VASCULAR DISEASE IN HIV/AIDS PATIENTS

J van Marle, L Tudhope, G Weir, K Botes

Objectives. An ongoing prospective clinical survey to determine the spectrum of vascular disease in HIV/AIDS patients and the risk factors affecting clinical outcome in order to formulate a management protocol for future use.

Methods. Comprehensive screening for risk factors for vascular disease as well as HIV/AIDS-related conditions. Disease pattern and presentation are noted and patients treated accordingly. Vascular emergencies are managed regardless of HIV status because this information is usually not available at the time of presentation. Elective management is based on immune status and risk stratification.

Results. 42 patients tested positive for HIV. The majority of patients presented with occlusive disease (57%), followed by anearysms (21%) and vascular trauma (19%). A variety of vascular surgical procedures were performed on 36 patients. There was no surgical mortality and 10 patients developed complications, including 2 amputations and 7 cases of minor wound sepsis. The 3 patients who received preoperative antiretroviral therapy showed a marked reduction in viral count and a significant improvement in CD4 T-cell count.

Conclusion. Surgery can be safe and effective in HIV-positive patients provided the necessary precautions are taken to reduce surgical morbidity.

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South Africa has one of the most rapidly expanding HIV epidemics in the world.[1] It is estimated that there were between 5 and 5.3 million HIV-positive people in the country by the middle of 2000. This represents approximately 11 - 12% of the population.[2]

The relationship between vascular disease and HIV infection is well documented. Patients may present with occlusive disease, aneurysms or the complications of hypercoagulability. They may also, however, present with the normal spectrum of vascular disease such as atherosclerosis or trauma where HIV positivity is an incidental finding.

Although the precise pathogenesis is still unclear, there are several clinical features suggestive of HIV-related vascular disease (Table I). We have noted a dramatic increase in the number of patients who are HIV-positive in our Vascular Unit over the past 2 years.

Unit for Peripheral Vascular Surgery, Pretoria Academic Hospital, University of Pretoria

J van Marle, MB ChB, MMed (Chir), FCS (SA)
L Tudhope, MB ChB, MMed (Chir)
G Weir, MB ChB, MMed (Chir)
K Botes, MB ChB

Table I. Clinical features suggestive of HIV-related vascular disease

Younger patient
Absence of typical risk factors for atherosclerosis
Multiple aneurysms
Atypical location of aneurysms
Features of immunodeficiency

OBJECTIVES

The present study forms part of an ongoing prospective clinical survey to determine: (*i*) the spectrum of vascular disease in HIV/AIDS patients; (*ii*) the risk factors affecting clinical outcome; (*iii*) the difference between HIV vasculopathy and atherosclerotic vascular disease; (*iv*) the effect of antiretroviral therapy on outcome; and (*v*) a management protocol for future use.

MATERIALS AND METHODS

In January 2002 we started with a programme of routine voluntary testing for HIV/AIDS. Patients were advised about the importance of knowing their HIV status in planning proper treatment. Informed consent was obtained in 82.1% of all admissions. Fourteen per cent of these patients tested HIV-positive. During the period January - October 2002, 42 HIV-positive patients were admitted to our unit. There were 38 males and 4 females, and the mean age was 37 years (range 21 - 60 years).

The most common presenting condition was occlusive disease (57%) followed by aneurysms (21%) and vascular trauma (19%). Two patients presented with widespread arterial and venous thrombosis due to hypercoagulability and 1 patient presented with a carotid body tumour. Table II depicts the

Table II. Spectrum of vascular pathology

		N
Occlusive disease		24
Aorto-iliac	5	
Femoro-popliteal	13	
Infra-popliteal	5	
Carotid	1	
Aneurysms*		9
Thoraco-abdominal	2	
Carotid	3	
Femoral	2	
Popliteal	1	
Multiple aneurysms	1	
Vascular trauma		8
Other		
Carotid body tumour		1

*Two patients had multiple aneurysms.

spectrum of vascular pathology and Figs 1 - 5 illustrate examples of the pathology encountered. Comprehensive screening for risk factors for atherosclerosis was carried out. The most common risk factor was a moderate smoking history of less than 10 pack-years in 50% of the patients. Four patients (9%) had moderately elevated triglycerides and 5 patients (11%) had hyperhomocysteinaemia. None of the patients had hypercholesterolaemia or diabetes mellitus. The 2 patients who presented with hypercoagulability complications had increased anticardiolipin antibodies.

Apart from the normal routine preoperative work-up for vascular patients, several additional tests were performed, viz. screening for sexually transmitted diseases, tuberculosis, viral hepatitis, CD4 T-cell count and HIV-1 RNA count. Eleven patients (26.2%) had a CD4 T-cell count of < 200 cells/μl, while 24 (57.1%) and 7 (16.7%) had counts of 200 - 500 and > 500 cells/μl, respectively.

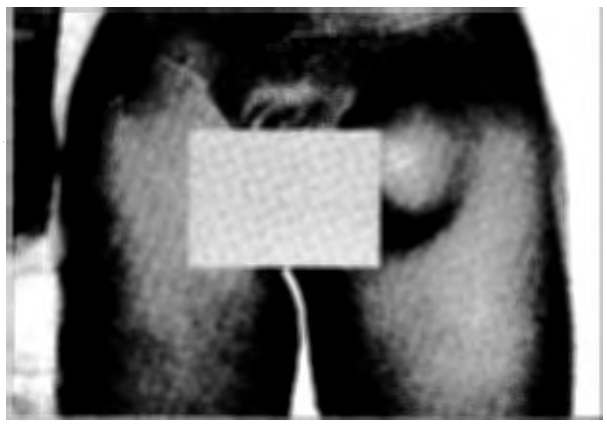

Fig. 1. Aneurysm of the common femoral artery.

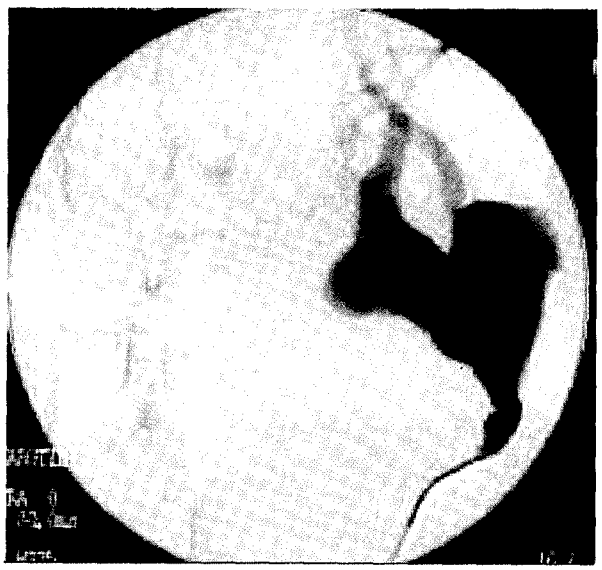

Fig. 2. Aneurysm of the carotid bifircation.

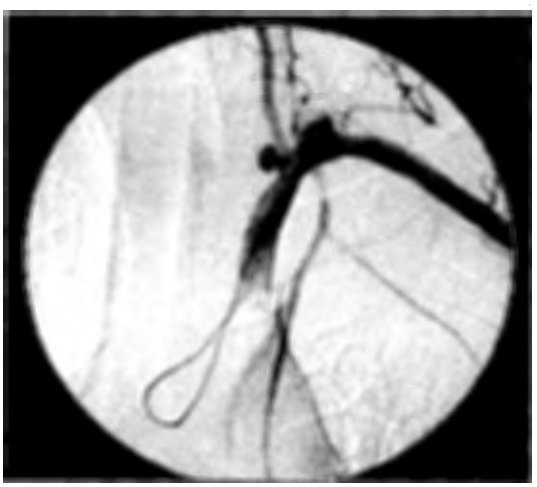

Fig. 3. Multiple aneurysms in a subclavian artery.

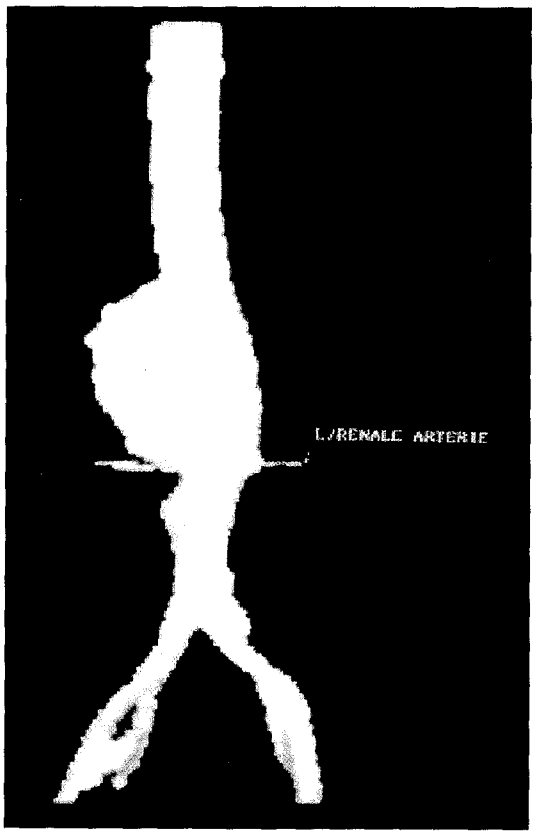

Fig. 4. Supra-renal aortic aneurysm.

MANAGEMENT

Patients who presented with vascular emergencies were managed regardless of HIV status because this information was not available at the time of presentation. Elective management was based on immune status, taking the CD4 T-lymphocyte count into consideration. When the CD4 T-cell count exceeded 500/μl, patients were managed according to standard vascular protocols appropriate for seronegative

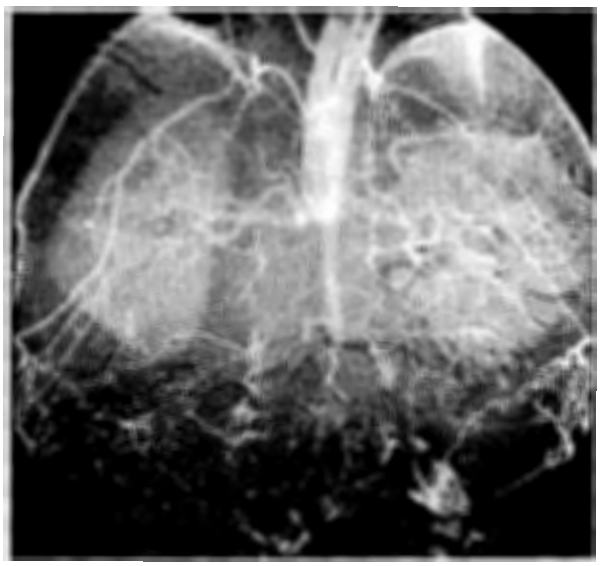

Fig. 5. Occlusion of the infra-renal abdominal aorta.

patients. If the CD4 T-cell count was between 200 and 500/μl a conservative alternative to surgery was used where possible. If surgery was unavoidable, however, we opted for a less invasive procedure, e.g. extra-anatomic bypass — procedures such as axillo-femoral or femoro-femoral bypasses were used rather than the more invasive aorto-bifemoral bypass. In patients with established AIDS (CD4 T-cell count < 200 μl) palliative treatment was given and surgery was only considered if it meant saving a life. Antiretroviral therapy was only available to 3 patients who had access to medical aid.

Five patients were treated conservatively and 1 patient is still awaiting surgery. A list of the elective surgical procedures is given in Table III. The vascular trauma involved repair of a stab wound to the right common carotid artery ($N = 1$), a gunshot wound to the right common iliac artery ($N = 1$), gunshot wounds to the common femoral arteries ($N = 2$) and gunshot wounds to the superficial femoral arteries ($N = 4$).

Table III. Elective surgical procedures

	N
Primary amputation	6
Femoro-popliteal bypass	6
Thrombo-endarterectomy	2
Axillo-bifemoral bypass	2
Ileo-femoral bypass	2
Femoral artery aneurysm repair	2
Femoro-femoral bypass	1
Femoro-distal bypass	1
Carotid aneurysm resection and bypass	1
Carotid endarterectomy	1
Carotid ligation	1
Lumbar sympathectomy	1
Thoracoabdominal aneurysm repair	1
Dissection carotid body tumor	1

Results

Two patients presenting with full-blown AIDS who received conservative palliative treatment were the only patients who died. There was no surgical mortality. Two patients required amputations (1 above the knee and 1 below the knee) after failed attempted revascularisation for critical limb ischaemia. There were 7 minor wound complications, viz. lymphocele and delayed wound healing and sepsis. A patient on whom a sternotomy was performed after penetrating chest trauma had postoperative respiratory problems for which he required prolonged intensive care unit (ICU) care. The 3 patients who received preoperative antiretroviral therapy showed a marked reduction in viral count and a significant improvement in CD4 T-cell count (Table IV).

Table IV. Response of CD4 T-cell count and viral load to antiretroviral therapy

	CD4 T-cell count (cells/μl)		HIV-RNA count (copies/ml)	
Patient	Pre Rx	Post Rx	Pre Rx	Post Rx
1	416	470	126 000	< 500
2	234	339	73 900	36 800
3	245	426	415 000	6 400

Rx = treatment.

Discussion

Joshi *et al.*[3] reported fibro-proliferative occlusive disease in the coronary arteries and Calabrese *et al.*[4] described systemic necrotising vasculitis involving the small vessels in patients with HIV infection. Du Pont's first report[5] on aneurysms associated with HIV was followed by many publications dealing with this issue.[6-8] HIV-associated aneurysms are typically multiple and often occur in atypical locations with a predilection for the carotid arteries.[9,10] Spontaneous arteriovenous fistula arising from HIV arteritis has recently been described.[11]

Typical histological features of HIV-associated vasculopathy have been described. Fibro-obliterative occlusive disease consisting of an inflammatory infiltrate of the endothelium by lymphocytes and mononuclear giant cells, with fragmentation of elastin fibres and intimal fibrosis resulting in luminal narrowing, is one feature.[3] HIV-related aneurysms have several histological features distinguishing them from degenerative and infective aneurysms. The principal feature is occlusion of the vasa vasorum by an inflammatory cell infiltrate.[12]

Although viral protein has been demonstrated in lymphocytes in arterial and aneurysmal tissue using immunohistochemical staining and polymerase chain reaction (PCR), the precise pathogenesis of vascular disease in HIV

infection remains unclear. Various hypotheses exist, including bacteraemia as a result of immunosuppression with secondary mycotic aneurysms, weakening of the arterial wall caused by a direct action of the virus itself, immune-complex mechanisms or by ischaemia of the wall resulting from occlusion of the vasa vasorum.

There is growing evidence that HIV influences the physiology of the vascular endothelium with the release of endothelial cell products, which may cause hypercoagulability.[13] The presence of anticardiolipin antibodies, protein S-deficiency and antithrombin deficiency contribute to the hypercoagulable state associated with HIV/AIDS.[14-16] Deep-vein thrombosis has been reported to occur 10 times more frequently in these patients than in the general population.[17] Protease inhibitor therapy also has certain class-specific metabolic side-effects, which may lead to accelerated atherosclerotic disease.[18]

There are various factors influencing the operative outcome of surgery in HIV-positive patients (Table V). HIV infection leads to a reduction in the CD4 T-lymphocyte count. Overall postoperative complications and delayed wound healing and infection are more common in patients with a CD4 count of < 200/μl.[19] There is, however, no significant difference in postoperative morbidity and mortality between HIV-positive patients with a CD4 T-cell count ≥ 500/μl and HIV sero-negative patients.[20]

Table V. HIV and surgery — factors influencing operative outcome

Immune status: CD4 T-cell count
Opportunistic infections
WBC count
Haematocrit
Nutritional state: decreased albumin
Type of operation
Emergency v. elective
Clean v. contaminated

WBC = white blood cell.

Plasma viral load is considered to be an excellent prognostic indicator of clinical outcome.[21] A significantly improved complication-free survival rate has been reported in patients with higher preoperative total white cell counts.[22] Low serum albumin and haematocrit levels have been associated with poor surgical outcome.[23] Savioz *et al.*[19] found a significant difference between clean and contaminated operations — with a CD4 count below 200/μl 'contaminated' surgery should only be performed when the procedure is unavoidable.[19] Opportunistic infections indicate immunodeficiency and result in poorer outcome of surgery.[24]

The surgeon must be aware of the many systemic effects of HIV/AIDS. This includes cardiac, pulmonary and central nervous system manifestations.[25,26]

As already mentioned, a CD4 count in excess of 500/μl is not associated with an increase in surgical morbidity or mortality.[20,27] Where the CD4 count is less than 500/μl, however, a conservative alternative to surgery or a less invasive surgical procedure should be considered. Patients with AIDS (CD4 count < 200/μl) have a median survival of a year, but palliative surgery should still be offered where it may alleviate symptoms and if it can be performed with minimum morbidity. For example, palliation may involve only an endarterectomy, profundoplasty or even lower limb amputation instead of an extensive bypass procedure for critical lower limb ischaemia. Ligation instead of repair of aneurysms may also be considered in this group.

Surgery for vascular emergencies is performed regardless of HIV status because HIV status and degree of immunodeficiency are often only available at a later stage. It has also been shown that the incidence of complications in trauma patients with HIV is directly associated with an increase in injury severity score, rather than the HIV status.[28] Where the HIV and immune status is known in patients who require emergency surgery, they are managed according to the principles described above.

The basic principles of vascular surgery also apply to HIV-positive patients — exclude or bypass diseased arterial segments and perform anastomoses to macroscopically normal tissue. Autogenous vein is the preferred conduit, and if vein is not available, PTFE or polyester grafts are used. The commercially available silver impregnated grafts are used if there is a high probability of sepsis. Standard antibiotic prophylaxis for vascular surgery using a first-generation cephalosporin is routinely used. However, Savioz *et al.*[19] have shown that 35% of infective complications in HIV/AIDS patients were caused by opportunistic infections outside the range of normal vascular prophylaxis. These complications require therapeutic antibiotic and antifungal treatment according to microscopy, culture and sensitivity. Patients with AIDS should receive prophylaxis against *Pneumocystis carinii* pneumonia as well as oral and oesophageal candidiasis.[19]

The necessary precautions against accidental exposure must be taken to protect health workers working with HIV/AIDS patients. Issues regarding exposure prophylaxis and therapy have been described in detail elsewhere.[29,30]

Highly active antiretroviral therapy (HAART) has been shown to be effective in patients with advanced immune suppression.[31] There is, however, concern about patient compliance and the long-term adverse effects of therapy. Peri-operative use of HAART at this stage, however, is limited to patients who require elective surgery that can be postponed for at least 3 months.

CONCLUSION

There is no documented evidence that surgery or any intervention hastens the disease process in HIV/AIDS. These interventions should therefore not be withheld because of HIV status and a concern for subsequent complications. Provided the necessary precautions are taken to reduce surgical

morbidity, surgery can be safe and effective in HIV-positive patients, without an increase in patient mortality.

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SCREENING FOR CHILDHOOD ANAEMIA USING COPPER SULPHATE DENSITOMETRY

M Funk, T Hambrock, G C van Niekerk, D F Wittenberg

Objective. To evaluate copper sulphate densitometry to screen for childhood anaemia in a primary care setting, with a view to identifying children requiring definitive diagnostic testing and treatment.

Design. A cross-sectional screening study. Results of densitometry with a copper sulphate solution of specific gravity (SG) 1.048, corresponding to a haemoglobin (Hb) concentration of 10 g/dl, were compared with laboratory Hb determination.

Setting. Outpatient department of Pretoria Academic Hospital (73 children) and a local crèche (27 children).

Subjects. One hundred consecutive children, aged between 6 months and 6 years, with informed written consent by parents.

Outcome measure(s). Accuracy of copper sulphate densitometry in screening for Hb concentration below 10 g/dl in terms of sensitivity, specificity, positive and negative predictive values, as well as likelihood ratio.

Results. The prevalence of anaemia (Hb < 10 g/dl) was 17% (95% confidence interval (CI) 10.2; 25.8). Copper sulphate densitometry had a sensitivity of 88.2% (95% CI 62.3; 97.9), a specificity of 89.2% (95% CI 79.9; 94.6), a positive predictive value of 62.5% (95% CI 40.8; 80.5) and a negative predictive value of 97.4% (95%CI 90.0; 99.5) in screening for anaemia. The likelihood ratio of a positive screening test was 8.17.

Conclusions. Copper sulphate densitometry was accurate in screening for childhood anaemia.

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Anaemia is the most common haematological disease of infancy and childhood. Iron deficiency anaemia due to inadequate intake of iron is common, especially between 9 and 24 months of age.[1] It may lead to tiredness, irritability and anorexia, as well as to dramatic manifestations such as cardiac

Department of Paediatrics and Child Health, Pretoria Academic Hospital and University of Pretoria

M Funk, MMed (Paed), FCPaed (SA)

T Hambrock, Medical student

G C van Niekerk, Medical student

D F Wittenberg, MD, FCPaed (SA)