Renal transplantation in South Africa

Treatment of end-stage renal disease (ESRD) in South Africa is an important public health issue. The prevalence of ESRD in South Africa is unknown. Data from Europe and the USA estimate the prevalence to be 790 and 1 400 per million population respectively.[1] The prevalence figures from the USA indicate a marked increase in the incidence of chronic renal failure (CRF) in the African American population, approximately fourfold greater than for the Caucasian American population, and thus the figures in South Africa are likely to approximate or exceed the US data. It is estimated from the Southern Africa Dialysis and Transplantation Registry that only about 99 cases per million population receive treatment.[2] There is therefore a huge shortfall of facilities to treat ESRD, and it is important to optimise treatment for ESRD in South Africa within the budgetary restrictions. Dialysis is not the solution. It is very expensive and offers treatment to only a small number of patients due to limited facilities and expense. Transplantation, on the other hand, is cost effective in the long term, offers the chance of full rehabilitation and can be offered to a greater number of patients provided that there is a sufficient supply of organs. Dialysis should only be seen as a staging procedure to transplantation in South Africa.

The National Department of Health (DOH) has produced guidelines for the provision of dialysis and transplantation, emphasising the following points. Firstly, there must be equitable access to treatment for all who require it. Secondly, the provision of dialysis and transplantation is very costly and therefore treatment for all is currently unaffordable. Consequently some degree of selection is needed. The DOH has indicated in the guidelines that the following considerations are the most important in selecting patients for treatment: (*i*) suitability for transplantation; (*ii*) age less than 65 years; (*iii*) compliance with treatment; and (*iv*) absence of other significant pathology that will interfere significantly with treatment.

It is vital that the results of transplantation are documented in South Africa to ensure optimal use of scarce resources. Most studies have originated from Europe or the USA. The Southern Africa Dialysis and Transplantation Registry has documented dialysis and transplant outcomes in South Africa, but the last reliable report was issued in 1994.[2] It is therefore timely that in this issue of the *Journal* Moosa presents a paper documenting the results of 542 patients receiving 623 cadaver transplants at the renal unit, University of Stellenbosch and Tygerberg Hospital from 1976 to 1999.[3] This is the first comprehensive paper from a single South African centre analysing transplant results over an extended period, and it focuses primarily on the impact of age, gender and race. Previous studies have suggested that older patients, blacks and women may have poorer outcomes. The reasons for these different outcomes are not entirely clear. It has been suggested that older people may be more prone to complications of immunosuppression due to declining immune function and altered drug metabolism with increased immunosuppression and susceptibility to infection.[4,5] The impact of gender on patient survival is controversial. Tröppmann *et al.*[6] and Gorlén *et al.*[7] reported increased mortality in women compared with men, but Arend and co-workers[8] reported a lower mortality rate. Possible explanations for the higher mortality in women include the presence of preformed cytotoxic antibodies from prior pregnancies resulting in increased likelihood of rejection, and different requirements with regard to immunosuppressive drugs. Blacks may have poorer outcomes because of lower socioeconomic conditions,[9,10] less HLAmatching of organs[10] and more severe hypertension,[11] which potentially impact on transplant outcomes.

The issues of race, gender and age are particularly important in South Africa for historical reasons. Blacks, women and the elderly are often the most marginalised sectors of our society. In addition the effects of immunosuppression on infectious diseases such as tuberculosis (TB) are important issues in a developing country.

The results of the paper presented by Moosa are relevant to renal transplantation in South Africa. In essence the paper found that there were no ethnic differences in outcome, but there was increased mortality in women and patients older than 40 years. Graft survival was good provided that it was censored for patient mortality.

In contrast to a previous report from the Baragwanath group[12] the finding by Moosa that there were no ethnic differences in outcomes is good news. However, there may be several reasons for this finding. The patients from Tygerberg Hospital are a highly selected group, which would tend to minimise the effects of socioeconomic deprivation. In addition because of the small donor pool in South Africa the majority of patients receive poorly matched cadaver transplants regardless of ethnicity.

The high mortality seen in women and in patients older than 40 years is a worrying problem and presents many challenges to nephrologists. In most centres worldwide the two leading causes of death are cardiovascular (CVS) complications and infection. These findings are confirmed by Moosa. In his report 36.1% and 40% of deaths were due to CVS disease or infection respectively.

It is often not recognised that patients with chronic renal failure are at high risk of CVS complications even in the absence of diabetes. It is now well established that an elevated creatinine and/or albuminuria are powerful independent CVS risk factors,[13-15] and these parameters have been incorporated in

the new European Hypertension Guidelines for CVS risk stratification.[16] This risk is probably due to a combination of longstanding hypertension, lipid abnormalities, diabetes mellitus and insulin resistance among other factors.

It is important to grasp that CVS disease is an important preventable cause of death. In general patients with renal disease have a 10-year CVS risk greater than 30%.[16] This implies that primary prevention of CVS disease is cost effective and the majority of patients should receive optimal blood pressure control (BP< 130/80 mmHg), statins to lower cholesterol and antiplatelet drugs like aspirin. However, in the state sector CVS therapy prevention is fraught with problems. Statin therapy is available only to a minority with familial hypercholesterolaemia and modern antihypertensive therapy is often simply unobtainable. It seems penny wise pound foolish to invest so much money, expertise and effort on dialysis and transplantation, only for the patient to die of CVS complications due to lack of availability of essential CVS drugs. Policy decisions based on drug costs alone rather than overall cost benefits seem to be rather short sighted.

Infection ranks with CVS disease as the other major cause of death in patients with ESRD especially during the transplant period due to the effects of immunosuppressive drugs. There is clearly a fine balance due to under or over immunosuppression, which may result in either rejection or susceptibility to infection respectively. Moosa found that women and patients older than 40 years had a higher mortality and suggests that this may be in part due to changes in the pharmacokinetics and dynamics in these groups. This is a reasonable hypothesis and there is an important need to explore this issue in special populations such as women and the elderly.

Death due to infection, like CVS disease, is also potentially preventable. In transplant patients this is generally due to opportunistic infections such as TB, *Pneumocystis carinii* pneumonia (PCP), and cytomegalovirus infection (CMV). In Moosa's paper these infections were not a major problem. TB or PCP caused only 9.7% and 5% of deaths due to infection respectively.[3] There were no reported cases of CMV infection. These findings are consistent with their policy of giving prophylaxis for TB, PCPand CMV. The majority of deaths were due to lung infection and septicaemia. We are not given further details of the exact causes of these infections and an important weakness of this paper is the lack of postmortem findings in these cases. It is the author's experience that disseminated TB or CMV may be an unexpected finding at postmortem examination. Nevertheless, infection in transplant patients should be seen as a life-threatening complication and investigated and treated aggressively.

In conclusion, Moosa should be congratulated on carefully documenting the outcomes of renal transplantation at Tygerberg Hospital from 1976 to 1999. The important findings in this paper are that outcome of renal transplantation in blacks is the same as for other ethnic groups, but survival is worse in women and patients older than 40 years. Graft survival was good provided that it was censored for death. These findings present important challenges to the practising nephrologist in South Africa.

Brian Rayner

Divisions of Nephrology and Hypertension
Groote Schuur Hospital and
University of Cape Town

1. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiac disease in chronic renal disease. *Am J Kidney Dis* 1998; **32:** S112-S119.
2. South African Dialysis and Transplantation Registry. *Combined Report of Maintenance Dialysis and Transplantation in the Republic of South Africa.* 1994.
3. Moosa MR. The impact of age, gender and race on patient and graft survival after renal transplantation: a developing country experience. *S Afr J Med* 2003; **93:** 689-695.
4. Doyle SE, Matas AJ, Gillingham K, Rosenberg ME. Predicting clinical outcome in the elderly renal transplant recipient. *Kidney Int* 2000; **57:** 2144-2150.
5. Hirokawa K. Understanding the mechanism of age-related decline in immune function. *Nutr Rev* 1992; **50:** 361-366.
6. Troppmann C, Gillingham KJ, Benedetti E, *et al.* Delayed graft function, acute rejection, and outcome after cadaver renal transplantation. The multivariate analysis. *Transplantation* 1995; **59:** 962-968.
7. Gorlén T, Abdelnoor M, Enger E, *et al.* Long term morbidity and mortality after kidney transplantation. *Scand JUrol Nephrol* 1992; **26:** 397-401.
8. Arend SM, Mallat MJ, Westendorp RJ, van der Woude FJ, van Els LA. Patient survival after renal transplantation; more than 25 years follow-up. *Nephrol Dial Transplant* 1997; **12:** 1672-1679.
9. Young CJ, Gaston RS. Renal transplantation in black Americans. *N Engl J Med* 2000; **343:** 1545-1552.
10. Butkus DE, Meydrech EF, Raju SS. Racial differences in the survival of cadaveric renal allografts. Overriding effects of HLAmatching and socioeconomic factors. *N Engl JMed* 1992; **327:** 840-845.
11. Cosio FG, Dillon JJ, Falkenhain ME, *et al.* Racial differences in renal allograft survival:the role of systemic hypertension. *Kidney Int* 1995; **47:** 1136-1141.
12. Modiba MC, Mzamane DV, Pantanowitz D, *et al.* Renal transplantation in black South Africans: the Baragwanath experience. *Transplant Proc* 1989; **21:** 2010-2011.
13. Jensen FS, Feldt-Ramussen B, Strangaard S, Schroll M, Borch-Johnsen K. Arterial hypertension, microalbuminuria, and risk of ischaemic heart disease. *Hypertension* 2000; **35:** 898-903.
14. Bigazzi R, Bianchi S, Baldari D, Campese VM. Microalbuminuria predicts cardiovascular events and renal insufficiency in patients with essential hypertension. *J Hypertens* 1998; **16:** 1325-1333.
15. Ruilope LM, van Veldhuisen DJ, Ritz E, Lüsher TF. Renal function; the Cinderella of cardiovascular risk profile. *J Am Coll Cardiol* 2001; **38:** 1782-1787.
16. Guidelines Committee. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; **21:** 1011-1053.