

Kidney Transplantation Among the Elderly: Challenges and Opportunities to Improve Outcomes



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Elderly patients (>65 years old) represent the fastest growing population among the ESRD patients and those awaiting kidney transplantation. There is ample evidence to suggest that kidney transplant in the elderly population offers the best chance of survival and improves health-related quality of life compared to remaining on dialysis. Although all these emerging facts are encouraging, this population brings with them complex medical problems including frailty, cognitive impairment, and multiple comorbidities. These issues can be barriers to transplantation and threaten the well-being of the patients after transplantation. Furthermore, aging results in changes to the immune system and affects the pharmacokinetics of immunosuppressants. All these changes can increase risk of complications such as infections and malignancy. Because death with a functioning graft is a common cause of graft loss, the new kidney allocation system has been implemented in an attempt to maximize allograft utilization and minimize unrealized graft years. This may result in longer wait-times for the elderly. In this review, we will highlight the barriers to kidney transplant, characterize transplant-related issues in the elderly, and propose alternative strategies under the new allocation system.

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The definition of an “elderly” person is somewhat arbitrary and usually refers to the age when one receives pension. Due to this lack of consensus in the age cutoff, present studies involving elderly patients suffer from a lack of uniformity and generalizability. In general, however, most studies define elderly patients as patients aged above 60 or 65 years. According to the most recent US Renal Data System annual report, the number of incident ESRD cases aged more than 65 years has increased dramatically over the past decade. Currently, elderly patients make up almost half the incident dialysis patients in the United States.¹ It is, therefore, not surprising that patients aged older than 65 years represent the fastest growing group on the wait-list with the numbers increasing from 6991 (12.9%) in 2003 to 20,115 (20.8%) in 2013.² This trend, although encouraging, fails to highlight the fact that the percentage of elderly patients wait-listed or transplanted within the first year of dialysis (9.9%) is still lower compared with the overall rate of 15.8% and is much lower compared to their younger counterparts, perhaps reflecting the reluctance and hindrance to refer elderly patients for transplantation (Fig. 1).¹ Advanced age per se is not a contraindication for transplantation, in fact, mounting evidence suggests that transplantation improves survival and quality of life in this group of patients.

The immunologic and metabolic changes that occur with aging put elderly transplant recipients at a heightened risk for infections and malignancies after transplantation. Managing the immunosuppression in this group of patients is a fine line between adequate and over immunosuppression.³ This review will highlight barriers to kidney transplantation in elderly patients with advanced CKD and characterize transplant-related issue for the elderly. We will also review the outcomes of kidney transplantation among the elderly and the influence of the new allocation policy on kidney transplant in the elderly.

BARRIERS TO KIDNEY TRANSPLANTATION IN ELDERLY TRANSPLANT CANDIDATE

With the mounting evidence that kidney transplantation offers improved survival and quality of life in ESRD patients, more elderly patients are currently being referred for transplant evaluation. This population of patients brings with them a unique set of problems, including frailty, cognitive impairment, and comorbidities less commonly seen in the other age groups.^{4,5} All these factors have been associated with morbidity and mortality after transplant.⁶ Geriatric assessment tools may provide useful information in evaluating the physical and cognitive function in these patients, as the standard workup does not always test for such things as frailty and cognitive function. Geriatric assessment tools that can be used as part of the workup include the Charlson Comorbidity Index, which assigns a score for each comorbid condition, and the sum of the scores from the different comorbid conditions is then used to predict mortality, the Lawton scale for instrumental activities of daily living, testing hand grip strength, evaluating gait speed, and administering either the mini-mental status examination or the Montreal Cognitive Assessment.⁷ The development of a model using the aforementioned assessment tools may help physicians counsel their elderly patients about

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challenges they may face after transplantation and whether kidney transplantation is the best choice for them.

Frailty and Transplantation

There have been a number of instruments developed to assess frailty. Frailty as a measure of physiological reserve was first described and validated by Fried and colleagues⁸ in the geriatric population. The concept of a frailty phenotype created by Fried and colleagues consists of 5 domains including shrinking (weight loss), weakness (decrease grip), exhaustion (effort and motivation), low physical activity, and slowed walking speed (15 feet). Each domain yields a score of 1 when present, and the higher the score, the higher the degree of frailty.^{8,9} In a systematic review of all the different tools used to assess frailty, de Vries and colleagues¹⁰ found that the frailty index was one of the better instruments developed to assess frailty as it covers all the frailty factors. The frailty index is a quantitative measure defined as the proportion of deficits (symptoms, signs, functional impairments, and laboratory abnormalities) present in an individual, which can be used to estimate survival probability.¹¹

Frailty has been shown by Makary and colleagues to be a risk factor for postoperative complications (odds ratio [OR] 2.54; 95% confidence interval [CI] = 1.12-5.77), prolonged hospital stay (OR 1.69; 95% CI = 1.28-2.23) and discharge to a skilled nursing facility (OR 20.48; 95% CI = 5.54-75.68). In the renal population, McAdams-Demarco and colleagues¹² showed that frailty is 5× higher in hemodialysis patients than in the community-dwelling older adults. The same author went on to show that in kid-

ney transplant recipients, the presence of frailty was associated with early hospital readmission within 30 days of kidney transplant discharge (45.8% vs 28%, $p = .005$)¹³ and with mortality, whereby frail recipients had a 2.17-fold increased mortality compared to non-frail recipients (95% CI = 1.01-4.65).¹⁴ Interestingly, this association was not due to age alone as younger, frail patients also had higher mortality compared to their non-frail counterparts. Although these data do not address the question of whether frail patients should remain on dialysis or be transplanted, it does highlight the need to risk stratify and possibly optimize the functional status of transplant candidate especially elderly ESRD patients before transplantation. Studies are needed to address whether improvement in frailty improves transplant outcomes.

Cognitive Impairment and Transplantation

The association between cognitive impairment and CKD is increasingly being recognized.^{15,16} The underlying mechanism is unclear, but possible mechanisms

proposed include silent ischemia and neural toxicity due to uremic toxins.¹⁶ The proportion of patients with cognitive impairment increases with increasing age; hence, with more elderly ESRD patients being referred for transplantation, transplant physicians will need to decide whether these patients are suitable candidates for transplantation. There is a scarcity of literature regarding the transplantation of patients with any degree of cognitive impairment. Available data suggest that patients with mental impairment have comparable outcomes compared to normal controls with minimal allograft loss due to noncompliance.^{17,18} However, the transplantation of patients with cognitive impairment will require significantly more resources and strong social support to ensure that the patients are compliant with their medications after transplant.

Comorbidity and Transplantation

Comorbidities such as diabetes and hypertension are commonly seen in patients with ESRD. With increasing age, the prevalence of comorbidities increases as well.

Not surprisingly, patients with more comorbidities have a higher risk of mortality after transplantation as shown in 2 separate studies by Grosso and colleagues and Karim and colleagues, respectively. The authors retrospectively studied 223 first time deceased donor kidney transplant recipients between 2000 and 2007 and found that increasing Charlson Comorbidity Index was associated with increased risk of death after transplantation. (hazard ratio [HR] 3.87; 95% CI = 1.06-14.06)^{19,20} Similarly, Karim and colleagues reviewed

19,103 patients transplanted in England from April 2001 through March 2012 and found that patients over 70 had an increased risk of death with a deceased donor transplant as time from transplantation progressed. At a median follow-up of 4.4 years, the risk of death was higher with certain comorbid conditions such as congestive heart failure, 60%, and peripheral vascular disease, 57.1%, compared with diabetes, 38%. The overall risk of death was attenuated if these elderly patients received a living donor vs a deceased donor transplant (20.7% vs 34.9%, $p = .002$).²¹ The current allocation system takes into account age, duration on dialysis, diagnosis of diabetes, and history of prior solid organ transplant. It does not take into account other comorbidities prevalent in the elderly population; thus, the onus of deciding whether the patient is a suitable candidate for transplant and whether this scarce resource is best used in elderly patients with limited life expectancy is on the evaluating physician. Wu and colleagues examined 266 patients aged more than

CLINICAL SUMMARY

- Kidney transplant in the elderly offers the best survival and improves health-related quality of life compared to remaining on dialysis.
- Elderly patients have complex problems such as frailty, cognitive impairment, and multiple comorbidities, all of which, threaten patient and allograft survival after transplant.
- Aging results in changes to the immune system and affects the pharmacokinetics of drugs, which may increase the risk of complications such as infections and malignancies after transplantation.
- The new allocation system, which emphasizes longevity matching, may result in longer wait-times for the elderly patients; hence, alternative strategies should be pursued.

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