Arteriovenous access outcomes in haemodialysis patients with HIV infection

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Abstract

Background. Arteriovenous (AV) grafts in haemodialysis patients usually fail due to thrombosis or infection. There is limited information on whether graft outcomes in HIV-positive haemodialysis patients differ from those in HIV-negative controls.

Methods. Using a prospective, computerized vascular access database, we identified retrospectively 15 HIV-positive dialysis patients having a graft placed during a 6.5-year period (January 1999 to June 2005), and compared their graft outcomes to those observed in 30 age-, sex- and access date-matched HIV-negative control patients. In addition, the outcomes of AV fistulas in 23 HIV-positive patients were compared with those observed in 32 matched HIV-negative controls.

Results. Thrombosis-free graft survival was substantially worse among the HIV-positive patients than in the HIV-negative controls (1-year survival, 17% vs 62%). The hazard ratio for graft thrombosis in the HIV-positive patients was 3.22 (95% CI, 1.66–10.32, P = 0.002). Infection-free graft survival was also lower in HIV-positive patients (hazard ratio 3.51; 95% CI, 1.21–18.85, P = 0.025). Finally, cumulative graft survival (from creation until permanent failure) tended to be lower in HIV-positive patients (1 year survival, 41% vs 65%, P = 0.07). The primary failure rate of fistulas (those never usable for dialysis) was similar in HIV-positive patients and in their controls (44% vs 41%, P = 0.83). Cumulative fistula survival was similar for HIV-positive and negative patients (hazard ratio 1.32; 95% CI, 0.65–3.58, P = 0.33).

Conclusion. AV grafts have inferior outcomes in HIV-positive patients as compared with HIV-negative patients, whereas fistulas have a similar survival in both groups.

Keywords: fistula; graft; HIV; infection; vascular access

Introduction

Arteriovenous (AV) grafts in haemodialysis patients usually fail due to thrombosis or infection [1,2]. There is limited information on whether graft outcomes in HIV-positive haemodialysis patients differ from those in HIV-negative controls [3–8]. Moreover, many of the published studies have been uncontrolled, making it difficult to evaluate whether the graft outcomes differed from those in HIV-negative dialysis patients [3,5,7]. There are contradictory reports about the impact of HIV infection on graft thrombosis. Whereas one study observed a higher risk of graft thrombosis among HIV patients [8], the second study observed no difference [6].

Due to their immunocompromised state, HIV-positive patients may be at increased risk of graft infection. Two studies reported a higher frequency of graft infection in HIV-positive patients, as compared with HIV-negative controls [4,8]. However, most (55–76%) of the HIV-positive patients in those reports had a history of intravenous drug abuse. Since the frequency of graft infection was also associated with intravenous drug use, it was not clear whether HIV infection itself was a risk factor for graft infection, or whether it was simply a marker of patients using intravenous drugs. Only a small minority (~15%) of HIV-positive dialysis patients at our medical center has a history of intravenous drug abuse, making it easier to evaluate the relationship between HIV infection and risk of graft infection.

The goal of the present study was to compare the outcomes of AV grafts and fistulas in HIV-positive haemodialysis patients with the respective outcomes observed in age-, sex- and access date-matched HIV-negative controls.
Methods

Study design

University of Alabama at Birmingham (UAB) nephrologists oversee the medical care of about 450 chronic haemodialysis patients at five dialysis units in metropolitan Birmingham. About 2–3% of the chronic haemodialysis population at UAB has HIV infection. UAB transplant surgeons place new vascular accesses in these patients. Subsequent access interventions and revisions are performed by the transplant surgeons or by the interventional radiologists. We identified all patients with HIV infection receiving haemodialysis at our institution during the 6.5-year period between 1 January 1999 and 30 June 2005. Institutional Review Board approval was obtained to review the patients’ medical records for research purposes. Using a retrospective case-control design, the vascular outcomes in the HIV-positive haemodialysis patients were compared with those observed in a matched group of HIV-negative patients.

Vascular access management

Each patient referred for placement of an upper extremity vascular access first underwent preoperative vascular mapping to assist the surgeon in selecting the optimal choice of access [9–11]. An ultrasound was used to quantify the diameters of the artery and vein, and to exclude stenosis or thrombosis of the draining vein. Fistulas were placed preferentially to grafts, and required a minimum artery diameter of 2 mm and a minimum vein diameter of 2.5 mm. Graft placement was reserved for those patients without suitable vascular anatomy for fistula creation. Preoperative vascular mapping was not employed prior to placement of thigh grafts.

Grafts were typically cannulated 2–3 weeks after their creation. Fistula cannulation was attempted 6–8 weeks after placement, provided that they were sufficiently matured. Fistulas that had failed to mature were evaluated sonographically, and subjected to surgical or radiological intervention in an attempt to salvage them.

Patients were referred for an elective fistulogram when there was a clinical suspicion of stenosis [12,13], and angioplasty was performed when a ≥50% stenosis was detected. Elective surgical revision was performed if the angioplasty was unsuccessful. Thrombosed accesses were referred to interventional radiology for mechanical thrombectomy, in conjunction with angioplasty of the underlying stenotic lesion. Surgical thrombectomy was attempted if the radiological thrombectomy was unsuccessful, or if the access re-thrombosed within 1 month. Infected grafts were treated initially with systemic antibiotics, and excised if the infection failed to resolve. An access was considered to have failed permanently if thrombectomy was not successful, or if it required excision due to infection.

Two full-time Vascular Access Coordinators in the Division of Nephrology scheduled all the access procedures, and maintained a prospective computerized database of all the interventions [14].

Data collection

The UAB computerized access database [14] was queried retrospectively to obtain a comprehensive list of all AV grafts placed in HIV-positive patients during the study period. For the purpose of analysis, only the first graft placed in each patient during the study period was included. By this process, we identified 15 HIV-positive patients receiving a first AV graft during the study period.

To obtain a group of age-, sex- and date-matched control patients, the following procedure was followed. For each index HIV patient receiving an AV graft, the computerized database was queried to generate a list of all patients receiving a graft in the 4-month time period starting 2 months before the index procedure and ending 2 months following the index case. We excluded from this master list any patients with HIV infection. We then selected patients of the same gender as the index case. Finally, we selected two HIV-negative patients whose age was closest to that of the index case, and not differing by more than 10 years. By this process we compiled a group of 30 matched HIV-negative control patients.

Similarly, query of the access database identified 23 HIV-positive patients receiving a first AV fistula during the same study period. Matched HIV-negative control patients receiving a fistula were identified using a similar protocol to that used to obtain a control group for the graft patients. However, we also required the HIV-positive and the control patients to be matched for the location of the fistula, as we have previously observed inferior survival of forearm fistulas, as compared with upper arm fistulas [9,15]. As a result of this additional restriction, we were able to identify two matched controls for nine HIV-positive patients receiving a fistula, but only one matched control for 14 of the patients.

Demographic and clinical information was collected on all study patients, including age, sex, race, and presence of diabetes, hypertension, peripheral vascular disease and serum albumin. A history of intravenous drug use (by self-report) was obtained from each HIV-positive dialysis patient. In addition CD4 counts were retrieved for all HIV-positive patients.

Statistical analyses

The clinical characteristics were compared between HIV-positive and HIV-negative patients using Student’s t-tests or Chi-square analysis, with a P-value <0.05 considered to be statistically significant. Thrombosis-free graft survival was calculated from the time of graft creation to the time of first thrombosis or failure. Infection-free graft survival was calculated from the date of its creation to the date of first graft infection. Cumulative graft survival was calculated from the date of its creation to the date of permanent failure, regardless of number of interventions. Graft survival was censored at the time of patient death, kidney transplant, transfer to an outside dialysis unit, or data analysis (30 June 2005). Primary fistula failure was defined as the inability of the fistula to be used for dialysis for at least 1 month, due to technical failure, early thrombosis, or failure to mature. Cumulative fistula survival was calculated from the creation date to the time of permanent failure, with primary failures considered to have an effective survival of ‘0 days’. Survival analysis techniques (Kaplan–Meier curves) were used to model access survival time, and the log rank test used to compare the access survival of patient subgroups.
Results

The HIV-positive dialysis patients receiving an AV graft were comparable to their matched, HIV-negative controls in terms of age, sex, race, diabetes, peripheral vascular disease, graft location, history of previous vascular access and serum albumin (Table 1). However, hypertension was significantly less common in the HIV-positive patients, as compared with their matched controls. Only 13% (2 of 15) of the HIV-positive patients had a history of intravenous drug use.

Among those patients receiving an upper extremity AV graft, the arterial diameters were slightly lower in the HIV-positive patients, as compared with the controls (4.5±0.3 vs 5.2±0.9 mm, P=0.03), but still well above the minimum 2 mm diameter required. In contrast, the venous diameters were not significantly different between the two study groups (5.0±0.6 vs 5.0±0.8 mm, P=0.78). Thrombosis-free graft survival was significantly lower in the HIV-positive patients than in the HIV-negative controls (Figure 1). The hazard ratio for graft thrombosis in the HIV-positive patients was 3.22 (95% CI, 1.66–10.32, P=0.002). Thrombosis-free graft survival at 1 year was 17% in the HIV-positive patients, as compared with 62% in the controls.

A graft infection occurred in 40% (6 of 15) of the HIV-positive patients and 17% (5 of 30) of the HIV-negative controls (P=0.09). Only one of the six HIV-positive patients with a graft infection had a prior history of intravenous drug use. The infection-free graft survival was significantly lower in the HIV-positive patients, as compared with the HIV-negative controls (Figure 2). The hazard ratio for graft infection in the HIV-positive patients was 3.51 (95% CI, 1.21–18.85, P=0.025). Infection-free graft survival at 1 year was 61% in the HIV-positive patients and 88% in the matched controls. The CD4 counts were similar in HIV-positive patients having a graft infection and those without an infection (274±175 vs 314±251, P=0.74). A CD4 count <200 was present in three of the six (50%) HIV-positive patients with a graft infection, and three of nine (33%) of those without a graft infection (P=0.52). Likewise, the baseline serum albumin was not different between HIV-patients with a graft infection and those without one (3.1±0.9 vs 3.4±0.6, P=0.46).

Finally, the cumulative graft survival (from initial placement to permanent failure) tended to be shorter in the HIV-positive patients (Figure 3). The hazard ratio for cumulative graft failure in the HIV-positive patients was 2.19 (95% CI, 0.92–6.74, P=0.07).

Table 1. Clinical features of graft study patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV</th>
<th>Control</th>
<th>P-value</th>
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<tbody>
<tr>
<td>N</td>
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<td>30</td>
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<tr>
<td>Age</td>
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<td>43±9</td>
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<td>Sex</td>
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<td>Male</td>
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<td>Female</td>
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<td>Race</td>
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<td>Black</td>
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<td>25 (83%)</td>
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<tr>
<td>White</td>
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<td>5 (17%)</td>
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<tr>
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<td>22 (73%)</td>
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<tr>
<td>Hypertension</td>
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<td>29 (97%)</td>
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<tr>
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<td>1 (3%)</td>
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<td>15 (100%)</td>
<td>29 (97%)</td>
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<td>Graft location</td>
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<tr>
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<td>4 (13%)</td>
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<td>Previous access?</td>
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<tr>
<td>No</td>
<td>9 (64%)</td>
<td>21 (70%)</td>
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<tr>
<td>Serum albumin (g/dl)</td>
<td>3.3±0.7</td>
<td>3.5±0.6</td>
<td>0.46</td>
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</table>

PVD, peripheral vascular disease. Previous access = fistula or graft.

HIV and AV access outcomes

Fig. 1. Thrombosis-free survival of grafts in HIV-positive and HIV-negative dialysis patients. Thrombosis-free survival was calculated from graft placement to the first graft thrombosis or permanent graft failure. P=0.002 by the log rank test.

Fig. 2. Infection-free survival of grafts in HIV-positive and HIV-negative dialysis patients. Infection-free survival was calculated from graft placement to the first graft infection. P=0.025 by the log rank test.
The cumulative graft survival at 1 year was 41% in the HIV-positive patients and 65% in the control group.

HIV-positive patients receiving a fistula were more likely to be black and less likely to have diabetes, as compared with the HIV-negative controls (Table 2). However, the two groups were similar in terms of their age, sex, frequency of hypertension and peripheral vascular disease. The primary fistula failure rate was similar in the two groups, being 44% in the HIV-positive patients and 41% in the control group (Table 3). Moreover, the distribution of reasons for primary failure was similar in the two groups. Cumulative fistula survival was comparable between the two patient groups (Figure 4). The hazard ratio for cumulative fistula failure in the HIV-positive patients was 1.32 (95% CI, 0.65–3.58, \( P = 0.33 \)).

Discussion

The higher risk of graft thrombosis in HIV-positive dialysis patients observed in the present study is in agreement with a previous report that found a 1-year primary graft patency of 49% in HIV-positive patients, as compared with 77% in HIV-negative controls [8]. Although the arterial diameters of vessels used for graft creation in HIV-positive patients were somewhat lower than those used in the control patients, they were still more than twice as large as the minimum diameters permitted. Thus, the higher thrombosis rate of grafts in the HIV-positive patients was probably not due to differences in the vessels used. The mechanism responsible for enhanced graft thrombosis in HIV-positive patients remains to be elucidated. A previous study from our institution found a lower graft patency in patients with hypoalbuminaemia [1]. The serum albumin levels in the current investigation were not significantly different between HIV-positive patients and the control group (Table 1), although the small numbers preclude a definitive conclusion about such an association. A hypercoagulable state in HIV-positive patients has been described [16], but we did not systematically evaluate for this problem in our study population.
HIV and AV access outcomes

The higher risk of graft infection in the HIV-positive patients observed in the present study is consistent with two previous investigations. Brock et al. [4] observed a graft infection in 37% of HIV-positive patients, as compared with 15% in the control group. Similarly, Curi et al. [8] reported a graft infection in 30% of HIV-positive patients, as compared with 7% in the controls. However, in previous publications the high risk of graft infection in HIV-positive patients was largely confined to those having a history of intravenous drug abuse. Thus, Curi et al. [8] found a 33% graft infection rate in HIV-positive patients with a history of intravenous drug use, as compared with 3% in those without such a history. Likewise, Eustace et al. [7] reported a 29% likelihood of graft infection among HIV-positive patients with a history of intravenous drug use, as compared with 0% in those without such a history. In contrast, the current study documented an increased risk of graft infection among HIV-positive dialysis patients, which could not be attributed to intravenous drug use. In fact, only one of the six HIV-positive patients who developed a graft infection had a history of intravenous drug use. Thus, the presence of HIV infection appears to directly predispose to a higher risk of graft infection. The precise mechanism is not clear, but did not appear to be related to hypoalbuminemia or a low CD4 count.

Given that most grafts fail due to thrombosis or infection, as well as the higher risk of both graft thrombosis and graft infection in HIV-positive patients, it is not surprising that the cumulative graft survival tended to be shorter in the HIV-positive patients than in the controls. The relatively small patient numbers likely accounts for the inability to show a statistically significant difference in cumulative graft survival between the two groups (P = 0.07).

In contrast to the observations on graft outcomes, fistula outcomes were comparable in HIV-positive patients and their HIV-negative controls. Specifically, both the primary failure rate and the cumulative fistula survival were similar in both groups. This observation is in agreement with a previous report by Curi et al. [8].

The current study has several strengths. First, all HIV-positive haemodialysis patients at the five dialysis centers were captured. Second, the low rate of intravenous drug use in the present study eliminated one potential confounding factor for graft infection in previous publications. Third, the use of matched controls minimized a potential selection bias. In particular, the process of date-matching the controls largely eliminated the possibility that changes in therapy or process of care over time might affect the vascular access outcomes.

Several limitations of this study should also be acknowledged. First, this was a relatively small sample size. Second, the results from our institution may not generalize to other dialysis centers. Finally, it is still possible that the matching process may have missed unmeasured differences in patient characteristics or treatment specifics between the HIV-positive patients and their controls.

Conclusion

Haemodialysis patients with HIV infection are much more likely to experience graft thrombosis and graft infection, as compared with HIV-negative patients. In contrast, the outcomes of fistulas in HIV-positive haemodialysis patients are comparable to those obtained in HIV-negative controls. Thus, the clinical advantage of fistulas over grafts appears to be more pronounced among HIV-positive haemodialysis patients, as compared with the general dialysis population.

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