
Nephrol Dial Transplant (1999) 14: Editorial Comments

Nephrol Dial Transplant (1999) 14: 1075

Ischaemic heart disease after renal transplantation: how to assess and minimize the risk

David C. Wheeler

Department of Nephrology, University Hospital NHS Trust, Birmingham, UK

Introduction

Advances in immunosuppressive therapy and in the treatment of opportunistic infection have greatly improved outcomes following renal transplantation, unmasking the clinical importance of co-morbid conditions associated with uremia. It is now well established that patients with chronic renal failure are at increased risk of cardiovascular disease [1]. Long-term follow-up studies suggest that this problem is attenuated, but is not corrected, by successful renal transplantation even when biases resulting from patient selection are taken into account [2]. Cardiovascular disease has now emerged, ahead of infection, as the leading cause of mortality in renal transplant recipients, particularly after the first year [3]. Since many of these individuals die with functioning transplants, these deaths represent an increasingly important cause of graft loss. In one study from Scandinavia, more grafts were lost from patient mortality than rejection during the 2–5 year post-transplant period (49 vs 41%). Ischaemic heart disease and other vascular events collectively accounted for 63% of these deaths [4]. Efforts to extend patient and graft survival will therefore become increasingly dependent on appropriate prevention and management of cardiovascular disease, rather than on further advances in immunosuppressive or antimicrobial therapy. The following brief comments describe how screening strategies could be used to exclude patients with significant coronary

Correspondence and offprint requests to: Dr David C. Wheeler MD MRCP, Department of Nephrology, University Hospital NHS Trust, Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TH, UK.
artery disease from transplant waiting lists and how the chances of developing disease might be minimized by appropriate risk factor modification. These approaches make sense when considering the allocation of cadaver kidneys, especially when organs are in short supply. Renal transplantation is generally cheaper than dialysis and death of a patient with a functioning kidney wastes the graft, thus negating the economic benefits of transplantation. Although not discussed, similar principles can be applied to detection and prevention of cerebrovascular, peripheral vascular, and left ventricular disease in patients considered for renal transplantation.

Assessing the risk of ischaemic heart disease

Perhaps not surprisingly, the presence of pre-transplant ischaemic heart disease has been shown to be a strong independent predictor of post-transplant cardiovascular events [5]. It therefore seems likely that operative risks could be minimized and graft survival improved if patients with established coronary disease were denied access to transplant waiting lists. In many cases, the presence of coexistent ischaemic heart disease will be clinically apparent. Guidelines drawn up by the American Society of Transplant Physicians recommend that individuals with angina pectoris, a history of myocardial infarction or congestive cardiac failure should undergo coronary angiography before any consideration is given to renal transplantation [6].

Many uremic patients will have clinically silent disease. Since it is generally not practical to perform coronary angiography on all individuals considered for transplant listing, other approaches have been recommended. These include stratification of asymptomatic patients based on the level of risk (as discussed below) and the use of non-invasive tests to pre-select patients in whom more detailed investigation is appropriate [6]. Pre-selection should increase the utility of screening tests that are likely to be more effective in a population where the incidence of the disease is high.

Such an approach proved to be effective in a prospective study of 189 consecutive patients referred for transplantation. Those without risk factors received no further cardiac investigation, whilst those considered at risk on the basis of clinical characteristics underwent thallium myocardial scintigraphy. Over a mean follow-up period of 47 months, cardiac mortality was considerably higher in the latter group (17 vs 1%, \( P < 0.001 \)). The presence of reversible or fixed perfusion defects on thallium scans allowing further stratification of patients according to the risk of cardiac mortality [7].

With or without patient pre-selection, the ideal screening strategy for high-risk asymptomatic patients has not been established. Whilst the use of exercise electrocardiography, thallium scintigraphy and dopamine echocardiography have been reported, it is unclear whether these tests have sufficiently high positive and negative predictive values to allow accurate pre-selection of patients for coronary angiography [6].

Dopamine stress echocardiography looks the most promising with a reported sensitivity of 95% and specificity of 86% when compared to coronary angiography in a group of unselected patients with end-stage renal disease [8]. However, local expertise is likely to be an important factor in determining the success of a screening strategy and many renal units have developed their own protocols accordingly. Even when coronary angiograms are performed, the value of this test in predicting future acute coronary events in the context of chronic renal failure has not been established.

Minimizing the risk of ischaemic heart disease

The detection of coronary artery disease will not only deny some patients a place on the transplant waiting list, but will also identify those most likely to benefit from medical or surgical treatment. Both percutaneous transluminal coronary angiography (PTCA) and coronary artery bypass grafting (CABG) relieve symptoms of angina in patients with chronic renal failure. However, when compared to individuals without renal failure undergoing CABG, periprocedural morbidity and mortality are increased as are restenosis rates following PTCA [9]. In a retrospective comparison of the two procedures, patients undergoing CABG were shown to have a lower incidence of recurrent angina, myocardial infarction and sudden cardiac death [10]. However, at the present time, there are no data confirming that such intervention improves survival in chronic renal failure. Thus it is unclear whether patients who have undergone revascularization procedures should subsequently be reconsidered for transplant listing.

Ischaemic heart disease remains a major cause of morbidity and mortality in the post-transplant period, even when efforts are made to exclude patients with pre-existing disease. In one follow-up study, 23% of patients who survived with a functioning graft for 15 years developed de novo coronary artery disease during this period [5]. It is therefore clear that preventative strategies are required to minimize the risks of ischaemic heart disease following renal transplantation.

Many risk factors for atherosclerosis can be identified in patients with chronic renal failure and may help to explain the markedly increased incidence of premature ischaemic heart disease in these individuals. These include smoking, hypertension, diabetes mellitus, dyslipidaemia, increased oxidant stress, elevated procoagulant activity, and hyperhomocysteinaemia [9]. However, to date there have been no prospective studies designed to demonstrate that modification of any risk factor will reduce the frequency of cardiovascular events, either pre- or post-transplantation. In the absence of these data, it is tempting to extrapolate from our knowledge based on the general population.

However, this approach should be cautious, since some studies have failed to demonstrate that commonly recognized risk factors such as hypertension and hypercholesterolaemia are independently associated with the development of coronary artery disease in the post-
transplant period [5]. Current recommendations aimed at minimizing the risk of cardiovascular disease complicating chronic renal failure emphasize cessation of smoking, avoidance of weight gain, dietary and lifestyle modification, optimization of diabetic control and treatment of hypertension and dyslipidaemia [9]. Strategies could also include dietary vitamin supplementation to reduce homocysteine levels and oxidant stress, antiplatelet drugs to decrease thrombogenic risk and correction of post-menopausal hormone deficiency. To maximize any potential benefits, risk factor management should ideally begin early in the course of renal disease, rather than in the post-transplant period. Benefits could include an increase in the proportion of patients suitable for transplant listing and improvements in the survival of individuals with chronic renal disease.

Conclusions

Ischaemic heart disease remains a major cause of morbidity and mortality in patients with chronic renal failure and markedly reduces life expectancy following renal transplantation. The detection, prevention and treatment of this and other cardiovascular diseases has become a management priority in individuals considered for renal transplantation. Future research should aim to establish the relationship between recognized risk factors and cardiovascular endpoints, the impact of risk factor modification on cardiovascular morbidity and mortality and whether active screening and revascularization programmes extend the lives of individuals with chronic renal failure, whether or not they are transplanted.

References