Geriatric Issues

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Kidney Transplantation in the Elderly

By Aneesha Shetty and John J. Friedewald

Epidemiology

Although there has been an overall slowing of incident cases of ESRD in the United States during the past several years, the elderly population continues to have the highest incident rates of ESRD (1) (Figures 1 and 2). This has significant implications for transplant centers, which are seeing a continual increase in the age of potential transplant recipients coming for evaluation. The continuing accumulation of data on outcomes in these patients should better inform the important addition to the pretransplantation screening process in elderly candidates. As shown by Fried et al. (4) using data from the Cardiovascular Health Study (Figure 3), evaluation of frailty domains would be an important addition to the pretransplantation screening process. Evaluation of activity, with poor outcomes in elderly transplantation patients and should be carefully evaluated during the pretransplantation screening process. Evaluation of activities of daily living and tests like “Timed Up And Go” are often used as a measure of disability. Assessment of cognitive impairment is crucial in elderly transplant recipients, given the higher risk for dementia resulting from vascular disease and metabolic derangement. Elderly patients are also more at risk for depression and are often in need of greater social support compared with their younger counterparts, and hence should undergo a careful psychosocial evaluation.

Frailty

Frailty has been recently shown to be an independent predictor of poor outcomes after kidney transplantation, including poor graft function, increased hospitalizations, and perioperative complications (3). The frailty phenotype meets three or more of the following five criteria: weight loss, weakness, slow gait, and decreased physical activity (Table 1) and can be evaluated by the use of different measures. Although frailty, typically characterized by sarcopenia, is often considered a precursor to disability, the relationship between frailty, disability, and comorbidity is complex, as shown by Fried et al. (4) using data from the Cardiovascular Health Study (Figure 3). Evaluation of frailty domains would be an important addition to the pretransplantation screening process in elderly candidates and may allow for better risk stratification and decisions about candidacy.

Candidacy

Kidney transplantation remains the treatment of choice for ESRD in elderly patients, providing a survival advantage and better quality of life when compared with dialysis (2). This benefit is especially seen with early transplantation, often facilitated by shorter wait times with the use of kidneys from donors with Kidney Donor Profile Index (KDPI) higher than 85 or living donor transplants. However, the benefit of transplantation in the elderly is contingent on selection of the appropriate candidate. Advanced age is often considered a relative contraindication for transplantation, but there is much variability in the actual age limit for transplantation among transplant centers in the United States. Moreover, chronological age alone seems to be a less important predictor of poor outcomes after transplantation when compared with factors like comorbidity burden, disability, and frailty. Cardiovascular disease, risk of infection, and malignancy are associated with poor outcomes in elderly transplantation patients and should be carefully evaluated during the pretransplantation screening process. Evaluation of activities of daily living and tests like “Timed Up And Go” are often used as a measure of disability. Assessment of cognitive impairment is crucial in elderly transplant recipients, given the higher risk for dementia resulting from vascular disease and metabolic derangement. Elderly patients are also more at risk for depression and are often in need of greater social support compared with their younger counterparts, and hence should undergo a careful psychosocial evaluation.

Table 1. Frailty characteristics

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<th>B. Cardiovascular Health Study Measure*</th>
<th>C. Presence of Frailty</th>
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<tbody>
<tr>
<td>Shrinkling: Weight loss (unintentional)</td>
<td>Baseline: ≥10kg lost unintentionally in prior year</td>
<td>Positive for frailty phenotype: ≥ 3 criteria present</td>
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<tr>
<td>Sarcopenia (loss of muscle mass)</td>
<td>Grip strength: lowest 20% (by gender, body mass index)</td>
<td>Intermediate or prefrail 1 or 2 criteria present</td>
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<td>Weakness</td>
<td>“Exhaustion” (self-report)</td>
<td>Walking time/15 feet: slowest 20% (by gender, height)</td>
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<td>Keats/week: lowest 20%</td>
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Figure 1. Rates of ESRD in the US

Figure 2. US rates of ESRD by age group

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Allocation

In December 2014, after nearly a decade of deliberation, a new kidney allocation system (KAS) was put into effect by the Organ Procurement and Transplant Network (OPTN). The effect of this new KAS on the elderly was carefully considered by the OPTN Kidney Committee. Elderly patients have received an increasing percentage of deceased donor kidneys over the past 2 decades based on their increasing share of the waitlist (Figure 4). Several policy components were predicted to lead to a decrease in the number of deceased donor kidneys allocated to candidates over age 65. The early returns from the first 5 months with the new KAS confirm the predictions (Figure 5), with a slight decrease in the percentage of deceased donor kidneys allocated to candidates over age 65 (5). This is primarily due to longevity matching, in which the 20 percent of kidneys predicted to function the longest based on the KDPI are allocated first to candidates in the top 20 percent of expected posttransplant survival (EPTS) (6, 7). Candidates over the age of 55 are not included in the top 20 percent of candidates based on the EPTS. Whether older candidates (and transplant centers) increase their acceptance of kidneys with shorter predicted longevity, from donors with KDPI greater than 85, remains to be seen. This approach has worked well in the Eurotransplant program but has not been as widely accepted in the United States. Discard rates for kidneys with KDPI are still as high as 60 percent (Figure 6). Coming to terms with the risks and benefits of transplanting higher-risk kidneys (in terms of KDPI) into higher-risk elderly candidates will be critical in the coming years to maintain timely access to deceased donor kidneys for older transplant candidates. It also highlights the growing importance of living kidney donation, not just for the older population but for all candidates.

Living donation

Expanding living donor kidney transplantation is an effective way to shorten wait times and improve outcomes among elderly ESRD patients. One way to achieve this goal is to increase the number of older living kidney donors. Although donors older than 65 years constitute a very small percentage of all living kidney donors, over the past decade the number of older living kidney donors has increased (8). Published data suggest, not surprisingly, that transplants from younger living donors have better outcomes than those from older donors. However, a review of registry data by Gill et al. (9) focusing on 1,133 transplants in recipients older than 60 years from relatively older living donors (>55 years) showed overall superior graft and patient survival compared with standard criteria donor (SCD) and expanded criteria donor (ECD) deceased donor transplants. When further stratification was made by donor age, allograft survival for recipients of kidneys from living donors 55 to 64 years old was similar to that achieved with younger living donor kidneys (Figure 7). Living donors aged 65 and older showed graft survival comparable with that of SCD transplants and superior to that of ECD transplants. Although long-term follow-up of donor outcomes is limited, there is no evidence to suggest that older donors have poorer outcomes than their younger counterparts, thus making pursuing living kidney donation relatively safe in selected elderly individuals.

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Kidney Transplantation

Access to transplantation in a highly regulated environment

A new crisis is looming in the field of kidney transplantation. Transplant center access to transplantation in a highly regulated environment continued from page 21

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Aging affects the immune system in multiple ways and is associated with inflammation, altered innate immunity, and altered cell-mediated immunity (10, 11). The latter is characterized by decline in the production of naive T cells, accumulation of senescent and exhausted T cells, and decline in T cell diversity. This suggests that the mechanisms governing rejection may differ in older and younger recipients. Delayed graft function, acute rejection with profound impact on graft function, and exaggerated chronic graft changes are more common in elderly transplant recipients. However, these patients are also more susceptible to infections and malignancies after transplantation, and this emphasizes the importance of a finely balanced immunosuppressive regimen.

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Management of immunosuppression in elderly transplant recipients

Aging affects the immune system in multiple ways and is associated with inflammation, altered innate immunity, and altered cell-mediated immunity (10, 11). The latter is characterized by decline in the production of naive T cells, accumulation of senescent and exhausted T cells, and decline in T cell diversity. This suggests that the mechanisms governing rejection may differ in older and younger recipients. Delayed graft function, acute rejection with profound impact on graft function, and exaggerated chronic graft changes are more common in elderly transplant recipients. However, these patients are also more susceptible to infections and malignancies after transplantation, and this emphasizes the importance of a finely balanced immunosuppressive regimen. Many transplant centers use interleukin-2 receptor antagonists for induction over lymphocyte-depleting agents, along with maintaining lower drug levels for maintenance immunosuppression to achieve a favorable risk-to-benefit profile. Other factors to be considered in the treatment of elderly kidney transplant recipients include drug interactions in the setting of polypharmacy and physiological impact of age on drug pharmacokinetics, pharmacodynamics, and adverse effects.

Summary

We have an aging ESRD population that presents specific challenges to the transplant community. There are less exaggerated differences in survival when transplantation is compared with dialysis in older patients. Yet, transplantation still may be the preferred therapy for ESRD in many elderly patients. Determining candidacy with objective measures of frailty and disability are crucial to supplement the traditional listing criteria. Maintaining access for older candidates is a looming issue that will need to be resolved at the federal level, but nephrologists must continue to advocate for their patients in this arena. Last, the approach to immunosuppression must be carefully tailored to the aging immune system, to avoid toxicity and maximize efficacy.

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Reference


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