Infected joint replacements in HIV-positive patients with haemophilia

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Joint replacement in HIV-positive patients remains uncommon, with most experience gained in patients with haemophilia. We analysed retrospectively the outcome of 102 replacement arthroplasties in 73 HIV-positive patients from eight specialist haemophilia centres. Of these, 91 were primary procedures. The mean age of the patients at surgery was 39 years, and the median follow-up was for five years. The overall rate of deep sepsis was 18.7% for primary procedures and 36.3% for revisions. This is a much higher rate of infection than that seen in normal populations. A total of 44% of infections resolved fully after medical and/or surgical treatment.

The benefits of arthroplasty in haemophilic patients are well established but the rates of complications are high. As this large study has demonstrated, high rates of infection occur, but survivorship analysis strongly suggests that most patients already diagnosed with HIV infection at the time of surgery should derive many years of symptomatic relief after a successful joint replacement. Careful counselling and education of both patients and healthcare workers before operation are therefore essential.

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Considerable joint degeneration occurs in 30% to 40% of patients with severe haemophilia, i.e., those having a factor-VIII activity of less than 1% of normal. The joints most commonly affected are the knee, elbow and ankle, with the shoulder and hip less so.

After the development of factor-VIII and factor-IX concentrates in the early 1970s, successful replacement of the hip and knee was undertaken in haemophilic patients, followed by that of the elbow, shoulder and ankle.

The technical challenges of arthroplasty were compounded by concerns of the risks to both patients and staff of the human immunodeficiency virus (HIV), which had been introduced into the haemophilic population through contaminated blood products between 1979 and 1985. A total of 1227 haemophilic patients has tested seropositive to HIV in the UK. The most useful measures of HIV progression, and susceptibility to opportunistic infection, are the CD4 lymphocyte count and the viral load measured as the level of HIV RNA. The latter has only recently been adopted for clinical use.

The high financial cost of a single joint replacement in a severe haemophilic and the assumed reduced life-expectancy in HIV-positive patients, has led many to urge caution. There has, however, been a steady improvement in the rates of survival of HIV-positive patients as a result of new drug regimens. Previous studies have not demonstrated a deleterious effect of major orthopaedic procedures on the progression of disease. To date most reports on arthroplasty in haemophilic patients have been either of small series or of individual cases. Inevitably, surgeon-dependent and centre-dependent factors, together with the case-mix, affect the results. Our study aimed to limit any such bias by combining the experience of many centres worldwide.

Patients and Methods

All the available sets of case notes for HIV-positive, haemophilic patients undergoing joint replacement proce-
dures were obtained from eight centres. We undertook a retrospective review of these using a standard form to capture details such as the type and severity of the haemophilia, the operative details, complications including infections and progression of HIV, noting CD4 counts when these had been measured. When available, microbiological findings were recorded as were, in the case of infection, the initial treatment and its outcome and details of any further management.

As part of the analysis of the data, survivorship was determined for those patients with a diagnosis of HIV infection at the time of primary surgery, using the date of death as the failure endpoint, and not excluding those patients with prosthetic infection. Aseptic survivorship was calculated for all primary prostheses, using the date of diagnosis of infection as the failure endpoint. Survivorship analyses were performed using the method described by Tew and Waugh.\textsuperscript{13}

Results

The details of 102 arthroplasties in 73 HIV-positive patients were available for detailed study. There were 74 replacements of the knee (72.5%), 27 of the hip (26.5%) and one of the elbow (1%). Of these, 91 were primary and 11 were revision procedures. The mean age at the time of surgery was 39 years (22 to 60, median 37). The mean duration of follow-up was 5.7 years (0.1 to 20.8, median 5.0). The median date of surgery was 1987 (1973 to 1998).

In 92% of patients a diagnosis of haemophilia A (factor-
VIII deficiency) was given, in 3% it was haemophilia B (factor-IX deficiency), and in 5% the diagnosis was not stated. Most patients (88%) had less than 1% factor-VIII or factor-IX activity (severe haemophilia).

For 53 arthroplasties (52%), the patient had been diagnosed as HIV-positive before surgery, and in 37 (36%) it had been made after the operation. In 12% the date of diagnosis was not known. Overall, preoperative CD4 counts were available for 50 of the procedures (49%). The mean CD4 count was $0.39 \times 10^{9} / l$ (0.03 to $1.30 \times 10^{9} / l$). The generally accepted mean in normal individuals is $0.8 \times 10^{9} / l$.

The rate of deep sepsis was 18.7% after primary procedures (17/91), 36.3% overall after revision procedures, 43% (3/7) in those revised for sepsis, and 25% (1/4) when revision was for other reasons. The mean time to the diagnosis of sepsis after the primary procedure was 47 months (2 to 190).

Of the 81 procedures in which infection did not develop, the CD4 counts had been measured before operation in 42 (52%) with a mean value of $0.40 \times 10^{9} / l$ (range 0.09 to $1.21 \times 10^{9} / l$). Of the 21 procedures which were complicated by infection, in eight (38%) the preoperative CD4 count was known with a mean value of $0.31 \times 10^{9} / l$ (0.03 to $1.30 \times 10^{9} / l$). The mean logarithmic CD4 count was significantly lower in the infected group (-22.42 v -21.78, Student’s t-test, p < 0.01).

Analysis of the overall survival of patients in which the diagnosis of HIV infection had been made before operation showed survivorship of 55% at ten years after operation (Fig. 1). Analysis of the sepsis-free survivorship of prostheses implanted in primary procedures showed survivorship of 71.8% at ten years and of 54.9% at 20 years (Fig. 2). In seven of 21 infected cases, organisms were cultured; in five they were Gram-positive cocci, and in the others diphtheroids and Klebsiella species.

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**Fig. 3**

Summary of results of the treatment of sepsis in 18 patients.
Figure 3 summarises the methods and results of treatment in patients in whom sepsis developed. These cases comprise all 17 primary procedures which became infected, and the single case revised for ‘aseptic loosening’, in which there was subsequent infection. The initial treatments were usually unsuccessful, with eradication of infection occurring in only four (22%) overall, and in only one of the 11 (9.1%) in which treatment was by antibiotics alone.

When initial treatment failed, seven patients (50%) were placed on long-term antibiotics and continued to be symptomatic, thus representing overall failure of treatment. In the remaining seven, further surgery was performed, resulting in the successful eradication of the infection in four (57%).

Discussion

Joint replacement in HIV-positive patients with haemophilia carries considerable risk. In addition to infection, it is more likely to be complicated by nerve palsy, impaired wound healing and the formation of haematomata.

Septic arthritis in the joints of haemophilic patients was rare before the appearance of HIV, but the risk increased several-fold after HIV infection.\(^9\)\(^14\)\(^15\) The spectrum of infecting organisms includes *Salmonella* and fungal species which are rarely found in HIV-seronegative individuals.

After arthroplasty in the normal population, rates of infection of up to 1.5% are currently considered to be acceptable.\(^6\)\(^16\) From an analysis of reports of 715 arthroplasties in haemophilic patients we calculated an overall rate of deep infection of 7.2%, regardless of HIV status. Only one infection was reported in the 11 studies completed before 1979,\(^7\) when HIV was introduced. When patients were known to be HIV-positive, we found an overall rate of infection of 11.7% compared with 18.7% in our study.

HIV-infected individuals differ widely in their rate of progression to AIDS, which is reflected in the rates of decline of CD4 lymphocyte counts. AIDS is more likely to develop once the CD4 count has fallen below \(0.2 \times 10^9\)\(^1\) (described as ‘severe immunodeficiency’), and the risk of death is low before the CD4 count has fallen below \(0.05 \times 10^9\)\(^3\). Viral load, which is measured as viral RNA titres, has been used more recently as a measure of control or progression of the disease, but was not available for the patients whom we studied.

A rate of infection of 26.1% has been reported in a group of HIV-positive patients in whom the CD4 count was below \(0.2 \times 10^9\)\(^1\).\(^17\) In our study patients with low CD4 counts before operation were more likely to develop deep sepsis. The mean preoperative CD4 count was less than \(0.2 \times 10^9\)\(^1\) in 62.5% (5/8) of the infected group, compared with 16.7% (7/42) in those not infected, and there was a significant difference between the mean logarithmic CD4 counts in the two groups.

We do not suggest that an absolute value for the CD4 count should be used to decide whether or not to offer surgery. This is because the rate of progression of the disease varies between individuals and, more importantly, because the combinations of highly active antiretroviral agents used today are much more effective at preserving the immune status than the regimens used even five years ago, and continue to improve. The British HIV Association has published guidelines, shortly to be updated, on suitable regimens for the initial treatment and for failures of treatment.\(^11\) With suitable patient selection, combining sound surgical technique with strict protocols for antisepsis in operating theatres, the risks of early infection should be kept to a minimum. Late infection is largely influenced by the medical control of HIV, but prompt and effective treatment when remote sepsis does develop, may protect implants from bacterial seeding.

It is now clear that long-term survival is a reality for a considerable proportion of the HIV-positive population. This has been brought about by improvements in medication and the use of combination therapies against HIV. Affected individuals have had to reassess their life goals, and their needs must be reflected in the treatment options offered to them.\(^18\)

In financial terms, the very high cost of arthroplasty is offset by a predictable reduction in the rate of joint haemarthroses, with a consequent reduction in the cost of replacement coagulation-factor. For knee arthroplasty the time to equivalence is 13 years,\(^19\) at which time our figures show a cumulative survivorship of 70.1%.

Our study has demonstrated high rates of infection after arthroplasty in haemophilic patients, particularly in those seropositive for HIV. Despite this, we feel that joint replacement can be of considerable value in improving the quality of life of those affected by haemophilic arthropathy, particularly when the surgery is performed in specialist centres in close consultation with physicians involved in the control of haemophilia and HIV.

For haemophilic patients in the developed world, there is evidence that better prophylaxis in childhood and adolescence is leading to a marked reduction in haemophilic arthropathy. It is also clear that the risk of HIV infection through contaminated blood products has significantly diminished with time since coagulation-factor concentrates have been subject to viricidal treatment. Treatment with other blood products carries some risk, but this is minimal. In the UK there have been no new HIV infections in haemophiliacs since 1986. However, most haemophilic patients worldwide do not have access to adequate prophylactic-factor replacement, and 50 million people are now infected with HIV.
References


