

Kidney Transplantation in Septuagenarians: 70 Is the New 60!



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Individuals 65 years or older account for 19.6% of the US population. In 2016, there were 296,229 patients aged 65 years or older, representing 41% of the total prevalent end-stage renal disease (ESRD) population. Moreover, 40% of all annual incident ESRD occurs in this age segment.¹ Despite the high incidence and prevalence of ESRD in the elderly and the known benefits of kidney transplantation over dialysis, only 20% of all transplant recipients were 65 years or older over the past 5 years (Figure 1). Various explanations have been offered for this finding. First, almost one-half of all patients older than 60 years on the waitlist for a kidney transplant will die before ever receiving a transplant.² Second, although outcomes of kidney transplantation in older patients have generally been favorable, detailed accounts of these outcomes from

nonregistry data are limited. The age cutoff used to study outcomes in older patients also has been variable among different studies, and the various risk factors that predict clinical outcomes in elderly transplant patients are not fully elucidated.³ Certainly, the presence of multiple comorbidities and potential alteration of the immune system, known as “immunosenescence” mortality, in elderly patients with ESRD is not trivial during the first year of transplant. Given the paucity of literature on this topic, there is a need to determine risk factors, modifiable and nonmodifiable, to predict early mortality and graft failure.

Lemoine *et al.*,⁴ in this issue of *Kidney International Reports*, examined various baseline and postoperative risk factors associated with the composite of early death and graft failure at 1 and 14 years after kidney transplantation in 171 patients from 4 medical centers in northwest France. The 1-year patient survival was 90.1%, paralleling 89.0% published by Heldal *et al.* (see [Supplementary Reference](#)) and higher than 80.9% following deceased donation reported by Rao *et al.*⁵ This superior

outcome occurred despite the lower rate of living donor kidney transplants. Indeed, the rates of living donation in France are lower than in the United States and should be further encouraged for patients in this age group.

Over the 14-year span of the study, there were 40 deaths, approximately one-half of which occurred within the first year after transplantation, and 6 within the first 3 months. This higher mortality in the early posttransplant period is well documented. Elderly recipients have a shorter life expectancy and more frequently die with a functioning graft. In their analysis, recipient death was the leading cause of graft loss. Analysis of recipients older than 70 in the Scientific Registry of Transplant Recipients revealed a patient’s risk of death at 45 days after transplantation was 2.26 times greater than for those on the waiting list. Importantly, this risk declined rapidly, and by 125 days, the mortality risk for both groups was equal. Mortality risk reduction was most pronounced long-term (>18 months) and was 56% lower for transplant recipients.⁵ However, as older patients with ESRD may not be referred or accepted as a kidney transplant recipient, the accuracy of these results is subject to selection bias. With the new allocation system that gives more points to those who have been on dialysis longer, we suspect it will take longer after transplantation to accrue a survival advantage over those waitlisted.

Infection was the most frequent cause of death; 58.8% at 1 year and 47.5% at 14 years. These results are in line with data from Lai *et al.*⁶ in which infection was responsible for 55.2% of patient mortality at

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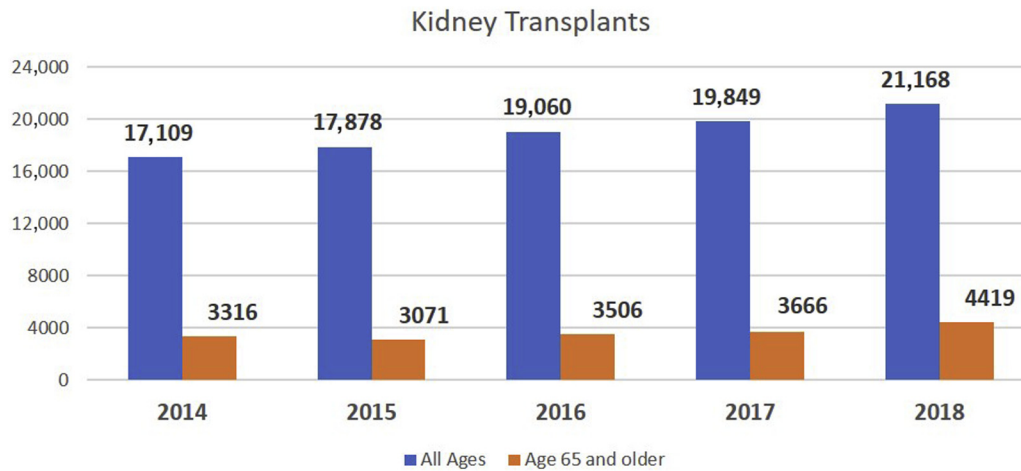


Figure 1. Annual number of elderly (≥ 65 years) receiving kidney transplantation in the US.

5 years. Of the infections reported by Lemoine *et al.*⁴ within the first year of transplantation, bacterial infections were the highest at 69.6%, evenly split between recurrent urinary tract infections (18.7%) and pneumonitis (19.6%). Viral infections were the second most frequent at 13.3%, led by cytomegalovirus infections. The authors raise a legitimate proposal to examine the potential benefit of prolonged cytomegalovirus prophylaxis in elderly kidney transplant recipients.

Given the increased infection risk with aging and its impact on mortality, it may be reasonable to consider less intense or no induction and minimize maintenance immunosuppression. However, the consequences of acute rejection may be more deleterious in the elderly. Lemoine *et al.*⁴ reported both HLA antibodies (odds ratio 2.1; 95% confidence interval [CI] 1.04–4.2) and biopsy-proven acute rejection (odds ratio 2.77; 95% CI 1.2–6.3) were independent risk factors for the composite of death or graft failure within the first year of transplant.

The choice of induction agent in the elderly kidney transplant recipient remains unclear. Gill *et al.*⁷ examined the risks of rejection at 1 year, functional graft loss,

and death by induction agents in kidney transplant recipients older than 60 years. Their study revealed a higher risk of rejection and graft loss with basiliximab versus antithymocyte globulin in high-risk recipients (hazard ratio 1.27; 95% CI 1.02–1.6). Certainly, finding the balance between infection and acute rejection is challenging. Future prospective trials comparing induction immunosuppression regimens in patients older than 70 may aid in delineating this risk-benefit profile.

Cardiovascular disease was highlighted as an independent risk factor for both graft failure and early death. Lemoine *et al.*⁴ showed arrhythmias, specifically atrial fibrillation and/or flutter, and congestive heart failure were significant cardiovascular events in the geriatric population. Similarly, Faravardeh *et al.*³ showed congestive heart failure at baseline evaluation was associated with graft failure (hazard ratio 3.85; 95% CI 1.85–8.03) and death (hazard ratio 1.84; 95% CI 1.2–2.83). In addition, in their 3-year mortality prediction model, Grams *et al.*⁸ found both congestive heart failure (odds ratio 0.74; 95% CI 0.65–0.85) and cardiac arrhythmia (odds ratio 0.64; 95% CI 0.55–0.75) associated with reduced 3-year

posttransplant survival in older adults. Interestingly, Lemoine *et al.*⁴ demonstrated that a left ventricular ejection fraction on echocardiography equal to or less than 56% was independently associated with early death or graft failure but is subject to verification bias. This is the first study to examine left ventricular ejection fraction as a potential predictor of the composite outcome of patient death or graft loss in patients with congestive heart failure. Furthermore, it reiterates the importance of properly evaluating the preoperative cardiovascular status of elderly transplant recipients. More importantly, clinicians should not underestimate these patients' cardiovascular comorbidities after the transplant.

Moving forward, distinctive issues needing further evaluation include the impact of kidney transplantation on the elderly patient's quality of life. Frailty has been defined as a phenotype of decreased physiologic reserve and vulnerability to stressors. Prior work has demonstrated that frailty is associated with delayed graft function, longer hospital stays, higher readmission rates, immunosuppressive intolerance, and mortality.⁹ Like frailty, cognitive impairment is highly prevalent

and poorly recognized before kidney transplantation in high-risk elderly patients. Severe cognitive impairment could increase the risk of poor outcomes and require the provision of strong social support after transplantation. Screening for frailty and cognitive impairment should become routine and more structured in elderly patient evaluation.

Collectively, the evidence supports a survival benefit in the elderly compared with dialysis. With most data focusing on short-term graft and patient survival, Lemoine *et al.*⁴ identified immunosuppression, infection, and cardiovascular disease as the predominant risk factors for these outcomes. We wonder whether incorporating frailty and cognitive function would provide better prognostication in this ever-expanding segment of renal transplant recipients.

DISCLOSURE

All the authors declared no competing interests.

SUPPLEMENTARY MATERIAL

Supplementary References.

Supplementary material is linked to the online version of the paper at www.kireports.org.

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