Survival in haemodialysis: is there a role for vascular access?

Sir,

Patient survival on haemodialysis is one of leading issues in dialysis. Age at the beginning of treatment, diabetes mellitus, nutrition, and probably adequacy of dialysis are the most frequently mentioned prognostic factors [1,2]. In a previous report we found that patients who survived 10 or more years on haemodialysis had significantly fewer vascular accesses than those who survived less than 10 years [3]; we speculated that this finding could be related to the better dialysis provided by better vascular access.

In order to further investigate this interesting finding we compared the 2.5-year survival of patients entering a single-centre dialysis programme. Between 1 January 1994 and 30 June 1996, 153 patients started an ambulatory dialysis programme in a single centre; by the end of this period, 24 patients had died, nine received a renal transplant, seven moved to other dialysis facilities and three recovered sufficient renal function to stop dialysis. A life table was made in order to compare survival between those patients with a single vascular access with those where more than one fistula (or PTFE graft) was necessary (Figure 1). These two groups were not significantly different in terms of age at the beginning of dialysis, diabetes mellitus, urea reduction ratio, neoplasia, or serum albumin. We found that even in this short period of follow-up, patients with a single vascular access had better survival than those with more than one fistula (log-rank test, $P<0.025$). This difference persisted even if diabetic patients are removed from analysis and could not be attributed to differences in age, nutritional status, prevalence of neoplasia, or other comorbidity. These results, if confirmed by other groups, suggest that good vascular access, regardless dialysis adequacy, is a novel prognostic factor in survival of haemodialysis patients, perhaps as an index of vascular background.

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**Editor’s note**

Please see the Editorial Comment by Woods and Port (pp. 657–659 in this issue).

Follow-up on a transplant recipient with chromomycosis

Sir,

Recently we reported a renal transplant recipient who developed cutaneous chromomycosis caused by *Aureobasidium pullulans*. The lesion was erroneously diagnosed as squamous-cell carcinoma and treated by surgical excision [1]. Twenty-eight months later, the same recipient developed a $1.2 \times 1$ cm painless purple nodule (Figure 1A) on the skin near the previous excision. This lesion resembled Kaposi’s sarcoma and was also excised. Histopathology (Figure 1B) and culture confirmed chromomycosis. No recurrence was subsequently seen during an 8-month follow-up period.

Recurrent lesions of chromomycosis in the same area, as our case, have often been reported [2,3], since the disease may spread by extension along lymphatics [2].

The two renal transplant recipients reported by Wackim *et al.* [3] developed two different cutaneous lesions. One of them presented recurrent purple nodules, and the other a verrucous skin lesion. Our patient developed both of them during his follow-up. Thus we had to consider two different differential diagnoses, first squamous-cell carcinoma [1] and second Kaposi’s sarcoma. The incidence is increased 400–500-fold in the renal transplant recipients over the population of the same ethnic origin [4].

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Herpes simplex virus as a sentinel lesion for cytomegalovirus infection

Sir,
Cytomegalovirus (CMV) infection, occurring usually within the first few months after transplantation, is a major cause of morbidity and mortality in transplant recipients, both bone marrow and solid organs. Like other members of the herpesvirus group, CMV possesses the cardinal characteristics of latency–reactivation and potential oncogenicity. This virus produces an infectious syndrome with frequent organ involvement (lung, liver, gastrointestinal, and retinitis). It is related to several complications such as increased immunosuppression, with a higher incidence of opportunistic infections and/or bacteriaemia, and acute and chronic allograft injury [1–4]. The diagnosis of CMV infection is based on laboratory tests including detection of virus markers (inclusion bodies and virus antigens, particles and/or genome), isolation of the virus by using tissue culture techniques, and detection of seroconversion or a significant rise in CMV antibody titer by serologic methods [1,5]. Because of the importance of this viral pathogen in clinical transplantation is necessary to optimize preventive measures. Recently, Lippmann et al. [4] have suggested that varicella zoster virus (VZV) and herpes simplex virus (HSV) diseases may serve as sentinel lesion for the CMV infection. We report a transplant recipient who developed seroconversion for CMV few days after HSV disease.

A 26-year-old female with end-stage renal disease secondary to vesicoureteral reflux received a renal transplantation in June 1996. Serologic studies immediately prior to transplantation for CMV and VZV showed IgG positive and IgM negative. She had not received neither vaccination nor passive immunoprophylaxis. Immunosuppression therapy consisted of antilymphocytic globulin, prednisone, cyclosporine-A and azathioprine. Two months after transplantation she presented a characteristic herpetic lesion on the right leg. Histocytopathologic study of material obtained from the cutaneous vesicles was characteristic of HSV infection. Interestingly, 20 days after the appearance of the cutaneous lesions a serologic study showed CMV-specific IgM antibodies without other signs or symptoms of CMV. The patient was treated with intravenous ganciclovir with prompt resolution of HSV disease. Four days after the end of ganciclovir therapy, serologic studies revealed negative CMV-IgM antibodies.

Although a variety of prophylactic regimens are prescribed based on viraemia, type of transplant, donor and recipient serostatus and use of antilymphocytresis [1], but has been reported that is related to allograft dysfunction [6,7]. Our case suggests that HSV may be associated with contemporaneous CMV infection, in agreement with the data reported by Lippmann et al. [4]. On this basis, HSV disease may serve as marker that identifies patients with a high risk to develop CMV infection, in whom the administration of specific antiviral therapy should be considered.

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Fig. 1. (A) painless purple nodule resembling Kaposi’s sarcoma; (B) spherical and septate hyphal fungal forms (arrow) were seen (H&E ×1000).
Recombinant human erythropoietin (Epoetin) and autologous blood transfusion in chronic haemodialysed patients: two observations

Sir,

Preoperative collection of autologous blood might seem impracticable in patients with chronic renal failure because they are so frequently anaemic, but it is really feasible, thanks to epoetin, as the two following cases testify.

Case 1

As a result of chronic rejection, Mr JB returned in haemodialysis 27 years after renal transplantation. Believing to have hitherto avoided infection by different viruses, he asked for autologous transfusions for the hip replacement which had to be carried out following a major detachment of the left acetabular cup with extensive destruction. His usual haemoglobin rate was 9.6 g/dl while he received a subcutaneous dose of 3000 IU of beta-epoetin (44.5 IU/kg) twice a week. This dose was progressively increased to 24000 IU per week and intravenous supplementation of 100 mg trivalent iron was administered at each dialysis session three times a week. Over 15 days, three units of 400 ml blood were collected, in each case on the day following dialysis. Mean haemoglobin was 10.2 g/dl before each donation. He was able to tolerate this programme of preoperative collection well without any complication of blood pressure or vascular access. His preoperative haemoglobin was 10.8 g/dl. Two blood units were returned to him during the operation, which was long and involved heavy blood loss, and the third during the dialysis session that followed. His subsequent progress was entirely satisfactory and his haemoglobin, which was at 7.3 g/dl on the first postoperative day, returned to preoperative levels within two months with the help of beta-epoetin and iron therapy.

Case 2

Mrs PC developed renal failure due to chronic interstitial nephritis and was treated with regular haemodialysis. When she received transfusions in cases of surgical operations, she tolerated them poorly, particularly because of chills and fever but without signs of alloimmunization. She was also frightened about the risks of viral transmission. Thus, when it was decided to perform a total hip replacement for a rapidly destructive arthritis, an autologous transfusion protocol was adopted. Her usual haemoglobin rate was spontaneously 9.8 g/dl. Thus, iron supplementation and subcutaneous injections of beta-epoetin were started: the initial dose of 2000 IU at each dialysis session (26 IU/kg three times a week) was rapidly doubled. Four units of 400 ml blood were collected, in each case the day after a dialysis session, with a good tolerance, pre-donation haemoglobin being at each time at an average of 10.4 g/dl. One dialyser coagulated 8 days after the dose of epoetin had been increased to 4000 IU. In view of this incident and the patient’s history of vascular access thromboses, she was treated with low-molecular-weight heparin (until the 15th postoperative day). Preoperative haemoglobin was 11 g/dl. Three blood units were returned to her during surgery and the fourth on the following day although haemoglobin rate was 11.3 g/dl. At the same time, epoetin was reduced in order to be stopped at the 18th postoperative day. Subsequently, haemoglobin has remained steady.

In an autologous transfusion programme, the addition of epoetin may permit such donation and to ensure an optimum yield of collected blood. It increases not only the quantity of blood that can be collected preoperatively, but also corrects pre-existing anaemia, minimizes or prevents the development of anaemia secondary to repeated collections, and finally corrects as swiftly as possible anaemia due to operative blood loss. Because of the expenses involved in autologous transfusion, epoetin should be used only for certain operations in patients for whom perioperative anaemia is likely to be harmful: those anaemic prior to surgery; those unable to tolerate without risks an aggressive preoperative blood donation, or with limited time available before surgery; polyclonally patients who are likely to tolerate homologous transfusions poorly or are at risk of harmful transfusion reactions.

Patients with chronic renal failure are therefore in many respects potential candidates for autologous transfusion, whether they are in predialysis phase or on dialysis, whether or not they have already had multiple transfusions, and whether or not they are candidates for a transplantation and must avoid HLA immunization. Before epoetin was available, autologous blood donation was not feasible. At the present time, the few studies on this subject [1–5] testify, as do our two case histories, to the merit and feasibility of an autologous blood programme using epoetin. These data, together with our own results, would suggest that in patients with chronic renal failure the additional cost would be lower than in non-anaemic patients because less epoetin can be used with good results: with their better tolerance of anaemia, these patients are likely to benefit from more aggressive protocols with lower limits to collection. For those on haemodialysis, regular trips for sessions and the ease with which epoetin can be administered and blood collected, minimize the constraints of such programmes and make them more readily acceptable—all the more so since these patients are often already very aware of the problems of transfusions.

Because little work has been done to date in patients with chronic renal failure to specify indications and detailed protocols, further observations should contribute to better define the correct implementation of this transfusion strategy, particularly the doses of epoetin and the limits to blood collection, taking into account the potential complications of thrombosis and hypertension, which conversely should be reduced by repeated collection and operative blood loss.

Reference:

Influence of overweight on survival of kidney transplant

Sir,

Obesity is associated with higher morbidity and mortality [1-3]. It is considered to be a general risk for surgical complications [4], and has been associated with poor graft and patient survival in kidney transplantation [5-7]. According to the standards determined at the First International Meeting on Body Weight Control [8], a BMI of 20–25 kg/m², 25–30 kg/m² and 30–40 kg/m², is considered to be normal, overweight and obese respectively. Although moderately overweight individuals comprise up to 45% of the entire population, there are no published studies that indicate whether or not overweight could be a risk for renal transplantation.

Influence of overweight on patient and graft survival and on associated morbidity was assessed in 562 cadaveric renal allograft recipients over 15 years of age. Mean follow-up was 58 months. Overweight was noted in 115 patients (group 1) and normal weight in 447 (group 2). Only 13 patients had a BMI > 30 kg/m². Patients in group 1 were older than those in group 2, 46.6 ± 10 vs 36.8 ± 12 years, \( P < 0.01 \), and there were no differences in BMI between males and females (both means 22.7 kg/m²). Donor age and sex, HLA matching, cold ischaemia time and revascularization time were similar in both groups.

Delayed graft function was more frequent in the overweight patients, 47 vs 35%, \( P < 0.05 \). Overall incidence of acute rejection was slightly lower in group 1, 52 vs 60%, NS. One-year graft survival was similar in both groups; 78.3% (\( n = 90 \)) in group 1 vs 78% (\( n = 341 \)) in group 2, NS. Five-year graft survival was also similar, 67.2% (\( n = 42 \)) vs 65.2% (\( n = 189 \)). Patient survival at 1 and 5 years was also similar. There were no differences in the percentage of patients with hypertension, infections, surgical complications, development of diabetes, hyperlipidaemia, or avascular osteonecrosis between both groups at the time of transplant. Days of hospitalization during the first year post-transplantation were also similar between the groups (36.5 ± 27.6 vs 39.7 ± 31.3 days, NS.). Serum creatinine at the end of the first year was 1.5 ± 0.6 mg/dl in group 1 and 1.7 ± 1 mg/dl in group 2, NS. Five years post-transplantation, serum creatinine was 1.5 ± 0.5 mg/dl and 1.5 ± 0.7 mg/dl respectively, NS. Although patients in group 1 received less cyclosporin (CsA) in relation to BMI than patients from group 2 during the first month post-transplantation, 9.5 ± 2.3 vs 12.4 ± 3.2 mg/kg/m², \( P < 0.001 \), whole blood levels of the drug were higher, 316 ± 98 vs 265 ± 90 ng/ml, \( P < 0.001 \). One year after transplant, CsA doses remained lower in Group 1, 8.5 ± 2.5 vs 11.3 ± 3 mg/kg/m², \( P < 0.001 \), and the higher blood levels were maintained, 258 ± 34 vs 218 ± 58 ng/ml, \( P < 0.001 \). (Table 1).

This is the first report regarding the impact of moderate overweight on renal transplantation therapy, and longer follow-up studies should be performed to confirm these observations. Overweight at the time of transplant, is not associated with a worse prognosis for the graft or the patient, at least during the first years post-transplantation. Moreover, patients with greater BMI require a smaller CsA dose to maintain therapeutic levels. The differences in CsA doses and blood levels between overweight and normal weight individuals are highly significant. We may not attribute the difference only to age, because all of our patients were older than 15 years.

Table 1. Morbidity in patients at the time of transplantation according to body weight

<table>
<thead>
<tr>
<th>Condition</th>
<th>Overweight n = 115 (%)</th>
<th>Normal weight n = 434 (%)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical complications</td>
<td>51</td>
<td>53</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>50</td>
<td>49</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9</td>
<td>5</td>
<td>NS</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>30</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>Ischaemia cardiopathy</td>
<td>8</td>
<td>5</td>
<td>NS</td>
</tr>
<tr>
<td>Aseptic necrosis of bonds</td>
<td>30</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>Infection (total)</td>
<td>60</td>
<td>61</td>
<td>NS</td>
</tr>
<tr>
<td>Infection/patient (n)</td>
<td>1.3 ± 2</td>
<td>1.6 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td>Delayed graft function</td>
<td>47</td>
<td>35</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>52</td>
<td>61</td>
<td>NS</td>
</tr>
<tr>
<td>Days of hospitalization (1st year)</td>
<td>36 ± 28</td>
<td>40 ± 31</td>
<td>NS</td>
</tr>
<tr>
<td>CsA (mg/kg/m²)</td>
<td>9.5 ± 2.3</td>
<td>12.4 ± 3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CsA (levels ng/ml)</td>
<td>316 ± 98</td>
<td>265 ± 90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine 1st year (mg/dl)</td>
<td>1.5 ± 0.6</td>
<td>1.7 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine fifth year (mg/dl)</td>
<td>1.5 ± 0.5</td>
<td>1.5 ± 0.7</td>
<td>NS</td>
</tr>
</tbody>
</table>
Dialysis-related amyloidosis (DRA) secondary to β₂M accumulation is a common complication of long-term dialysis therapy and is responsible for significant morbidity and potential mortality among dialysis patients [1,2]. A recent study by Hakim et al., comparing low-flux biocompatible polymethylmethacrylate membrane (PMMA) versus low-flux less biocompatible cellulose membrane (T175), shows that the use of biocompatible dialysers leads to lower serum β₂M concentrations [3]. Moreover it has been shown that routine use of polyacrylonitrile (PAN) membrane reduces the positive balance of β₂M in the body by 50% and that patients dialysed chronically on PAN have a lower incidence of carpal-tunnel syndrome when compared to those dialysed with cuprophane membrane [4]. Furthermore it has been suggested that membranes that activate complement cascade participate in the development of amyloid bone disease by both increasing the release of β₂M and by providing an environment in which the products of complement activation, reactive oxygen species, and activated neutrophils result in modification and polymerization of β₂M, enhancing their deposition [5]. One disadvantage, however, to the long-term use of high-flux biocompatible membrane is their greater cost.

We retrospectively analysed five chronic haemodialysis patients who had been dialysed sequentially with three different dialysis membranes: CA210 (cellulose acetate, less biocompatible membrane, KOA = 930; Baxter HealthCare Corp., McGaw Park, IL, USA), CT190 (cellulose triacetate, high-flux, more biocompatible membrane, KOA = 920; Baxter HealthCare Corp.), and F80 (polysulphone, high-flux and very biocompatible, KOA = 945; Fresenius Corp., Bad Homburg, Germany). The demographics of the group were African-American, four patients; male, four patients. End-stage renal disease was due to hypertension, diabetes mellitus, focal glomerulosclerosis, chronic glomerulonephritis, and unknown aetiology, one case in each category. The patients' age was 55 ± 7 years (mean ± SEM; range, 30–70 years). The length of time on dialysis was 114 ± 35 months (range, 20–235). Each patient had been dialysed with each membrane for a mean of 8 months (range, 3–16). There were a total of nine serum β₂M measurements while the patients were dialysed on CA210 membrane, 16 measurements on CT190, and 16 measurements on F80 membranes. Serum β₂M (mg/dl) was significantly lower with the F80 membrane (42 ± 3.3, mean ± SEM) and CT190 (43 ± 2.7) than the CA210 membrane (75 ± 7.4; P < 0.0001 for F80 or CT190 versus CA210; P = not significant for F80 versus CT190; for statistical analysis groups were compared using ANOVA with Bonferroni/Dunn post hoc correction). Serial serum β₂M concentrations of each patient on different dialysis membranes is shown in the figure.

Our results suggest that high-flux biocompatible membranes e.g., CT190 and F80 are equally effective in significantly reducing serum β₂M when compared to less biocompatible high-efficiency membrane CA210. This is the first direct comparison of serum β₂M in patients dialysed on CT190 and F80, and CA210 membranes.

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![Fig. 1. Serial serum β₂M concentrations in five patients sequentially dialysed with three different dialysis membranes. CA, CA210; CT, CT190; F, F80.](image)