Infra-inguinal Arterial Reconstruction for Peripheral Arterial Disease

The Curaçao Experience

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ABSTRACT

Background: *The prevalence and treatment of peripheral arterial disease in the Caribbean is not well documented. The aim of this study was to review the results from a small hospital in the Caribbean.*
Methods: *One-hundred and eight infra-inguinal arterial reconstructions on 90 patients were retrospectively reviewed. Patients were classified according to the categories suggested by the* Ad Hoc *Committee on Reporting Standards of the Joint Councils of the Society for Vascular Surgery. Follow-up ranged from 0 to 103.1 months. The Kaplan-Meier method was used to visualize survival, limb salvage rates and primary and secondary patency rates. Cox regressions were used to identify potential risk factors.*
Results: *The limb salvage rates were 74.5% after one year and 71.4% after five years. Overall primary patency rates were 67.0 % after one year, 63.4% after three years and 50.8 % after five years. Overall secondary patency rates were 86.4% after one year and 75.1% after five years. The primary patency rate for autologous saphenous vein was 82.4% (SE 7.5%) after five years. The primary patency rates for prosthetic grafts were 62.1% (SE 8.5%) after one year, 56.9% (SE 9.2%) at three years and 37.9% (SE 16.7%) after five years.*
Conclusion: *Infra-inguinal arterial bypass surgery is feasible in small Caribbean hospitals showing results comparable to major studies.*

Reconstrucción Arterial Infrainguinal en la Enfermedad Arterial Periférica

La Experiencia de Curazao

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RESUMEN

Antecedentes*: La prevalencia y el tratamiento de enfermedad arterial periférica en el Caribe no están bien documentados**.** El objetivo de este estudio fue examinar los resultados de un pequeño hospital en el Caribe.*
Métodos: *Se examinaron retrospectivamente ciento reconstrucciones arteriales infrainguinales en 90 pacientes**.** Los pacientes eran clasificados según las categorías sugeridas por el* Comité Ad Hoc *para el Reporte de Normas de los Consejos Unidos de la Sociedad de Cirugía Vascular. El seguimiento tuvo un rango de 0 a 103.1 meses. Se usó el método Kaplan-Meier con el objeto de ver las tasas de supervivencia, salvamento de la extremidad, y tasas primarias y secundarias de permeabilidad. Se usaron regresiones de Cox para identificar los factores de riesgo potencial.*
Resultados: *Las tasas de salvamento de miembro fueron 74.5% después de un año y 71.4% después de cinco años. Las tasas generales de permeabilidad primaria fueron 67.0% después de un año, 63.4% después de tres años y 50.8% después de cinco años. Las tasas generales de permeabilidad secundaria fueron 86.4% después de un año y 75.1% después de cinco años. La tasa de permeabilidad primaria para la vena safena autóloga fue 82.4% (SE 7.5%) después de cinco años. Las tasas de permeabilidad primaria para los injertos prostéticos fueron 62.1% (SE 8.5%) después de un año, 56.9% (SE 9.2%) a los tres años y 37.9% (SE 16.7%) después de cinco años.*

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Conclusión: *La cirugía de bypass arterial infrainguinal es factible en hospitales caribeños pequeños que muestran resultados comparables a los de estudios importantes.*

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INTRODUCTION

In modern western society, infra-inguinal arterial reconstruction for symptomatic and limb threatening ischaemia has become the preferred treatment by many surgeons. Alternatives like sympathectomy and conservative measures for critical limb ischaemia have shown poor long-term results (1–4). Patients presenting with symptoms of occlusive arterial disease like ischaemic rest pain, ischaemic ulcer or gangrene often have multiple risk factors including advanced age, diabetes, history of smoking, hypertension, hyperlidaemia, renal and cardiac disease. Patient's delay in seeking treatment is in several cases an important factor leading to major amputations. A study to determine the results of infra-inguinal bypass surgery on the island of Curaçao was conducted at the department of general surgery of the St Elisabeth hospital.

The department of general surgery of the St Elisabeth hospital is comprised of five general surgeons who together perform 2500 surgical procedures minor and major (the whole range except fractures, neurosurgery and cardiac surgery) on a yearly basis. The department also serves as a rotation for medical interns from Groningen University of the Netherlands. Curaçao, (171 square miles) is the largest of the five islands of the Netherlands Antilles and has a total population of approximately 145 000. Over fifty nationalities comprise the cosmopolitan population. The capital city, Willemstad combines a modern business infrastructure with the charm of historic Dutch colonial architecture.

We retrospectively reviewed the eight-year experience with infra-inguinal arterial reconstruction for peripheral arterial disease (PAD) to obtain data on risk stratification and outcome of these patients.

SUBJECTS AND METHODS

One hundred and eight infra-inguinal arterial reconstructions were performed upon 90 patients at the St Elisabeth Hospital, Curaçao, Netherlands Antilles, between June 1989 and December 1997.

Patients were classified according to clinical categories suggested by the *Ad Hoc* Committee on Reporting Standards of the Joint Councils of the Society for Vascular Surgery (5). A risk factor review was performed on each patient and included diabetes, smoking, hypertension, hyperlipidaemia, renal function and cardiac disease (5). All patients were assessed pre-operatively by a combination of noninvasive studies and angiography. Doppler ultrasonography with calculation of ankle/brachial index was performed whenever possible. All patients underwent angiography. All extremities had arteriosclerotic vascular disease as noted on angiography. These included segmental occlusions involving the superficial femoral artery, the popliteal artery and the tibial arteries.

Graft patency was determined by physical examination with assessment of palpable pulses in the graft and distally, supplemented by doppler ultrasonography. Continued or complete healing of the open lesions was further evidence of adequate perfusion in the presence of a patent graft. Graft occlusion was determined by clinical and non-invasive examination. Follow-up ended with occlusion of the graft, death of the patient, amputation of the extremity that had bypass surgery or patients who were lost to follow-up. Limb salvage was defined so that amputation to transmetatarsal level was considered as a salvaged limb. Infected tissue was often thoroughly débrided, requiring digit or metatarsal amputation. Any amputation above this level (*eg* Syme's, Chopard's) was considered to be limb loss.

Kaplan-Meier estimates were used to construct survival curves for first patency, second patency, limb salvage and survival. The standard error (SE) was calculated for each estimate of patency, survival and limb salvage, respectively. Extremities that required amputation, despite a patent graft, were considered as limb loss for the limb salvage calculation but patent for the graft patency analysis. In extremities in which graft thrombosis occurred but limb salvage was accomplished, the graft was considered thrombosed for the analysis of patency but the limb was considered as salvaged for the analysis of limb salvage. Any graft thrombosis or revision occurring at any time, including the first 48 hours after implantation, was considered graft failure for calculation of primary patency.

Cox regression has been used to compare the hazards for each of the considered events between the levels of the following factors: gender, hypertension, hyperlipidaemia, smoking behaviour, diabetes mellitus, type of material (prosthetic versus autologous), presence of cardiac disease and presence of renal disease. Due to the small number of patients contributing two observations in the analysis, it was not possible to take into account the clustering in the data statistically (108 procedures for 90 patients). Since multiple risk factors were identified for amputation, a multivariable Cox regression was performed to detect which of these risk factors remained significant (after correcting for the other risk factors). Due to the exploratory character of the study, no corrections have been made for multiple testing. P-values < 0.05 were considered statistically significant. All analyses have been performed using the statistical package SAS (version 9.1)

RESULTS

Patients ranged in age from 36 to 88 years with a mean age of 65.4 ± 10.1 years. There were 59 (65.6%) men and 31 (34.4%) women. Patients were followed from zero to 103.1 months with a mean follow-up of 10.1 months.

According to clinical categories suggested by the Ad Hoc Committee on Reporting Standards of the Joint Councils of the Society for Vascular Surgery (5), 35 (32.4%) extremities had gangrene (grade III, category 5), 10 (9.3%) extremities had non-healing ischaemic ulcers (grade III, category 5), 30 (27.8%) extremities had ischaemic rest pain (grade II, category 4), 25 (23.1%) extremities had severe claudication (grade I, category 3) and eight (7.4%) extremities had moderate claudication (grade I, category 2). Critical limb ischaemia (CLI) was defined as ischaemic rest pain and tissue loss associated with ischaemia (Grade II and III, categories 4, 5 and 6). Indications for operation for the different levels of distal anastomosis are listed in Table 4.

Of the patients studied, fifty-six had diabetes mellitus (62.2%), of which 28 patients had insulin dependent diabetes and 28 patients had non-insulin dependent diabetes. Thirty-eight had a history of smoking (42.2%), 30 had hypertension (33.3%) and 14 had hyperlipidaemia (15.6%). Nineteen patients (21.1%) had serum creatinine levels greater than 2.5 mg/dl of normal serum level of creatinine. Eight of the 19 patients had chronic renal failure with four of them being on chronic haemodialysis. Forty-two patients (46.6%) had cardiac disease. The risk assessment of patients undergoing infra-inguinal bypass surgery is outlined in Table 1.

Table 1: Risk assessment of patients undergoing infra-inguinal bypass surgery

Diabetes mellitus$^{\Omega}$	56 (62.2)
Tobacco use$^{\Xi}$	38 (42.2)
Hypertension$^{\Phi}$	30 (33.3)
Hyperlipaemia$^{\Psi}$	14 (15.6)
Renal insufficiency^{X}	19 (21.1)
Cardiac disease$^{\Lambda}$	42 (46.6)

Values in parenthesis are percentages.
$^{\Omega}$ Receiving oral agents or insulin.
$^{\Xi}$ History of tobacco use in the last 10 years or ongoing use.
$^{\Phi}$ Receiving treatment with drugs.
$^{\Psi}$ Serum cholesterol elevated.
^{X} Serum creatinine more than 2.5 mg/dl.
$^{\Lambda}$ Remote or recent myocardial infarction, controlled and uncontrolled arrhythmia, stable and unstable angina pectoris, compensated and uncompensated heart failure.

An autologous saphenous vein was used as the bypass conduit in 34 procedures (31.5%). The *in situ* technique was used in 21 constructions to the extremities (19.4%), nine were to the below-knee popliteal artery (42.9%), four were popliteotibial constructions (19.0%), five were femorotibial constructions (23.8%) and three were popliteopedal constructions (14.3%). Reversed autologous vein harvested from the ipsilateral or contralateral extremity was used as a bypass in 13 procedures (12.0%), four femoropopliteal bypasses to the below-knee popliteal artery (30.8%), two femoropopliteal bypasses to the above-knee popliteal artery (15.4%), two popliteotibial bypasses (15.4%), three femorotibial bypasses (23.1%) and 2 popliteopedal bypasses (15.4%), respectively. A polytetrafluoroethylene (PTFE) graft was used in 66 procedures (61.1%), in 60 operations (90.9%), a PTFE femoropopliteal bypass to the above-knee popliteal artery, in four operations (6.1%), a PTFE femoropopliteal bypass to the below-knee popliteal artery and in two operations (3.0%), a PTFE femorotibial bypass, respectively.

Dacron graft was used in four procedures (3.7%) to above-knee popliteal artery. A composite graft was used in four procedures (3.8%). One composite graft was a sequential graft consisting of a PTFE graft originating from the common femoral artery to the above-knee popliteal artery and an *in situ* vein originating distal to the PTFE graft to the posterior tibial artery. The remaining composite grafts consisted of PTFE and reversed saphenous vein.

The proximal anastomosis was on the common femoral artery in 93 cases (86.1%). The superficial femoral artery served as inflow artery in four cases (3.7%). The popliteal arteries above or below the knee served as inflow artery in 11 cases (10.2%). The distal anastomosis was on the above-knee popliteal artery in 66 cases (61.1%). The below-knee popliteal artery served as outflow artery in 17 cases (15.7%). The anterior tibial artery served as outflow artery in four cases (3.7%); the posterior tibial artery served as outflow artery in 15 cases (13.9%). The dorsalis pedis artery served as outflow artery in six cases (5.6%). The distributions of graft types for the levels of distal anastomosis are listed in Table 5**.**

There were no intra-operative deaths. Sixteen of the 90 patients had died during the follow-up period. The operative 30-day mortality was seven, with a further 10 late deaths for an overall mortality rate of 18.9% for all patients (Table 2).

Table 2: Mortality, early (30 days) and late

Early (< 30 days)	
Cardiac and respiratory	5
Unknown	2
Late	
CVA	1
Cardiac and respiratory	7
Unknown	1
Septic shock	1

CVA = cerebrovascular accident

Postoperative complications are listed in Table 3**.** The patient's survival rate (by Kaplan-Meier methods) was 87.7% at one year and 63.2% at five years, respectively (Fig. 1).

Twenty-six patients required limb amputation. Twenty-three of these patients had diabetes which is 41.1% of known patients with diabetes. Amputation was performed upon one patient who had initially been operated upon for claudication (3.8%). This patient had graft occlusion and subsequently satisfied criteria for critical limb ischaemia with rest pain and tissue loss. All other 25 amputations were performed on patients who presented with critical limb ischaemia. Eighteen

Table 3: Postoperative complications

Wound infection	3
Post-op bleeding	7
CVA	3
Congestive heart failure	2
Graft infection	1
Urinary tract infection	1
Compartment syndrome	1
Hypoglycaemia	1
Sepsis	1
Epileptic insult	1
Lung embolism	1

CVA = cerebrovascular accident

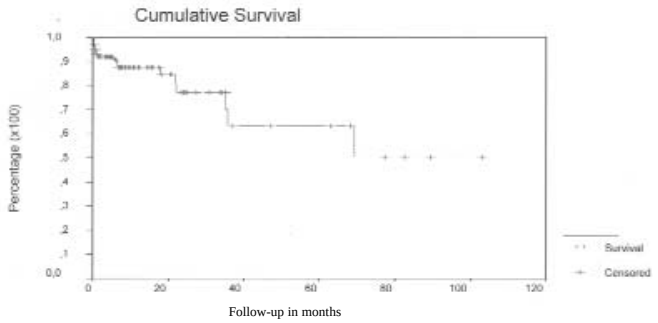

Fig. 1: Cumulative survival.

patients underwent major amputation either above the knee or below the knee despite having patent grafts because of progression of tissue loss (13 patients) or sepsis (five patients). Limb salvage rates for all patients were 74.5% at one year and 71.4% at five years, respectively (Fig. 2). Peri-

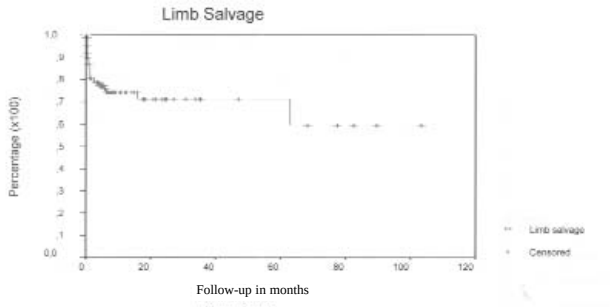

Fig. 2: Limb salvage.

operative early (< 48 hours) graft thrombosis occurred in four patients. These grafts were successfully revised and considered thrombosed in the primary patency analysis. The overall primary patency rates for all grafts to all levels were 67.0% (SE 6.4%) at one year, 63.4% (SE 6.9%) at three years and 50.8% (SE 12.6%) at five years, respectively. (Fig. 3) The overall secondary patency rates for all grafts to all levels were 86.4% (SE 4.6%) at one year and 75.1% (SE 8.9%) at five years, respectively (Fig. 4).

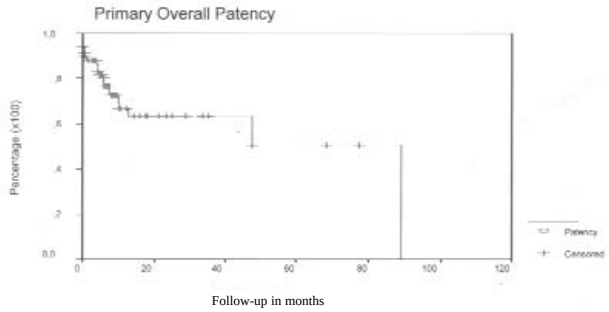

Fig. 3: Primary overall patency.

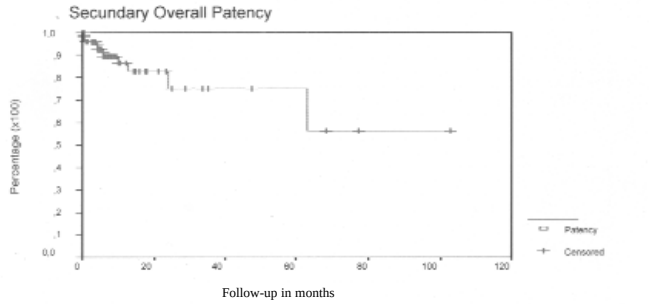

Fig. 4: Secondary overall patency.

There was no significant difference in patency rates between grafts performed for claudication and grafts performed for CLI. The cumulative patency rates of autologous saphenous vein and prosthetic grafts to all levels are illustrated in Figure 5. The primary patency rate for autologous

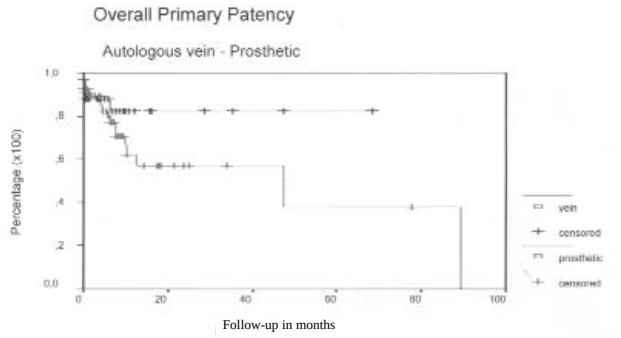

Fig. 5: Overall patency

saphenous vein was 87.9% (SE 5.7%) at five years. The primary patency rates for prosthetic grafts were 62.1% (SE 8.5%) at one year, 56.9% (SE 9.2%) at three years and 37.9%

Table 4: Number of grafts to above knee, below knee and distal positions according to operative indication

	Claudication	CLI
Above knee	24	42
Below knee	2	15
Distal	7	18

CLI = critical limb ischaemia

Table 5: Number of grafts performed to the above knee, below knee and distal positions according to graft type

	PTFE	RSV	SSV	Dacron	Composite
Above knee	60	2	0	4	0
Below knee	4	4	9	0	0
Distal	2	7	12	0	4

PTFE = polytetrafluoroethylene, RSV = reversed saphenous vein, ISSV = in situ saphenous vein

(SE 16.7%) at five years, respectively. There was no significant difference in patency rates between autologous saphenous vein and prosthetic graft types ($p = 0.21$). Most grafts to the above knee position were PTFE. The small numbers of other graft types to the above knee position prevented meaningful comparison of patency rates.

In univariable Cox regression analysis, tobacco use, hyperlipaemia, diabetes mellitus and female gender were all statistically associated with a poor outcome defined as graft failure, major amputation or death (Table 6). These variables were selected for multivariable Cox regression analysis on amputation. This resulted in a model where tobacco use ($p = 0.01$) and female gender ($p = 0.02$) were the best predictors for amputation (Table7).

Table 6: Results from univariable Cox regression.

		95% CI		
Variable	**Hazard Ratio**	**Lower**	**Upper**	**p-value**
Secundary Patency	**Graft failure**			
Tobacco use				0.034
Not smoking (reference category)	–	–	–	–
Not known	10.212	1.046	99.726	0.046
Ex-smoker	24.630	2.056	295.088	0.011
Smoker	4.710	0.539	41.137	0.16
Limb Salvage	Amputation			
Tobacco use				0.005
Not smoking (reference category)	–	–	–	–
Not known	3.231	1.321	7.907	0.010
Ex-smoker	0.725	0.092	5.719	0.76
Smoker	0.487	0.166	1.433	0.19
Hyperlipaemia				0.0064
No hyperlipaemia (reference category)	–	–	–	–
Hyperlipaemia	0.197	0.018	2.193	0.19
Not known	1.867	0.438	7.951	0.40
Diabetes Mellitus	6.127	1.837	20.436	0.0032
Female	3.926	1.795	8.586	0.0006
Death	Death			
Hyperlipaemia				0.0023
Not hyperlipaemia (reference category)	–	–	–	
Hyperlipaemia	–	–	–	0.001
Not known	0.513	0.165	1.594	0.25

Hazard Ratios, 95% confidence intervals and p-values are shown for significant factors. Note that no significant ($p < 0.05$) predictors were identified for primary patency. Due to sampling zeros (none of the patients with hyperlipaemia died), the estimate for the Hazard Ratio equals $-\infty$ or $+\infty$. Calculation of confidence intervals is not feasible and the p-values are derived from a likelihood-ratio test.

Table 7: Results from the multivariable Cox regression on amputation.

		95% CI		
Variable	**Hazard Ratio**	**Lower**	**Upper**	**p-value**
Limb Salvage	Amputation			
Tobacco use				0.01
Not smoking (reference category)	–	–	–	–
Not known	5.032	1.911	13.251	0.0011
Ex-smoker	1.265	0.145	11.053	0.83
Smoker	2.087	0.481	9.049	0.33
Hyperlipaemia				0.064
No hyperlipaemia (reference category)	–	–	–	–
Hyperlipaemia	0.109	0.009	1.272	0.07
Not known	1.272	0.287	5.642	0.75
Diabetes Mellitus	3.350	0.819	13.696	0.09
Female	3.249	1.167	9.043	0.02

Hazard ratios and 95% confidence interval (CI) are presented for all predictors in the model.

DISCUSSION

We have reviewed the results for infra-inguinal bypass surgery during an eight-year period on the island of Curaçao, showing results that compare with other published series, with a five-year primary and secondary patency rate of 50.8 and 75.1 per cent respectively, operative mortality rate of 17.7 per cent and a limb salvage rate at five years of 71.2 per cent.

The use of prosthetic graft for the above knee arterial reconstruction remains a controversial issue after many decades of consideration. Although better patency rates are achieved using autogenous saphenous vein, there is still a preferential use of PTFE graft for above the knee arterial reconstruction among many surgeons. These preferences are based on the following arguments: a) there is substantial evidence that good short-term results can de achieved using prosthetic grafts for above the knee bypass surgery (6); c) saving the vein for later use, especially for coronary artery bypass grafting or for revisional bypass surgery and d) the most important reason for using prosthetic graft in the above knee bypass has to do with morbidity and costs. Reconstructive surgery with prosthetic graft is done fast. The graft is tunnelled deep or subcutaneously and the whole procedure can be completed in one to two hours by most experienced surgeons. Morbidity is low, resulting in a shorter length of stay and less costs.

Many debates during the last decade has centred on the use of reversed and *in situ* saphenous vein as the conduit of choice for infragenicular procedures with neither clearly proving to be the better graft (7–10). This unit adopted the

policy to use RSV or ISSV as the conduit of choice for all infragenicular reconstructions, with the choice of PTFE when no vein is available. Composite grafting using PTFE and a distal vein segment were the next options. This policy has meant that vein use for infragenicular grafts was 90.5 per cent in this department.

In previous studies, it has been shown that people of African origin have a higher prevalence of PAD and were more likely to undergo infra-inguinal bypass surgery. They are at a greater risk of having an amputation (up to two times) compared to patients of Caucasian origin; this is especially evident among women of African origin (11). Diabetes and a different pattern of PAD development have been identified as important factors contributing to the disparity between Caucasians and Africans (12–14). A racial breakdown of the population of Curaçao reveals that the majority (80%) of the population is of West African origin, 10% of West European origin and the rest of Asian or Latin American origin. The Afro-Caribbean majority on Curaçao however is not a homogeneous group (15–19). This must be taken into account when comparing the results of this study with the results in the literature for African Americans. Diabetes is the second most common disease, after high blood pressure, on the island of Curaçao (20). The prevalence of diabetes in this study group was 62.2%. Twenty-three of the twenty-six patients who had an amputation were known to have diabetes. A further breakdown of the amputees reveals a higher number of female patients, fifteen compared to eleven male patients. An observation that is consistent with previous reports showing higher rates of amputation in female diabetic patients with PAD (12). The latter observation is formally confirmed by detection of gender as a significant risk factor, in the univariable setting, as well as in the multivariable model. Also for diabetes mellitus, the obtained hazard ratios revealed an increase risk for amputation. Although large in actual value (HR = 3.35), this effect was only suggestive in the multivariable model.

At the time of initial presentation, 47% of patients had CLI defined as ischaemic rest pain and tissue loss associated with ischaemia (Grade II and III, categories 4, 5 and 6). This advanced stage of PAD, at the time of initial patient encounter, has been clearly identified as an important risk factor for graft related events and subsequent amputations (21). Possible explanations for late patient encounter in the study group when an advanced stage of PAD was present are asymptomatic presentation of PAD, a delay in the diagnosis of PAD due to atypical presentation especially in the diabetic, lower physical activity levels resulting in less complains of intermittent claudication and patients delay in the seeking of medical treatment (22)**.**

We also observed that the majority of graft failures were associated with CLI (Grades II and III, categories 4, 5 and 6) at initial presentation. Graft failure usually leads to subsequent limb loss and higher mortality rates as reported by others (23–27). The overall graft failure in the present study resulted in limb loss in seven cases (26.9%) of which four were due to early graft failure. In the study group, however, we could not prove the above-mentioned relationship between CLI, time of initial patient encounter, graft failures and amputation due to the small numbers.

Tobacco use has clearly been identified as a risk factor contributing to development and progression of PAD. There is extensive evidence that cessation of smoking even after bypass surgery improves the outcome in patients undergoing surgery. Ongoing tobacco use after surgery increases the risk for graft failure and amputation to threefold of the normal risk (28). In our group, tobacco use was identified as a significant risk factor, in the univariable setting, as well as in the multivariable model.

After bypass surgery, a long-term commitment to careful postoperative surveillance is mandatory, as re-interventions (15.7% in this study) are frequently required. Higher primary patency rates associated with duplex surveillance and elective revisions of failing/failed grafts will then be achievable. Postoperative duplex surveillance is still recommended after bypass surgery to asses patency, as re-interventions (15.7% in this study) are frequently required. However, a recent prospective randomized controlled study by Davies *et al* concluded that intensive surveillance of vein grafts with duplex ultrasonography compared to close clinical surveillance did not show any benefits in terms of limb salvage or improvement of quality of life (29). Duplex surveillance only added to the financial costs. We believe that for vein and prosthetic bypasses duplex ultrasonography is still a useful surveillance technique to detect failing infra-inguinal grafts (30–32).

In conclusion, the home physician has an important role in recognizing patients with PAD as early referral to the vascular surgeon can make the difference in limb salvage procedures. There must be an understanding of the natural history of chronic lower extremity ischaemia especially in Afro-Caribbean patients before making decisions regarding therapeutic options. Clearly, mild ischaemia as evidenced by claudication does not place the patient at significant risk for limb loss. Initial conservative treatment emphasizing abstinence from tobacco products, control of underlying medical maladies, antiplatelet therapy, statin therapy and an exercise programme along with patient reassurance, will adequately treat the majority of claudicates (33–35). When ischaemia or tissue loss is present, patient education regarding foot care and avoidance of trauma are beneficial. Such a policy of risk modification may than improve the quality of life with a further decrease of resource utilization in the care of PAD patients (36, 37). A vascular laboratory with all the facilities for patients' assessment and post-operative surveillance will be a major asset in small Caribbean hospitals in order to achieve better results.

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