Anaemia and congestive heart failure early post-renal transplantation

Richard Borrows, Marina Loucaidou, Gary Chusney, Sarah Borrows, Jen Van Tromp, Tom Cairns, Megan Griffith, Nadey Hakim, Adam McLean, Andrew Palmer, Vassilios Papalois and David Taube

West London Renal and Transplant Centre, Hammersmith Hospital, Du Cane Road, London W12 0HS, United Kingdom

Abstract

Background. Anaemia is common following renal transplantation and is associated with the development of congestive heart failure (CHF). However the prevalence of anaemia in the first year following transplantation and the association between anaemia occurring early and the development of CHF have been understudied.

Methods. In this study, 132 incident patients undergoing tacrolimus and mycophenolate mofetil-based renal transplantation were studied for the prevalence of, and risk factors for, anaemia and CHF in the early period post transplantation.

Results. Anaemia occurred in 94.5% and 53.1% of patients at 1 week and 12 months, respectively, and was associated with allograft dysfunction, hypoalbuminaemia, higher mycophenolic acid (MPA) levels, bacterial infection and hypoalbuminaemia. The association with hypoalbuminaemia may reflect the presence of chronic inflammation post transplantation. Of patients displaying haemoglobin <11 g/dl, 41.1% and 29.4% were treated with erythropoiesis stimulating agents (ESAs) at 1 and 12 months respectively. CHF developed in 26 patients beyond 1 month post transplantation, with echocardiographic left ventricular systolic function preserved in all but one. CHF was associated with anaemia and lower haemoglobin, allograft dysfunction, duration of dialysis and left ventricular hypertrophy on echocardiography prior to transplantation, suggesting the aetiology of CHF may involve the interplay of diastolic cardiac dysfunction, pre-load mismatch and after-load mismatch.

Conclusions. Modification of risk factors may improve anaemia management post transplantation. Reducing the prevalence of anaemia may in turn reduce the incidence of CHF—these observations support the need for clinical trials to determine how anaemia management may impact CHF incidence.

Keywords: anaemia; congestive heart failure; kidney transplant

Introduction

Post-transplantation anaemia (PTA) remains a significant problem following renal transplantation, particularly with use of potent contemporary antiproliferative agents such as mycophenolate mofetil (MMF) and sirolimus [1–11]. Many recent studies have concentrated on PTA at or beyond 12 months post-transplantation, often in stable patients many years following transplantation [1–7]; recent studies specifically addressing risk factors for PTA during the first 6 months are scarce, despite suggestion that distinction be made between early and late PTA based on occurrence before or after 6 months [2,8,9]. Certainly most recovery of erythropoiesis occurs early post transplantation [10]. A predominantly paediatric study showed that anaemia at 3 months is associated with reduced renal function and the use of prednisolone [11]. In adult recipients, anaemia at 6 months has been associated with reduced renal function [12], African American race [12], female sex [12,13] and the use of sirolimus versus mycophenolate mofetil [4,14]. Immunosuppression protocols in these studies of early PTA were variable, and in contrast to current practice were often based on ciclosporin and azathioprine.

In turn, PTA is associated with congestive heart failure (CHF), a significant cause of morbidity and mortality following renal transplantation [15–18]. Detailed reports of CHF post-transplantation are limited to one single-centre study, one dual-centre study and two analyses of the United States Renal Data System (USRDS). Despite highest CHF incidence during the first year post-transplantation, only two of these reports (one single-centre study; one registry analysis) investigated risk factors for CHF during this period [15,17]. Both studies found an association between CHF early post-transplantation and anaemia, highlighting the potential importance of early PTA, although the first report focussed exclusively on diabetic patients predominantly undergoing combined kidney–pancreas transplantation [15], and the other is prone to the limitations (as well as advantages) of registry data [17]. Other data that exist have focussed on CHF occurring later following transplantation [16,18].

The main aims of this study were to investigate the association between PTA (assessed serially during the
first year post-transplantation) and the subsequent development of CHF early in the post-transplantation period, and secondly to identify other factors associated with CHF. In addition, the risk factors for early PTA in patients undergoing standardized tacrolimus and MMF-based immunosuppression with anti-CD25 monoclonal antibody induction and a steroid sparing regime were investigated.

**Subjects and methods**

**Patients**

Data were prospectively collected on 132 consecutive renal transplant recipients undergoing renal transplantation and follow-up at a single centre between 2001 and 2003. All patients received tacrolimus (Prograf®; Fujisawa) and mycophenolate mofetil (MMF; Cellcept®; Roche). Tacrolimus was administered from the first day post-transplantation in all patients at 0.1 mg/kg twice daily, adjusted to a whole-blood trough level of 10–15 ng/ml in the first year, and 8–10 ng/ml thereafter (enzyme immunoassay; IMx® tacrolimus II; Abbott Laboratories, IL, USA). MMF was administered at 750 mg twice daily and increased to 2 g per day if tolerated. Total 12-h predose plasma mycophenolic acid (MPA) levels were measured by an enzyme-mediated immuno-technique (EMIT; Dade Behring, UK). However the clinical team was blinded to the results of the MPA analysis throughout, with decisions to change the MMF dose made on clinical grounds alone. Corticosteroids were administered as a steroid-sparing regime: intravenous methylprednisolone (500 mg) pre-operatively followed by oral prednisolone 1 mg/kg/day for the first 3 days, reducing to 0.5 mg/kg/day from Day 4, stopping after Day 7. Steroid therapy was re instituted in the event of an acute rejection episode.

**Pre-transplantation screening and post-transplantation clinical assessment**

All patients underwent detailed clinical assessment and cardiac investigation prior to activation on the transplant waiting list. Most patients underwent echocardiography (n = 104; 79%), assessed at a mean of 14 ± 7 months prior to transplantation. All patients studied by echocardiography displayed left ventricular ejection fractions of >50%. In addition, all patients over the age of 50 years, all diabetic patients and all patients with previously documented (or history suggestive of) cardiovascular, cerebrovascular or peripheral vascular disease (n = 39; 29%) underwent coronary angiography and revascularization (if necessary) prior to waiting list activation.

Post-transplantation follow-up was conducted at the single centre, with patients advised to attend the centre’s assessment unit in the event of intercurrent illness. De novo CHF was defined in concordance with previous studies of transplant recipients and dialysis patients as dyspnoea in association with two of the following: raised jugular venous pressure, pulmonary crepitations on auscultation, chest X-ray evidence of pulmonary hypertension or pulmonary oedema [16,19]. CHF was studied beyond 1 month post-transplantation to avoid the initial post-transplantation period that is associated with significant shifts in intravascular and extravascular volume, often aggressive fluid administration by the transplant team and transplant recipient, and marked changes in renal allograft function.

**Data collection**

Haemoglobin levels were measured daily, as part of the complete blood count, during the initial post-transplantation period, and then at each clinic attendance following discharge. The analysis of haematological parameters focussed on values obtained at 1, 3, 6 and 12 months. Anaemia was defined according to the World Health Organization (WHO) and Clinical Practice Guidelines for Outpatient Surveillance of Renal Transplant Recipients [8]:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>haemoglobin &gt;13 g/dl (males), &gt;12 g/dl (females);</td>
</tr>
<tr>
<td>Mild</td>
<td>haemoglobin between 12.1 and 13 g/dl (males), between 11.1 and 12 g/dl (females);</td>
</tr>
<tr>
<td>Moderate</td>
<td>haemoglobin between 11.1 and 12 g/dl (males), between 10.1 and 11 g/dl (females);</td>
</tr>
<tr>
<td>Severe</td>
<td>haemoglobin ≤ 11 g/dl (males), ≤10 g/dl (females).</td>
</tr>
</tbody>
</table>

Donor and recipient variables with the potential to impact haemoglobin levels and anaemia were collected: donor source (live/deceased donor); recipient demographic data (age; sex; ethnicity; diabetic status); prior use of antiproliferative agents (azathioprine; cyclophosphamide; MMF) due to previous transplantation or treatment of immune-mediated disease; delayed graft function (DGF; requirement for dialysis during the first post-operative week). The following information for the sampling points at 1, 3, 6 and 12 months was collected: renal function [creatinine and estimated glomerular filtration rate (eGFR)]; mean blood pressure; serum albumin, ferritin, C-reactive protein and intact parathyroid hormone (PTH); comodication [MMF dose and plasma MPA predose level; corticosteroid usage; angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor blocker (ARB) usage]. Episodes of biopsy-proven acute rejection and bacterial sepsis (the positive identification of a bacterial organism from blood or body fluid culture in the presence of fever, with resolution following antibiotic therapy) since the previous sampling point were noted.

Development of CHF beyond 1 month post-transplantation was ascertained by systematic review of patient records at regular intervals. The association between CHF and the following clinical characteristics was investigated: haemoglobin; renal function (creatinine and eGFR); serum albumin; mean arterial blood pressure; use of ACEI or ARB (versus neither). In addition, the following variables were also analysed for a relationship with CHF; age; sex; time on dialysis; diabetes as a cause for end-stage renal failure; LVH on echocardiography prior to transplantation, defined as the easily measurable and widely accepted criteria of interventricular septal thickness >1.2 cm or posterior wall thickness >1.1 cm [20].
Statistical analysis

Analysis was performed using Stata (version 7.0; Stata Corporation, USA). Haemoglobin levels at different times were compared using ANOVA for repeated measurements, with post hoc testing between specific groups. Bonferroni correction was applied for multiple comparisons. Continuous (haemoglobin level) and categorical (anaemia) data were examined by linear and logistic regression, respectively. All continuous data were normally distributed. Time post-transplantation was examined as an independent variable, and consequently there were several measurements from each subject. Therefore, a variation of standard regression analysis known as the ‘random effects’ model (multilevel modelling) was used to allow for the repeated measures.

Due to the distribution of grades of anaemia over the course of the study (see the Results section and Figure 1), examination of anaemia focussed on severe anaemia at 1 month, combined moderate and severe anaemia at 3 and 6 months, and any grade of anaemia at 12 months. Cox proportional hazards regression examined associations between explanatory variables and the subsequent development of CHF. For all models, a joint examination of variables showing an association on univariate analysis was performed in a multivariate fashion. A backward stepwise selection procedure was used to construct the multiple regression model, with a subsequent forward selection process to confirm the robustness of the final model. A two-tailed \( P \)-value <0.05 was considered significant.

Results

Clinical outcomes

Two patients experienced technical graft failure during the first week. Demographics of the remaining 130 studied patients are shown in Table 1. Two patients died during the study period: one from progressive cardiac failure at 6 months and one from sepsis at 8 months. All other patients were followed for a minimum of 12 months [median 26 months (range 12–40)]. In addition to these deaths with graft function, there was one further graft lost to chronic allograft nephropathy. Therefore, overall actuarial survival with graft function was 96.2%.

Haemoglobin levels and anaemia prevalence during the first year post-transplantation

Haemoglobin levels changed significantly over time (\( P < 0.001 \) by ANOVA). Mean haemoglobin before transplantation was 12.2 ± 1.5 g/dl, and fell to 10.4 ± 1.1 g/dl by 1 week post-transplantation (\( P < 0.001 \)). Haemoglobin levels were 10.7 ± 1.2 g/dl by 1 month post-transplantation, and subsequently rose to 11.8 ± 1.3 g/dl, 12.0 ± 1.4 g/dl and 12.7 ± 1.5 g/dl by 3, 6 and 12 months post-transplantation (\( P = 0.004 \) for 1 month versus 3 months; \( P = 0.009 \) for 6 months versus 12 months). Multivariate associations with haemoglobin levels during the study are shown in Table 2. Estimated GFR and serum albumin at the equivalent sampling point, haemoglobin at the previous sampling point, estimated GFR and serum albumin at the equivalent sampling point, haemoglobin at the previous sampling point, male sex and time post-transplantation were positively associated with haemoglobin levels; bacterial infection since the previous sampling point and higher predose plasma MPA level (calculated as the median value since the previous sampling point) were negatively associated with haemoglobin levels.

The prevalence of anaemia (defined in the Methods section) is shown in Figure 1. With the exception of recipient sex (which was not entered as an explanatory variable as the WHO definition of anaemia is sex-specific), the variables
Time post-transplantation f 0.06 0.03, 0.16 0.01
MPA level e 1.4 and 2.3

The purpose of subsequent analysis these two patients were
pharyngeal and treated with angioplasty and stent deployment. For
underwent magnetic resonance angiography of the renal
and 3 beyond 12 months. Twenty-one of these patients
9 between 3 and 6 months, 5 between 6 and 12 months
these, 11 patients developed CHF between 1 and 3 months,
Twenty-eight patients developed CHF beyond 1 month. Of
CHF following transplantation

| Table 2. Haemoglobin levels post-transplantation: multivariate analysis |
|-----------------------------|-----------------------------|------------------|
| Effect | 95% CI | P-value |
| Serum albumin a | 0.72 | 0.49, 1.19 | 0.005 |
| eGFR b | 0.67 | 0.46, 1.03 | 0.002 |
| Male sex | 0.79 | 0.51, 1.37 | 0.003 |
| Hb at prior sampling point c | 0.81 | 0.42, 1.42 | 0.004 |
| Bacterial infection d | −0.82 | −1.29, −0.53 | 0.003 |
| MPA level e | −0.51 | −0.98, −0.26 | 0.005 |
| Time post-transplantation f | 0.06 | 0.03, 0.16 | 0.01 |

Effect shown is the actual change in haemoglobin (g/dl) for each described change in the explanatory variable.

aEffect for 10 g/dl rise in serum albumin; mean values (g/dl) at Months 1, 3, 6 and 12: 36.7 ± 5.3, 39.2 ± 4.8, 40.4 ± 3.7 and 41.3 ± 2.7 respectively.
bEffect for 10 ml/min rise in eGFR; mean values (ml/min) at Months 1, 3, 6 and 12: 36.0 ± 15.5, 41.8 ± 13.1, 44.1 ± 12.5 and 48.1 ± 11.5 respectively.
cEffect for 1 mg/l rise in haemoglobin at the previous sampling point; mean values (g/dl) at Week 1, Months 1, 3 and 6: 10.4 ± 1.1, 10.7 ± 1.2, 11.8 ± 1.3 g/dl and 12.0 ± 1.4 respectively.
dNumber of patients experiencing bacterial infections between transplantation and Month 1, between 1 and 3 months, between 3 and 6 months and between 6 and 12 months: 34 (26%), 27 (21%), 23 (18%) and 16 (12%) respectively.
eEffect for 1 mg/l rise in the median MPA level in the time since the last measurement; mean values (mg/l) at Months 3, 6 and 12: 2.7 ± 1.2, 2.5 ± 1.4 and 2.3 ± 1.4 respectively.
fEffect shown per month post-transplantation.

associated with lower haemoglobin levels in the previous analysis were also associated with grade of anaemia when this was substituted for haemoglobin level in the multivariate model, with the effect predictably in the opposite ‘direction’ (data not shown).

No associations were found between the prevalence of anaemia and the use of ACEI, ARBs, PTH levels or serum ferritin. Other markers of iron storage (such as serum transferrin, transferrin saturation and percentage hypochromic red blood cells) were not collected.

Use of erythropoiesis stimulating agents (ESAs)

European Best Practice Guidelines [21] suggest haemoglobin be maintained above 11 g/dl in transplant recipients, and do not discriminate between males and females. Of 73 patients displaying haemoglobin <11 g/dl at 1 month post-transplantation, 30 (41.1%) were treated with ESAs. At 3, 6 and 12 months post-transplantation the corresponding figures were 5/36 (13.9%), 4/27(14.9%) and 5/17 (29.4%) respectively.

CHF following transplantation

Twenty-eight patients developed CHF beyond 1 month. Of these, 11 patients developed CHF between 1 and 3 months, 9 between 3 and 6 months, 5 between 6 and 12 months and 3 beyond 12 months. Twenty-one of these patients underwent magnetic resonance angiography of the renal transplant artery. Significant transplant renal artery stenosis (TRAS) was found in two patients (both 2 months post-transplantation), confirmed on digital subtraction angiography and treated with angioplasty and stent deployment. For the purpose of subsequent analysis these two patients were not considered to experience CHF, as TRAS may mimic the clinical presentation of CHF. For the 26 remaining patients with CHF (20%), 6 required hospital admissions for symptom control. All 26 patients (including the 6 requiring admission) displayed a rapid symptomatic response upon initiation of diuretic therapy.

Multivariate Cox regression analysis revealed CHF beyond 1 month was associated with lower haemoglobin levels and renal impairment at 1 month, and longer duration of dialysis (Table 3).

Next, haemoglobin level was replaced by anaemia in the regression analysis. Due to the distribution of anaemia severity, this analysis focussed on severe anaemia at 1 month as the independent variable (Hb <11 g/dl and <10 g/dl for males and females respectively; n = 62; 47.7%). CHF beyond 1 month was associated with the presence of severe anaemia (relative risk: 2.68; 95% CI: 1.39–4.81; P = 0.03). The substitution of anaemia in the analysis did not materially alter the associations of CHF with renal function or time on dialysis.

Finally, subanalysis was performed for the 103 patients undergoing echocardiography prior to transplantation, of whom 63% (65/103) displayed LVH. CHF developed in 30% (20/65) of patients with LVH versus 11% (4/38) of those without LVH (P = 0.01). Multiple regression analysis revealed that the presence of LVH was associated with the development of CHF beyond 1 month (relative risk: 1.93; 95% CI: 1.33–2.84; P = 0.03). In these models, the association between CHF and haemoglobin/anaemia, and with eGFR, remained significant (P < 0.05 for all); however time on dialysis lost significance in this multivariate model.

Because of potential colinearity between haemoglobin/anaemia and eGFR, the analyses were repeated omitting firstly haemoglobin/anaemia and then eGFR from the models. No material difference in the results for the remaining variables in the models was seen.

Hypoalbuminaemia was associated with CHF on univariate analysis (P = 0.01), but not in the multivariate model.

All patients experiencing CHF underwent echocardiography. In all cases except one, left ventricular systolic function was preserved (ejection fraction >50%). The exception to this developed progressive CHF, resulting in death at 6 months post-transplantation.

Two patients developed stable angina during follow-up. Neither had a prior history suggestive of ischaemic heart disease. Coronary angiography revealed flow-limiting
coronary stenoses in both patients, with successful angioplasty and stent insertion resulting in symptom resolution.

Discussion

This analysis shows a high incidence of anaemia during the first year following renal transplantation coupled with low ESA usage and extends the understanding of factors associated with haemoglobin and PTA early post-transplantation in a population undergoing standardized tacrolimus and MMF-based immunosuppression in a steroid-sparing protocol. Importantly, reductions in haemoglobin and anaemia early post-transplantation were associated with a subsequent clinical diagnosis of CHF, most episodes of which occurred in the first 12 months following transplantation. In addition, other factors associated with CHF early post-transplantation are described, in particular impaired graft function and LVH (by echocardiogram criteria), the latter observation being a novel finding. The study therefore extends the understanding of CHF occurring early post-transplantation that, although common, has been little studied hitherto.

The significant burden of PTA in stable renal allograft recipients is well recognized [1–7]. The current study confirms these observations in the early period post-transplantation. A gradual rise in haemoglobin occurred during the first year, with PTA prevalence similar to the study by Mix [13], and increase of haemoglobin levels similar to (but slightly lower than) the study by Turkowski–Duhem in which haemoglobin levels of 12–13 g/dl were specifically targeted by the use of ESAs [14]. In the current study, ∼50% of patients remained anaemic by WHO criteria at 12 months. This is in keeping with the results of previous studies in stable renal allograft recipients [2,3,7,12]. In agreement with the results of the European TRESAM study [3], ESAs were underutilized when benchmarked against published guidelines [21].

PTA was associated with a number of risk factors previously described in stable allograft recipients: inferior red cell indices were associated with allograft dysfunction, bacterial infection and higher MPA levels so extending recognized risk factors for anaemia to the early stages post-transplantation in a population undergoing steroid-sparing renal transplantation [1–7,10–13,22].

The association between hypoalbuminaemia and PTA may relate to an increase in biologically active unbound MPA in hypoalbuminaemia patients [23], or may reflect the mutual association between chronic inflammation, hypoalbuminaemia and erythropoietin resistance that is gaining increasing recognition in dialysis patients [24]: the current study supports the proposal that the so-called MICS syndrome (malnutrition–inflammation complex syndrome) may also play a role in the development of anaemia in transplant recipients [25].

No relationship was seen between haemoglobin and the simple marker of iron storage, ferritin. A previous study has shown an inverse association between ferritin and haemoglobin [7], probably a consequence of the dual role of ferritin as a marker of iron storage and chronic phase reactant, rendering the lack of association in the current study less surprising. No relationship was seen between haemoglobin values and the acute phase reactant CRP. This lack of association has been observed previously, and may reflect deficiencies in the ability of CRP to detect chronic low-grade inflammation in immunosuppressed transplant recipients [7]. Previous studies have nevertheless shown associations between haemoglobin and markers of iron status. Percentage hypochromic red blood cells (%HRBC) is emerging as a reliable marker of iron status [7] by virtue of its lesser dependence on factors such as inflammation, diet and nutritional status than other traditional markers of iron storage, thereby better reflecting iron available for erythropoiesis [7,26]. Unfortunately %HRBC was not assessed in the current study, and warrants further investigation in future.

Rigatto et al. have proposed that the pathogenesis of CHF in transplant recipients is a progressive cardiomyopathy as a result of the interplay between baseline left ventricular geometry, the development of cardiac damage due to longstanding anaemia and hypertension, and the presence of ischaemic heart disease [16]. The current study supports a similar, but not identical, schema for the pathogenesis of CHF early following transplantation: we propose an interaction between low haemoglobin levels, renal impairment and LVH.

Previous studies have shown an association between anaemia and CHF [15–17], and although the results of these studies complement the current analysis the results are not readily comparable: in the study from Djamali [15], all patients were diabetic, most had undergone combined kidney–pancreas transplantation and a composite end point was studied (CHF; cardiac death; myocardial infarct; angina). The registry data analysis by Lentine [17] found an association between CHF (occurring at any time post-transplantation, rather than specifically during the first year) and anaemia, although both CHF and anaemia were defined by Medicare claims, and therefore precise data are not available. Rigatto studied only patients developing de novo CHF after the first year post-transplantation, although it was clear from their study that clinical heart disease was common during the first 12 months, occurring in 20% of patients [16]. The current study showed a similar early incidence; the low incidence of CHF beyond 12 months post-transplantation was similar in the two studies. Anaemia is associated with peripheral vasodilatation and subsequent salt and water retention secondary to activation of the renin–angiotensin system, resulting in an increase in cardiac strain [27]. Severe anaemia occurring early post-transplantation may be a modifiable risk factor for CHF. In addition, previous studies have shown associations between PTA and mortality in prevalent renal transplant recipients [1,28], although data are conflicting [29]. To date, no large-scale randomized trials of anaemia management in renal transplant recipients has been conducted, and therefore robust evidence to support a benefit of anaemia correction in transplant recipients is currently lacking.

The current study also confirms the association between CHF and renal impairment seen in other analyses of CHF beyond 12 months [16,18], thereby extending these associations to the early stage post-transplantation. The association
likely reflects impaired fluid volume regulation. We have used the term ‘CHF’ rather than ‘fluid overload’, ‘volume expansion’, ‘salt and water retention’ or other such phrases for a number of reasons: firstly, it is ultimately the failure of the heart to cope with the strains put upon it (by either anaemia or renal impairment) that results in the constellation of clinical features described in this article; secondly, the task force of the European Society of Cardiology has defined acute heart failure as symptoms and signs related to systolic or diastolic dysfunction, pre-load mismatch or after-load mismatch, and point out that extra-cardiac pathologies may result in acute heart failure [30]—indeed this group specifically cites anaemia and renal impairment as causes of CHF; third, the definition is similar to that used by previous authors who importantly showed increased mortality in patients displaying ‘CHF’ [16]. We believe that ‘CHF’ represents logical terminology and avoids the somewhat circular argument that currently exists regarding the definition of the described clinical scenario.

An association was also seen between time on dialysis and CHF, as seen in some [18], but not all [15–17] previous analyses. This independent association disappeared when LVH was analysed as a covariate. This study is the first to show an association between echocardiographic indices of LVH and clinical CHF in renal transplant recipients. Systolic function was preserved in all but one of the study group, who may therefore best fit the syndrome of heart failure with preserved ejection fraction (HFrEF) that is believed to be largely, if not completely, due to diastolic dysfunction [31]. LVH is associated with diastolic cardiac dysfunction in both the general population [32] and renal allograft recipients [33]. Furthermore, in non-renal patients with a clinical diagnosis of CHF in the presence of LVH (using the same definition as the current study) and preserved (>50%) ejection fraction, diastolic dysfunction (assessed by cardiac catheterization and direct pressure measurement) is universal [20]. We acknowledge the lack of detailed echocardiographic measures of diastolic function in this study, but suggest that diastolic dysfunction is the most likely explanation for the association between LVH and CHF for the reasons described above.

All patients underwent post-transplant monitoring via a single centre, and were advised to contact the transplant unit in the event of intercurrent illness (rather than their primary care practitioner or alternative facilities), and none were lost to follow-up during the study duration, thereby lessening the likelihood that data collection for CHF incidence is incorrect. Nevertheless, there remains potential in an observational study such as this for non-uniform ascertainment in these patients.

In summary, this study highlights the factors associated with haemoglobin levels and PTA, and demonstrates an association between low haemoglobin levels, impaired renal function and LVH with CHF following renal transplantation. These observations suggest the need for further studies and trials to assess the impact of anaemia treatment on CHF. It remains to be seen whether the development of CHF in the early period post-transplantation is associated with increased mortality as has been seen in other studies of CHF occurring beyond 12 months, and whether anaemia and allograft dysfunction result in a progressive cardiomyopathy as suggested previously. Future studies detailing cardiac parameters and their evolution in renal transplant recipients may shed light on the mechanism of CHF in these patients, and the complex interaction between the heart and kidney.

Conflict of interest statement. None declared.

References


33. Huting J. Course of left ventricular hypertrophy and function in end-stage renal disease after renal transplantation. *Am J Cardiol* 1992; 70: 1481–1484

Received for publication: 2.6.07
Accepted in revised form: 18.10.07