FRACTURE FIXATION IN HIV-POSITIVE PATIENTS: A LITERATURE REVIEW

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INSTRUCTIONAL ARTICLE

Introduction

There is a paucity of literature involving the management of fractures in HIV-infected individuals. In sub-Saharan Africa there is a 'double epidemic' of musculoskeletal trauma and human immunodeficiency virus (HIV) infection, both of which affect young economically active people. This review aims to clarify whether fractures should be managed any differently in HIV-positive compared to HIV-negative patients. The orthopaedic surgeon should consider the following aspects: (1) the risk of post-operative wound infection, (2) delayed fracture union, (3) risk of late implant sepsis, (4) co-existing osteoporosis, and (5) HIV transmission to the healthcare worker.

The extent of the problem

An estimated 68 per cent of the world’s HIV-positive population resides in sub-Saharan Africa. In Southern Africa HIV and road traffic injury are the two leading causes of death affecting young economically active adults in the 15 to 44 year age group. In HIV endemic areas, between 16 and 30 per cent of trauma patients requiring surgery are HIV-positive. At Johannesburg Hospital trauma unit the prevalence of HIV in patients being attended for major trauma was found to be 30 per cent. Despite the scale of the problem, there is a paucity of literature on this subject and what there is mostly predates the widespread availability of antiretroviral therapy.

The human immunodeficiency virus

The human immunodeficiency virus is a retrovirus which encodes its genome in RNA and transcribes genome copies to DNA using the enzyme reverse transcriptase. This occurs within host cells containing the CD4+ receptor, typically the T-helper lymphocyte. There is a progressive depletion of the CD4+ cells, reversal of CD4/CD8 ratio and dysregulation of B-cell antibody production. Antiretroviral medication restores the CD4 cells and reduces the viral load, sometimes to undetectable levels, and when used appropriately, can convert HIV into a chronic manageable disease.

Post-operative wound infection

The early literature suggested that HIV-positive individuals had an increased risk of wound infection following fracture fixation. The risk appeared to be greater in those with symptomatic HIV disease and in open fractures. Hoekman compared rates of wound infection in seronegative patients (5%), asymptomatic seropositive patients (0%), and symptomatic seropositive patients (24%). There was a significant increased risk of postoperative wound infection in symptomatic seropositive patients (p= 0.01). A shortcoming of this study was the failure to use prophylactic antibiotics in all patient groups. Jellis found an infection rate of 40 per cent in symptomatic HIV disease.
The HIV-negative group also had a relatively high rate of infection (12%). These earlier studies were retrospective, not blinded, and ‘infection’ was not defined objectively. More recently a prospective single blind controlled study involved 41 HIV-positive and 141 HIV-negative patients.6,7 The patients were staged clinically and CD4 cell counts determined, wound infection was assessed objectively using a wound score, antibiotic prophylaxis was used in all patients, and both study and control groups were matched in terms of type of implants and type of procedures. The major finding in closed fractures was that HIV-positive patients had a low rate of wound infection (3.5%), comparable to the HIV-negative control group (5%).

However in open fractures, the risk of wound infection increased dramatically (42%).6 It would seem that the risk of infection relates to the presence of bacteria at the site of surgery, rather than the stage of disease. There was no relationship demonstrated between CD4 cell count and infection risk. A further study analysed internal fixation of open fractures of the tibia in 27 patients, seven of whom were HIV-positive. There was a significant increased risk of infection in HIV-positive patients (p<0.02), while differences in union rates were not significant. In HIV-negative patients internal fixation of Gustilo-Anderson grade 1 and 2 compound fractures have acceptably low rates of infection.7 However this practice may be dangerous in HIV-positive patients. External fixation is the safer option in immunocompromised individuals, especially in compound fractures involving the tibia. Although there is a slightly greater risk of pin track sepsis with external fixation, in most cases it is manageable with antibiotics and pin site care.4

All patients should be clinically evaluated for signs of HIV disease and staged using one of the staging systems available. The Centre for Disease Control (CDC) (Table I) has devised a more comprehensive staging system than the World Health Organisation (WHO) (Table II), involving the use of both clinical and laboratory markers.

### Table I: Centre for Disease Control (CDC) staging system of HIV

<table>
<thead>
<tr>
<th>CD4+ cell category</th>
<th>Clinical category</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥500</td>
<td>A1</td>
</tr>
<tr>
<td>200-499</td>
<td>A2</td>
</tr>
<tr>
<td>&lt;200</td>
<td>A3</td>
</tr>
<tr>
<td></td>
<td>B1</td>
</tr>
<tr>
<td></td>
<td>B2</td>
</tr>
<tr>
<td></td>
<td>B3</td>
</tr>
<tr>
<td></td>
<td>C1</td>
</tr>
<tr>
<td></td>
<td>C2</td>
</tr>
<tr>
<td></td>
<td>C3</td>
</tr>
</tbody>
</table>

A: Asymptomatic, B: Symptomatic, C: Aids-defining illness

Offering voluntary counselling and testing (VCT) to all patients with compound fractures with a view to avoiding internal fixation where possible may not be a viable option and may delay initial surgical debridement. In areas with high prevalence of HIV, it is probably safer to treat compound fractures with external fixation initially, unless facilities for rapid counselling and testing are available. The rate of post-operative wound infection can be decreased in all patients, both HIV-positive and -negative, in a stable theatre environment, by meticulous surgical technique and the use of prophylactic antibiotics. The use of prophylactic co-trimoxazole in HIV-positive patients with low CD4 cell counts may play a role in preventing *Pneumocystis carinii* pneumonia and toxoplasmosis.10 The most common organism causing wound infection in both seropositive and seronegative individuals is *Staphylococcus aureus*.11 Unusual organisms occur rarely.4

External fixation is the safer option in immunocompromised individuals, especially in compound fractures involving the tibia.

### Table II: World Health Organisation staging of HIV

<table>
<thead>
<tr>
<th>WHO Stage</th>
<th>Characterised by</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Acute (primary) HIV infection or latent, asymptomatic infection or persistent generalised lymphadenopathy</td>
<td>Acute seroconversion illness in some patients</td>
</tr>
<tr>
<td>II</td>
<td>Cutaneous manifestations</td>
<td>Herpes zoster, seborrhoeic dermatitis, recurrent upper respiratory infections, less than 10 per cent weight loss</td>
</tr>
<tr>
<td>III</td>
<td>More severe infections</td>
<td>Pulmonary tuberculosis less than one year ago, severe bacterial infections, weight loss greater than ten per cent, chronic diarrhoea greater than one month duration</td>
</tr>
<tr>
<td>IV</td>
<td>Aids-defining illness</td>
<td><em>Pneumocystis carinii</em> pneumonia, toxoplasmosis, cryptosporidiosis, cytomegalovirus disease/retinitis, extra-pulmonary tuberculosis</td>
</tr>
</tbody>
</table>
Fracture union and HIV

There is no proven association between HIV and impaired union in closed fractures. Fracture union may be impaired in HIV-positive individuals for several reasons, as follows: There is a strong association with reduced bone mineral density (BMD). In HIV-negative patients low BMD is associated with reduced fracture healing. HIV is associated with increased levels of pro-inflammatory cytokines including interleukin one, six and tumour necrosis factor. These cytokines may lead to desensitisation of bone repair processes. A similar mechanism involved in the aetiology of osteonecrosis may also impair fracture healing. Arteriolar blood supply may be impaired due to a microthrombotic/microvascular effects. Osteonecrosis commonly involves the femoral head. It is related to protease inhibitors, hyperlipidaemia, corticosteroid, alcohol and drug abuse. Corticosteroid use is greater among HIV-positive patients, and is known to impair bone healing. There is a higher non-union rate in open fractures.

Risk of late implant sepsis

The waning immunity associated with progression of HIV is likely to lead to activation of latent bacteria already present on implants, or late haematogenous seeding of bacteria onto implants. In the short term there are no increased sepsis rates up to about one year. This implies that fractures can safely be taken to union in most cases. It is not so clear what the risk of late infection is likely to be.

A retrospective assessment of 40 HIV-positive individuals who presented with late sepsis following fracture fixation and union suggests an increased rate of infection in the HIV population. Patients presented at an average of 36 months following the initial operation. Erythrocyte sedimentation rate (ESR) was elevated and albumin levels were low in all patients. Approximately 50% of patients had a low haemoglobin. The risk of refracture after early implant removal must also be kept in mind, especially since HIV may be associated with delayed fracture union.

Fixation in osteoporotic bone

The causes of osteoporosis in HIV disease include low body weight, drugs such as steroids, protease inhibitors, biochemical factors involving tumour necrosis factor, osteoprotegerin and abnormal vitamin D metabolism, and patient inactivity especially in the later stages.

The osteoporosis associated with protease inhibitor use improves spontaneously with time. A large population-based study in the USA found that fracture prevalence was significantly higher in HIV-infected versus HIV-non-infected patients (p < 0.0001). Despite this there is currently no evidence to suggest that HIV-positive patients should be screened or treated for osteoporosis any differently from the general population. In younger active patients pathological fracture risk is still low. The patient with advanced stage disease who is bedridden is at risk for fragility fractures. General measures to improve BMD may be used in conjunction with fracture fixation including encouraging regular weight-bearing exercises, maintenance of adequate body weight, calcium and vitamin D supplementation, and avoiding steroid use, smoking and alcohol. In HIV-positive patients who are found to be osteoporotic, consider the use of locking plates, cement augmentation of screws, hydroxyapatite-coated pins in external fixators, longer plates to distribute load over larger area, and good bone contact to augment healing. Intramedullary nails are biomechanically superior to plates and are preferred in osteoporotic bone. Pathological fractures in HIV-positive patients may be related to malignancies such as lymphoma, leukaemia, multiple myeloma, secondary deposits, and in bone weakened by infection.

HIV and hepatitis B transmission to the healthcare worker

The high prevalence of HIV among trauma patients in our setting makes HIV transmission to the surgeon during operative procedures a major concern. Orthopaedic surgery may pose an even greater risk due to the presence of sharp bone fragments, sharp instruments and power tools which may aerosolise viruses. True aerosols which remain suspended for long periods of time are probably an extremely low risk mode of transmission. The risk of transmission is increased when the operation lasts more than 3 hours or when blood loss exceeds 300 ml. A prospective study conducted in Zambia revealed that the risk of patient-to-surgeon transmission was 1.5% over five years, 15 times higher than that for a surgeon working in Europe. Strict adherence to universal precautions including protective eyewear, masks, gowns impermeable to body fluids, and boots as standard equipment are widely recommended. Newer glove designs such as cotton inner gloves or stainless steel mesh gloves may improve protection but are costly and decrease the sensitivity of the surgeon’s hands. Two pairs of latex gloves reduce the risk of exposure from glove defects from 17 per cent to 5 per cent. The surgeon involved in the case should ideally be a more experienced surgeon wherever possible. The seroconversion rate from a single exposure of hepatitis B is about 30% (compared to about 0.3% for HIV), making it obligatory for hepatitis B vaccination to be universal among healthcare workers.
Conclusion
We remain at the epicentre of this dual epidemic of trauma and HIV infection. While post-operative wound infection in compound fractures is significantly increased, the infection rate in closed fractures is comparable to that in HIV-negative patients provided optimum surgical conditions exist. Ultimately fracture treatment must be individualised depending on the bone involved, clinical presentation and host factors, antiretroviral medication, nutritional state, and surgical facilities available. The need for implant removal after union, delay in fracture union and the influence of antiretroviral medications still need to be answered by further research.

No benefits of any form have been received from a commercial party related directly or indirectly to the subject of this article.

References
6. Harrison WJ, Lewis CP, Lavy CB. Wound healing after implant removal after union, delay in fracture union and the influence of antiretroviral medications still need to be answered by further research.

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