exact test

Significant contra lateral ICA disease requiring CEA was present in 32 (12%) patients. 15 of these were diabetic and 17 non-diabetic with no significant difference between the two groups ( $p=0.2212$ ). (Table 4D.IV)

Ninety three (35%) patients required carotid shunt insertion. Forty one patients had DM and 52 were non-diabetic. This difference was statistically significant with a p value of 0.0469.

Carotid patch was used in 26 (10%), nine of whom patients were diabetic and 17 non-diabetic ( $p=0.9167$ )

Table 4D.IV

Contra lateral ICA status, shunting and carotid patch.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>264</b>	<b>94 (36)</b>	<b>170 (64)</b>	
Contralateral ICA stenosis	32 (12)	15 (47)	17 (53)	0.2212
Shunt insertion	93 (35)	41 (44)	52 (56)	0.0469
Carotid patch	26 (10)	9 (35)	17 (65)	0.9167

DM: diabetes mellitus, ICA: internal carotid artery, P-value: Fisher exact test

**Results (Table 4D.V)**

The stroke rate was 4% (10 patients), four of whom had DM and six non-diabetic (table 4D.V). There was no statistical significant difference between the two groups ( $p=0.9675$ ).

Six patients (2%) complicated with TIA. One patient was diabetic and five non-diabetic. ( $p=0.5831$ ).

Haematoma that required exploration was a complication in 6 (2%) patients, with two being diabetic and four non-diabetic ( $p=0.7538$ ).

Post operative transient hypoglossal nerve palsy was present in 3 (1%) patients. Two of whom were diabetic and one non-diabetic ( $p=0.6005$ ).

One patient who was diabetic complicated with hyperperfusion syndrome. There was no statistical significant difference between the two groups ( $p=0.7633$ ). This patient responded well to treatment.

Two (0.8%) patients demised. These two patients did not have diabetes mellitus, but there was no statistical significant difference when compared with those who were diabetic ( $p=0.7532$ ). One patient died following a myocardial infarction and the other following a massive stroke.

Table 4D.V:

One month morbidity and mortality following carotid endarterectomy surgery.

	<b>TOTAL (%)</b>	<b>DM (%)</b>	<b>NON-DM (%)</b>	<b>P-VALUE</b>
<b>TOTAL</b>	<b>264</b>	<b>94 (36)</b>	<b>170 (64)</b>	
Stroke	10 (4)	4 (40)	6 (60)	0.9675
TIA	6 (2)	1 (17)	5 (83)	0.5831
haematoma	6 (2)	2 (33)	4 (37)	0.7538
Transient hypoglossal nerve palsy	3 (1)	2 (67)	1 (33)	0.6005
Hyperperfusion syndrome	1 (0,4)	1 (100)	0	0.7633
Death	2 (0,8)	0	2 (100)	0.7532

DM: diabetes mellitus, TIA: transient ischaemic attack, P-value: Fisher exact test

## **CHAPTER 5**

### **5. Discussion**

#### **5.A Open abdominal aortic surgery**

There is little written on the influence of diabetes mellitus on early outcome following open abdominal aortic surgery. Aortic disease generally affects older patients as it is usually associated with atherosclerosis and similar overall results have been reported by other authors in relation to aortic surgery<sup>20-30</sup>.

In terms of demographics in this study there was no significant difference in the median age between diabetics and non-diabetics, but there were more male patients with aortic disease, which is in keeping with reports from other authors<sup>21,23,31</sup>.

As with other studies abdominal aortic aneurysm was more common among whites<sup>20,21</sup>.

Cigarette smoking and hypertension were the most common risk factors for both occlusive and aneurysmal aortic disease in keeping with other reports<sup>20,21,31</sup>. There were no significant differences between diabetics and non-diabetics in the present study.



The majority of patients with aneurysmal disease were asymptomatic, and in those with occlusive disease the majority presented with critical limb ischaemia.

Surprisingly very few patients (4%) had hyperlipidaemia. This has also been noted in previously published studies from Durban<sup>25,32</sup>. Presumably may be the incidence of hyperlipidaemia is low in this group of patients.

The incidence of symptomatic ischaemic heart disease among diabetics was significantly higher ( $p < 0.0001$ ), which has been noted in earlier studies in cohorts of patients with atherosclerotic peripheral arterial disease<sup>33-35</sup>.

Diabetes mellitus was significantly associated with an increased incidence of post operative myocardial infarction ( $p < 0.0001$ ), not surprisingly if one takes into account the higher incidence of ischaemic heart disease among those with DM. Mulaudzi et al made the same observation among those that had femoro-popliteal bypass surgery<sup>32</sup>.

Despite the increased incidence of ischaemic heart disease and postoperative myocardial infarction among diabetic patients, congestive cardiac failure did not occur more frequently ( $p = 0.2609$ ) and was mainly due to cardiomyopathy.

Among patients who had abdominal aortic aneurysm repair the incidence of graft sepsis was not significantly different between the two groups.

The incidence of graft sepsis was significantly higher ( $p < 0.00001$ ) among diabetic patients who had aorto-bifemoral bypass, due most likely to the groin incision. These results are similar to those found in other vascular surgical procedures such as femoro-popliteal bypass<sup>32</sup>.

The mortality rate for these patients that had open aortic surgery was 4%. This is similar to that reported by other authors<sup>12,13,25,31</sup>. There was a significantly higher mortality rate among diabetics ( $p = 0.0335$ ), which is in part due to the higher incidence of MI.

Very few patients in this study (4,%) were on statins. This may be explained by the fact that majority of these patients were referred to us by general practitioners who might not be aware of their importance in atherosclerotic disease. It has been shown that tight blood pressure and glycaemic control and statins do reduce the incidence of post operative cardiovascular complications<sup>35-37</sup>. Statins therapy would almost certainly impact favorably on these results.

## **5.B Peripheral bypass procedures**

There is little to be found in the literature that specifically addresses the influence of diabetes mellitus on early perioperative morbidity and mortality, which this study attempts to address in relation to peripheral bypass surgery. Overall, co-morbidity profiles in the two groups of patients were similar although non-diabetics had a preponderance of males and a much high incidence of cigarette smoking. There was a higher incidence of hypertension in diabetics.

The majority of patients who had a peripheral bypass procedure had presented with critical limb ischaemia, which is in keeping with the policies of the unit<sup>25 32</sup>.

In general diabetics are known to have an increased incidence of septic complications. Graft infection was significantly more common among diabetic patients. There was no relationship between graft infection and the presence of preoperative tissue loss on the extremity.

Strict aseptic technique at surgery and tight blood glucose control can assist in reducing the incidence of graft infection.

Postoperative cardiovascular complications were significantly increased in those who were diabetic. This concurs with the finding of several authors and is mainly due to the increased incidence of associated cardiovascular disease in those diabetics who present with peripheral arterial occlusive disease<sup>2,6,11,33,35</sup>. As the majority of the patients in this

study had critical ischaemia, the incidence of cardiovascular disease would be expected to be even higher as its incidence increases with the severity of peripheral arterial disease<sup>38</sup>. Of interest is the fact that all patients who had cardiovascular complications were Indians, which is probably due to the fact that there is a higher prevalence of diabetes in this population.

Overall in this series, those who developed myocardial infarction did not have symptomatic coronary artery disease. This calls into question how aggressive one needs to be in the preoperative workup. There remains no consensus but most authors suggest that only those who have symptomatic coronary artery disease should be referred to a cardiologist for assessment<sup>39,40</sup>. Others have shown that routine extensive cardiac assessment for all patients presenting with peripheral arterial disease does not reduce the morbidity and mortality rate<sup>39,40</sup>.

It is our practice to refer patients with symptomatic coronary artery disease for cardiological assessment. What we do not know is whether we should be more aggressive with our Indian diabetic patients as they have demonstrated a higher incidence of cardiovascular complication even though they were asymptomatic at presentation.

Strong evidence has emerged in support of beta blockade and statins administration to reduce the incidence of perioperative cardiovascular complications<sup>35-38,41-44</sup>. Few patients in this study were referred to us on beta blockers and statins. Hopefully the importance of this will be realized and more patients will be placed on this therapy.

These procedures have a low mortality rate with no significant differences between the two groups. Even though this was not statistically significant, the six patients who died had presented with critical ischaemia.

It is important then for these patients with PAD to have a comprehensive clinical history and examination to identify those with suspected significant coronary artery disease. This group of patients will require further cardiological assessment.

### **5.C Lower extremity major amputation**

Lower extremity major amputation is a demoralizing event and has a major physical, psychological and social impact.

Atherosclerotic peripheral arterial disease has been shown to be the major cause of lower extremity limb amputation as with this study<sup>45</sup>. The older age group is in keeping with other studies<sup>46,47</sup>.

As cigarette smoking is a major risk factor for atherosclerosis and this might in part explain the male preponderance among these patients in the present study as shown by other authors<sup>46,48-51</sup>.

Among the Indian patients who had major amputations there were significantly more patients with DM (P=0.0095).

The majority of patients undergoing major amputation (80%) presented with tissue loss. The main problem in our community is the late request for medical care with patients presenting with far more advanced disease. The late presentation is also common among diabetic patients due to peripheral neuropathy that lowers pain perception<sup>52</sup>.

Risk factors for atherosclerosis and their prevalence are similar to those from previous publications<sup>25,26,29,30,32,53</sup>.

The high incidence of ischaemic heart disease in this group of patients is a reflection of the fact that all had critical limb ischaemia<sup>11</sup>.

Myocardial infarction as a complication was significantly higher among diabetics ( $p=0.0433$ ). This would be expected as there is a higher incidence of coronary artery occlusive disease among patients with critical limb ischaemia, which in turn is greater in diabetic<sup>11,32,33,35</sup>.

Surprisingly the incidence of stump sepsis was not significantly higher among diabetics.

Patients in this study died from myocardial infarction. It is then not surprising that significantly more patients with diabetes mellitus died following major lower extremity amputation.

To reduce the rate of lower extremity major amputation one has to control the risk factors.

The majority of patient in this study were smokers and elimination of this risk factor would certainly reduce the amputation rate<sup>54</sup>.

Tight blood pressure control has also been shown to reduce the stroke and myocardial infarction rate<sup>36</sup>.

Treating patients with statins would possibly retard the progression of atherosclerosis and thereby reduce the amputation rate, as well as reducing the cardiovascular complication rate<sup>55-57</sup>.

Patients with DM should have their blood sugar level tightly controlled. Special attention should also be placed on foot care as this will reduce the incidence of diabetic foot ulcers thereby possibly decreasing the need for amputation<sup>58</sup>.

These patients with peripheral arterial disease should be given antiplatelet therapy in order to reduce the incidence of cardiovascular complications<sup>44,59</sup>.



## **5.D Carotid endarterectomy**

Stroke is one of the leading causes of death in western countries<sup>60-62</sup>. Stroke also has major physical, psychological and social adverse effects.

For those with carotid artery disease carotid endarterectomy has been shown to effectively reduce the incidence of cerebrovascular incidents<sup>60-66</sup>.

This is known to be a disease of an older population group<sup>60-69</sup>, but in this study those patients that had DM tended to be younger and as with other studies there was a male preponderance<sup>60,61,67-69</sup>.

The majority of patients were Indians and there were significantly more diabetics ( $p < 0.0001$ ) in this group. This is probably due to the high prevalence of cigarette smoking, hypertension and diabetes mellitus in this community.

Of interest is the low incidence of carotid disease among Africans even though that of peripheral arterial disease is high, reasons for this remain unclear and there may well be a genetic factor.

In our practice duplex ultrasound is the diagnostic tool of choice with angiography when indicated<sup>70,71</sup>.

Among those who were offered carotid endarterectomy symptomatic patients were in the majority. This is similar to previous publications from this institution<sup>68,69,72</sup>. There was

no significant difference in terms of indications for surgery between diabetics and non-diabetics. Our indications for carotid endarterectomy are similar to the guidelines given by major trials in carotid artery disease<sup>60-66,73</sup>.

The total carotid shunt insertion rate was 35%. We shunt selectively when the mean stump pressure is less than 50mmHg. Selective shunting and the use of mean stump pressure of 50mmHg as threshold is effective in preventing peri-operative cerebrovascular complication<sup>67,68,74,75</sup>. This shunt rate is comparable to that of other authors<sup>67,68,74,75</sup>.

The peri-operative stroke rate was 4% which is acceptable<sup>60-68,73 74</sup>. There was no significant difference between the diabetics and non-diabetics. This result differs from that of Schlueter et al who found that there was an increased risk of stroke and death among diabetics<sup>76</sup>. This study does support results from other studies in showing no significant difference in perioperative outcome among the two groups<sup>15,18,77,78</sup>.

Post operative hypoglossal nerve palsy was present in 1% in this study. This is much lower than the up to 8% stated by other authors<sup>79</sup>. This might be due to the experience and the guidance of those performing carotid endarterectomy.

Hyperperfusion syndrome is a very rare complication<sup>80,81</sup>. This complication did not have significant differences between the two groups.

The mortality rate in this study was 0,8% with no difference between the two groups.

This is comparable to that reported previously<sup>15,18,60-62,67,68,73,74,77,78</sup>.

Cessation of cigarette smoking, control of hypertension and diabetes mellitus and treating these patients with antiplatelets agents and statins will probably retard disease progression and also improve the peri-operative results<sup>82-85</sup>.

### **5.E. Best medical therapy**

Life style modification forms a major part of best medical therapy. There is a high incidence of cigarette smoking in our patients and reduction of this would possibly improve outcome<sup>11,54</sup>.

The community should be encouraged to exercise<sup>11,54</sup>.

Tight control of risk factors for atherosclerosis, hypertension and diabetes mellitus should be customary in all patients<sup>35,36 45</sup>.

Patients with atherosclerotic disease should be treated with an antiplatelet agent and statins<sup>35,36,44,45</sup>.

We have not been paying enough attention to best medical therapy as indicated by few numbers of patients on best medical therapy when referred to a vascular surgery unit. If we offer best medical therapy to all our patients our results would possibly improve.

## **CHAPTER 6**

### **6. CONCLUSION**

This is retrospective study and as such it has some limitations. Some patients might not have been included in the study and some of the information might have been lost. The numbers in this study are large and these limitations would appear not to have influenced the outcome of this study.

This study has shown that diabetes mellitus has diverse influence on the early outcome following different vascular surgical procedures.

Diabetic patients who had open abdominal aortic surgery had significantly increased incidence of myocardial infarction and mortality rate.

Graft infection was significantly higher in diabetics who had aorto-bifemoral bypass.

For those that had peripheral bypass procedures diabetes mellitus significantly increased the incidence of graft sepsis and that of cardiovascular morbidity.

Diabetic patients who had major lower extremity amputations had significantly increased incidence of myocardial infarction and that of the mortality rate.

Diabetes mellitus did not have an influence on the early outcome of those that had carotid endarterectomy.

## CHAPTER 7

### References:

1. Zimmet P, Alberti KGMM, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 414(6865), 782-787 (2001). .
2. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993;16(2), 434-444.
3. Movahed M-R, Hashemzadeh M, Mazen Jamal M. Diabetes mellitus is a strong, independent risk for atrial fibrillation and flutter in addition to other cardiovascular disease. *Int. J. Cardiol.* 2005;105(3), 315-318.
4. Fang ZY, Prins JB, Marwick TH. Diabetic cardiomyopathy: evidence, mechanisms, and therapeutic implications. *Endocr. Rev.* 2004; 25(4), 543-567.
5. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA* 1979; 241(19), 2035-2038. .
6. Garcia MJ, McNamara PM, Gordon T, Kannel WB. Morbidity and mortality in diabetics in the Framingham population. Sixteen year follow-up study. *Diabetes* 1974; 23(2), 105-111.
7. Cohn PF, Fox KM, Daly C. Silent Myocardial Ischemia. *Circulation* 2003; 108(10), 1263-1277. .
8. Fazzini PF, Prati PL, Rovelli F et al. Epidemiology of silent myocardial ischemia in asymptomatic middle-aged men (the ECCIS Project). *Am. J. Cardiol.* 1993; 72(18), 1383-1388.
9. Koistinen MJ. Prevalence of asymptomatic myocardial ischaemia in diabetic subjects. *Br. Med. J.* 1990;301(6743), 92-94. .
10. Janand-Delenne B, Savin B, Habib G, Bory M, Vague P, Lassmann-Vague V. Silent myocardial ischemia in patients with diabetes: who to screen. *Diabetes Care* 1999;22(9), 1396-1400.
11. Criqui HM, Langer RD, Fronc A, Feigelson HS, et al. Mortality over a period of 10 years in patient with peripheral arterial disease. *N Engl J Med* 1992;326:381-6.
12. Hallin A, Holmberg L. Literature Review of surgical management of abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg.* 2001;22: 198-204.
13. Harris, RA, Hardman, DT, Fisher, C, et al. Aortic reconstructive surgery for limb ischaemia: immediate and long-term follow-up to provide a standard for endovascular procedures. *Cardiovasc Surg* 1998; 6:256.
14. Axelrod DA, Upchurch GR Jr, DeMonner S, Stanley JC, Khuri S, Daley J, et al. Perioperative cardiovascular risk stratification of patients with diabetes who undergo elective major vascular surgery. *J Vasc Surg* 2002;35:894-901.
15. Aziz I, Lewis R, Baker JD, deVirgilio C. Cardiac morbidity and mortality following carotid endarterectomy: the importance of diabetes and multiple Eagle risk factors. *Ann Vasc Surg* 2001;15:243-46.
16. Caron B, Rockman, Stephanie S, Saltzberg, Thomas S, Maldonado, et al. The safety of carotid endarterectomy in diabetic patients: clinical predictors of adverse outcome. *J Vasc Surg* 2005;42: 878-83.)

17. Salenius JP, Harju E, Riekkinen H. Early cerebral complications in carotid endarterectomy: risk factors. *J Cardiovasc Surg (Torino)* 1990; 31:162-7.
18. Akbari CM, Pomposelli FB Jr, Gibbons GW, Campbell DR, Freeman DV, Logerfo FW. Diabetes mellitus: a risk factor for carotid endarterectomy? *J Vasc Surg* 1997;25:1070-6.
19. Ballotta E, Da Giau G, Renon L. Is diabetes mellitus a risk factor for carotid endarterectomy? A prospective study. *Surgery* 2001;129: 146-52.
20. Dawson I, Sie RB, van Bockel JH. Mass or high risk screening for Abdominal Aortic Aneurysm, *Br J Surg* (1997);84: 293-9.
21. Wilmink AB, Quick BT. Epidermiology and prevention of abdominal aortic aneurysm, *Br J Surg* (1998);85: 155-62.
22. Madiba TE, Abdool-Carrim ATO et al. Management of graft occlusion following aortobifemoral bypass. *Cardiovascular journal of South Africa* 2000;2:77-80.
23. Madiba TE, Mars M, Robbs JV. Aortobifemoral bypass in the presence of SFA occlusion. Does the profunda femoris artery provide adequate run-off? *J R Coll. Surg. Edinburgh* 1998;43(5):310-313.
24. Madiba TE, Mars M, Robbs JV. Choosing the proximal anastomosis in aortobifemoral bypass. *BJS* 1997;84:1416-1418.
25. Madiba TE, Robbs JV. Aortoiliac occlusive disease in the different population groups- clinical pattern, risk profile and results of reconstruction. *SAMJ* 1999;12:1288-1292.
26. Murabito JM. Intermittent claudication. A risk profile from the Framingham Heart study. *Circulation* 1997;96:44-49.
27. Nair R, Robbs JV, Chetty R et al. Occlusive arterial disease in HIV infected patients: a preliminary report. *Eur J Vasc Endovasc Surg* 2000;20:353-357.
28. Robbs JV, Late revascularization Of Lower Limb Following Acute Arterial Occlusion, *Br J Surg*, 1979,66 (2) 129-31.
29. Selvin, E, Erlinger, TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. *Circulation* 2004; 110:738.
30. Smith, SC Jr, Milani, RV, Arnett, DK, et al. Atherosclerotic vascular disease conference: Writing Group II: risk factors. *Circulation* 2004; 109:2613.
31. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM and Scott RA et al., The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial, *Lancet* 360 (9345) (2002 November 16), pp. 1531–1539.
32. Mulaudzi TV, Robbs JV , Paruk N, Pillay B, Madiba TE, Govindsamy V. The influence of diabetes on short-term outcome following femoro-popliteal bypass. *CVJA* 2009;20(3):184-186.
33. Manson JAE, Colditz GA, Stampfer MJ, Willett WC, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. *Arch Intern Med.* 1994;121:912-918.
34. Garcia MJ, McNamara PM, Gordon T, Kannell WB. Morbidity and mortality in diabetes in the Framingham population. Six year follow-up. *Diabetes.* 1974;23:105-111.

35. United Kingdom Prospective Diabetes Study Group. UK Prospective Diabetes Study 23: risk factors for coronary artery disease in non-insulin dependent diabetes. *BMJ*.1998;316:823-828.
36. United Kingdom Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ*.1998;317:703-713.
37. Fleisher LAM. Evaluation of the Patient With Cardiac Disease Undergoing Noncardiac Surgery: An Update on the Original AHA/ACC Guidelines. *International Anesthesiology Clinics* 2002; 40: 109-20.
38. Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, et al. The prevalence of peripheral arterial disease in a defined population. *Circulation*. 1985;71:510-515.
39. Auerbach A, Goldman L. Assessing and reducing the cardiac risk of noncardiac surgery. *Circulation* 2006; 113: 1361–1376.
40. Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery – executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on perioperative Cardiovascular Evaluation for Noncardiac Surgery). *J Am Coll Cardiol* 2002; 39: 542–553.
41. Collins R, Macmahon S. Blood pressure, antihypertensive drug treatment and the risk of stroke and of coronary heart disease. *Br Med Bull*.1996;50:272-298.
42. Hypertension Detection and Follow-up Program Cooperative Group. Mortality findings for stepped-care and referred-care in the Hypertension Detection and follow-up Program, stratified by other risk factors. *Prev Med*. 1985;14:312-335.
43. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA*. 2001;286:1317-1324.
44. Antiplatelet Trialists' Collaboration: Collaborative overview of randomised trials of antiplatelet therapy. I: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *Br Med J* 1994; 308: 81-106.
45. Feinglass J, Brown JL, LoSasso A, et al: Rates of lower-extremity amputation and arterial reconstruction in the United States, 1979 to 1996. *Am J Public Health* 1999; 89:1222-1227.
46. Tunis SR, Bass EB, Steinberg EP: The use of angioplasty, bypass surgery, and amputation in the management of peripheral vascular disease. *N Engl J Med* 1991; 325:556-562
47. Van Buskirk A, Barta PJ, Schlossbach NJ: Lower extremity amputations in New Jersey. *N J Med* 1994; 91:260-263.
48. Tunis SR, Bass EB, Klag MJ, et al: Variation in utilization of procedures for treatment of peripheral arterial disease. *Arch Intern Med* 1993; 153:991-998
49. Most RS, Sinnock P: The epidemiology of lower extremity amputations in diabetic individuals. *Diabetes Care* 1983; 6:87-91.
50. Dillingham TR, Pezzin LE, MacKenzie EJ: Incidence, acute care length of stay, and discharge to rehabilitation of traumatic amputee patients: an epidemiologic study. *Arch Phys Med Rehabil* 1998; 79:279-287



51. Ebskov LB: Lower limb amputations for vascular insufficiency. *Int J Rehabil Res* 1991; 14:59-64.
52. Kannel WB, Risk factors for atherosclerotic cardiovascular outcomes in different arterial territories. *J Cardiovasc Risk* 1994;1:3333-3339.
53. Desai Y, Robbs JV. Staged below knee amputations for septic peripheral lesions due to ischaemia. *BJS* 1986;73(5):392-4.
54. Lassila R, Lepantalo M: Cigarette smoking and the outcome after lower limb arterial surgery. *Acta Chir Scand*1988;154:635- 640
55. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994;344:1383-1389.
56. Kjekshus J, Pedersen TR: Reducing the risk of coronary events: evidence from the Scandinavian Simvastatin Survival Study (4S). *Am J Cardiol* 1995;76:64C- 68C.
57. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20, 536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360: 7-22.
58. American Diabetes Association: Preventive foot care in people with diabetes (Position Statement). *Diabetes Care*2003; 26 (Suppl. 1):S78 -S79.
59. American Diabetes Association: Aspirin therapy in diabetes (Position Statement). *Diabetes Care* 2003; 26 (Suppl. 1):S87-S88
60. European Carotid Surgery Trialists Group: Randomized Trial of Endarterectomy for recent Symptomatic carotid Stenosis. Final results of MRC European Carotid Surgery Trial (ECST). *Lancet*. 1998: 351-1387.
61. Ferguson GG et al. The NASCET Surgical Results in 1415 patients. *Stroke*. Sep 1999; 30: 1751-1758.
62. Naylor AR et al: Overview of the principal results and secondary analyses from the European and North American randomized trials of endarterectomy for symptomatic carotid stenosis. *Eur J Vasc Endovasc Surg*. 2004 Jan;27(1):107-8.
63. Halliday A et al.; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group (2004) Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 363: 1491 - 1502
64. Hobson R et al. (1995) Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Study. *JAMA* 273: 1421 - 1428.
65. Mayberg MR et al. (1991) Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. Veterans Affairs Cooperative Studies Program 309 Trialist Group. *JAMA* 266: 3289 - 3294.
66. North American Symptomatic Carotid Endarterectomy Trial Collaborators (1991) Beneficial effect of carotid endarterectomy in symptomatic patients with highgrade carotid stenosis. *N Engl J Med* 325: 445 - 453
67. Mulaudzi TV, Pillay W, Pillay B, Robbs JV. Transient ischaemic attack: Is computed tomography worthwhile? *CVJS* 2005 July/August;16(4):212-4.
68. Kadwa AM, Robbs JV: Carotid Endarterectomy in Durban. The First 10 years. *SAMJ*. April 1993; 83: 248-252.

69. Robbs JV, Hoffman M. Carotid Endarterectomy after recent cerebral infarction. *European Journal Of Vascular & Endovascular Surgery*. July 1999; 18: 6-10.
70. Logason K, Karacagil S, Hardermark H. Carotid endarterectomy based on duplex scan findings. *European J Vasc Endovasc Surg* 2002;36:9-15.
71. Kadwa AM, Robbs JV, Abdool-Carrim ATO. Arch angiography prior to carotid endarterectomy. Is its continued use justified? *Eur J Vasc Endovasc Surg* 1997;13:527-530.
72. Mulaudzi TV, Biccard BM, RobbsJV, Paruk N, Pillay B, Rajaruthnam P. Carotid artery stump pressure and associated neurological changes in predominantly symptomatic carotid artery disease patients undergoing awake carotid endarterectomy. *CVJSA*, in press. (accepted October 2008). .
73. Rothwell PM, Goldstein LB. Carotid endarterectomy for asymptomatic stenosis – Asymptomatic Carotid Surgery Trial. *Stroke* 2004;35:2425.
74. Woodworth GF, McGirt MJ, Than KD et al. Selective versus routine intraoperative shunting during carotid endarterectomy: a multivariate outcome analysis. *Neurosurgery* 2007Dec;61(6):1170-7.
75. Jacob T, Hingorani A, Asher E. Carotid artery stump pressure (CASP) in 1135 consecutive endarterectomies under general anaesthesia: an old method that survived the test of times. *J Cardiovasc Surg (Torino)* 2007 Dec;48(6):677-81.
76. Schlueter M, Reimers B, Castriota F et al. Impact of diabetes, patient age, and gender on the 30-day incidence of stroke and death in patients undergoing carotid artery stenting with embolus protection: a post-hoc subanalysis of a prospective multicenter registry. *J Endovasc Ther* 2007 Jun;14(3):271-8.
77. Enzo Ballotta, Giuseppe Da Giau, Laura Renon. Is diabetes mellitus a risk factor for carotid endarterectomy? A prospective study. *Surgery* 2001;129:146-52.
78. Giuseppe Raimondo Pistolese, Annalisa Appolloni, Sonia Ronchey, Eugenio Martelli. Carotid endarterectomy in diabetic patients. *J Vasc Surg* 2001;33:148-54.).
79. Sajid MS, Vijaynagar B, Singh P, Hamilton G. Literature review of cranial nerve injuries during carotid endarterectomy. *Acta chir belg* 2007;107:25-28.
80. Atnip RG. Post-operative cerebral hyperperfusion associated with impaired cognitive function in patients undergoing carotid endarterectomy. *Perspectives in Vascular Surgery and Endovascular Therapy* 2005;17(4):379-381.
81. Ogasawara K, Sakai N, Kuroiwa T et al. Intracranial Hemorrhage associated with cerebral hyperperfusion syndrome following carotid endarterectomy and carotid stenting; retrospective review of 4494 patients. *J Neurosurg* 2007 Dec;107(6):1130-1136.
82. Markus HS, Droste DW, Kaps M et al. Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using Doppler embolic signal detection (CARESS). *Circulation* 2005;111:2233-2240.
83. Cannon CP. Effectiveness of clopidogrel versus aspirin in preventing acute myocardial infarction in patients with symptomatic atherothrombosis (CAPRIE trial) *Am J Cardiology* 2002 Oct;90:760-762.
84. Perler BA. Should statins be given routinely before carotid endarterectomy? *Perspect Vasc Surg Endovasc Ther* 2007 Sep;19(3):240-5.

85. Wang JG, Staessen JA, Yan L et al. Carotid intima-media thickness and anti-hypertensive treatment. A meta-analysis of randomized controlled trials. *Stroke* 2006;37:1933.