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Receiving a Kidney Transplant in the Ninth Decade of Life

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Abstract

Kidney transplantation in individuals in their ninth decade of life was once unthinkable, but in recent years an increasing number of octogenarians have been considered for and received kidney transplants. Although this trend validates that there is no age limit beyond which kidney transplantation is prohibitive, the overall experience of kidney transplantation among octogenarians remains limited. The early experience with kidney transplantation in recipients aged 80 years or older has been reasonably successful in regards to patient and graft survival, prompting us to reevaluate the merits of kidney transplantation among elderly individuals with end-stage renal disease. In this article, we review the literature concerning kidney transplantation in the elderly and discuss the outcomes associated with transplantation in those in their ninth decade of life. **(Trends in Transplant. 2011;5:121-7)**

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Key words

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Introduction

There are an increasing number of older patients in the end-stage renal disease (ESRD) population. United States Renal Data Systems (USRDS) data report that there were 26,852 patients with ESRD who were aged ≥ 80 years in 2000; by 2008, this number increased to 46,080[1]. Factors such as an increased life expectancy of the general population and advances in the treatment of cardiovascular diseases and malignancy are thought to have played a role in the increasing prevalence of the elderly among the ESRD population[2]. The vast majority of octogenarians with ESRD are maintained on dialysis for renal replacement therapy and only a small number are considered kidney transplant candidates. Nevertheless, the kidney transplant waiting list in the USA has seen an increasing number of octogenarians join its ranks in the past decade. In 2000, only 32 candidates aged ≥ 80 were listed active on the waiting list; this number increased over sevenfold to 238 by the end of 2008[1]. Of these, only a select few became kidney transplant recipients.

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Although more octogenarians have become kidney transplant candidates in recent years, the above statistics indicate that less than 1% of octogenarians are considered for kidney transplantation in the USA, as defined by registration for kidney transplantation. Clearly, kidney transplantation is reserved for only a highly selected segment of the octogenarian population. Inevitable questions therefore arise: what factors are associated with waitlist mortality or successful kidney transplantation among the elderly? How do post-transplant outcomes among octogenarians compare with those of younger populations? Should the nephrology community place greater emphasis on kidney transplantation for octogenarian ESRD patients? In an effort to address these questions, we review the literature concerning kidney transplantation in the elderly and discuss the outcomes associated with transplantation in those in their ninth decade of life.

Access to the Kidney Transplant Waiting List and Transplantation

There are limited data addressing kidney transplant waitlist practices in octogenarians; consequently, an assessment of waitlist practices for octogenarians must be extrapolated from data concerning other elderly candidates. In the elderly, access to transplantation can be limited by either a reduced likelihood of waitlisting and/or a decreased probability of transplantation once waitlisted. When access to transplantation is defined as registration for deceased-donor transplantation or receipt of a live-donor kidney transplant, access decreases with advancing age and is limited to a greater extent among elderly women than men[3]. Each decade increase in age is associated with a 30% decrease in registration for deceased-donor transplantation or receipt of a live-donor kidney transplant[3]. In particular, females older than 75 have a 59% lower access to transplantation compared to age- and comorbidity-matched males[3]. These disparities may be related to negative patient or provider characterizations of overall health, whether true or unrealized, and it is postulated that elderly women are more likely than men to be characterized as too frail for transplantation[3]. Once waitlisted, there is no difference in the likelihood of transplantation between elderly women and men[3].

In a single-center study out of Glasgow, waitlisting practices and outcomes among 1,513 incident dialysis patients categorized by age from 1992 to 2008 were examined[4]. Of the 319 patients ≥ 75 years old, only 0.8% (three patients total) were listed for a deceased-donor transplant within one year of starting dialysis and no patients aged ≥ 75 received a deceased-donor transplant within five years of dialysis initiation. Strikingly, only 12% of those aged ≥ 75 remained alive at the end of the follow-up period.

In comparison to the UK, where recipient age and age disparity between donor and recipient are weighted so as to prioritize allocation of younger donors to younger recipients, recipient age is not a factor in allocation of deceased-donor allografts ≥ 35 years old in the USA. Overall, older patients are less likely to receive a deceased donor transplant than their younger counterparts (RR of deceased-donor transplant, ≥ 60 vs. 18-39: 0.71; $p < 0.001$)[5], although older candidates in recent years have been more likely to receive a transplant than in years past. A recent USRDS study reported that incident ESRD patients aged 60-75 were twice as likely to receive a transplant in 2006 compared to 1995 (HR: 2.01; 95% CI: 1.85-2.19), although the cumulative probability of kidney transplantation in 2006 was still only 7.3% at three years[6]. This study did not restrict the population to waitlisted patients only, and therefore

it is probable that the majority of these patients were not realistic transplant candidates. Among waitlisted patients, the likelihood of death on the waiting list was lower in 2006 than in 1995 (HR: 0.74; 95% CI: 0.60-0.91).

A Scientific Registry of Transplant Recipients (SRTR) study investigated waitlist mortality and time to deceased-donor transplantation among 54,699 candidates ≥ 60 years old listed between 1995 and July 2007[7]. Of patients who were aged ≥ 70, 59% received a deceased-donor transplant within five years of listing. The five-year probability of deceased-donor transplantation among all candidates aged ≥ 60 listed in region 5, which carries the longest waiting times in the USA, was 49%. It is important to note that probability estimates for deceased-donor transplantation in this study were censored for death, delisting, and receipt of a living-donor transplant. Censoring for death and delisting can lead to an overestimate, whereas censoring for living-donor transplantation results in an underestimate of the probability of transplantation. Therefore, the reported probability of transplantation from this study may be misleading. This study also reported that the five-year probability of mortality among those aged ≥ 70 was 57%. This mortality figure may be overinflated, as subjects who received a transplant were censored from the analysis.

The above studies underscore that kidney transplantation is generally reserved for a select minority of elderly ESRD patients. Access to transplantation is limited by a low likelihood of waitlisting and a high probability of mortality once waitlisted.

Posttransplantation Patient and Graft Survival in the Elderly

The Eurotransplant Senior Program (ESP) provides an opportunity to evaluate outcomes associated with the elderly recipient of an older donor. The ESP was implemented in 1999 and designed to expand the deceased-donor pool by matching older donors with older recipients (both ≥ 65 years old). Kidneys are allocated locally according to wait time and blood group compatibility. A five-year analysis of patient and graft survival after the implementation of the ESP was published in 2008[8]. The ESP participants had lower five-year patient and graft survival compared to older recipients (60-64 years old) of younger kidneys and younger recipients of older donors (≥ 65 years old) allocated under the Eurotransplant Kidney Allocation System (ETKAS), but it should be noted that recipients were younger in the comparator groups and that mortality comparisons were not made with a concurrent waitlisted control group. Although age-matching of older donors to older recipients was associated with inferior outcomes than that of younger donors to older recipients, the ESP system may yet be beneficial for elderly recipients. There was a shorter waiting time to transplant (3.6 vs. 4.6 years for older recipients of younger kidneys; $p < 0.001$)[8], which might offset the lower graft survival observed among the ESP participants[9,10].

There is limited data concerning transplantation specifically in octogenarians. We previously reported posttransplantation outcomes among 199 kidney transplant recipients aged ≥ 80, comparing patient and graft survival to those of recipients aged 60-69 and 70-79[11]. The median age of patients in the ≥ 80 year-old category was 81 (25^{th}, 75^{th} percentile: 80, 82), and therefore observations gleaned from the ≥ 80 year-old group mainly represent recipients in their early 80s and are not necessarily applicable to those in their later 80s. Although surgical mortality is a principal concern of transplantation in the elderly, no difference in 30-day mortality was observed between the three groups

(HR ≥ 80 vs. 60-69: 1.67; 95% CI: 0.69-4.05) and overall mortality in all groups within the first 30 days was low (60-69: 1.4%; 70-79: 1.5%; ≥ 80: 2.5%). An increase in mortality among ≥ 80 year-old compared to 60-69 year-old recipients was not observed until 105 days posttransplantation (HR: 1.83; 95% CI: 1.03-3.25). Over the course of the two-year follow-up period, ≥ 80 year-old recipients had a 2.42-times increased risk of death versus 60-69 year-olds (95% CI: 1.91-3.06). Cumulative survival among octogenarian recipients at two years was 73%, which is better than that reported for an 80-84 year-old dialysis patient[1].

Despite proportionally more expanded criteria donors (ECD) and fewer living-donor transplants in the ≥ 80 year-old group, there was no difference in death-censored graft survival at two years compared to those aged 60-69 and 70-79 (60-69: 93%; 70-79: 92%; ≥ 80: 91%; p = NS)[11].

Effect of Donor Characteristics on Posttransplant Outcomes

Deceased-donor transplantation in octogenarians is more common than living-donor transplantation. Of the 199 patients ≥ 80 years old transplanted in the USA from 2000 to 2008, 83.4% of recipients received a deceased-donor transplant[11]. Of deceased donor recipients, 56.7% received an ECD transplant. There are no studies that have directly compared outcomes associated with donor type in octogenarians, but several studies have examined the association of donor age on patient and graft survival among other elderly recipients.

In a study of elderly kidney transplant recipients aged ≥ 60 from 1996 to 2005, allograft survival of recipients of older living donors (> 55 years), younger living donors (≤ 55 years), standard criteria donors (SCD), and ECD kidneys were compared[12]. After adjusting for confounding factors, older living-donor recipients had similar allograft survival to younger living-donor recipients (HR: 1.00; 95% CI: 0.47-2.13) and SCD recipients (HR: 1.66; 95% CI: 0.83-3.32) and superior survival to ECD recipients with follow-up to four years (HR: 2.36; 95% CI: 1.18-4.74). Similarly, there was no difference in patient survival after multivariate adjustment between recipients of older living donors and younger living donor (HR: 1.46; 95% CI: 0.51-4.11) and SCD recipients (HR; 2.21; 95% CI: 0.83-5.90) and greater patient survival compared to ECD recipients (HR: 2.84; 95% CI: 1.06-7.59).

Older donor age is a risk factor for graft loss and mortality among ECD recipients. There is a 24% increased risk of graft loss (adjusted HR: 1.37; 95% CI: 1.19-1.59) and 21% increased risk of death (adjusted HR: 1.21; 95% CI: 1.15-1.64) associated with recipients of a donor kidney aged ≥ 70 compared to donor age 60-69[13]. The difference in graft survival may be due to death with graft function. When comparing death-censored graft survival, there was no difference between recipients of donors ≥ 70 years old compared to 60-69 (HR: 1.18; 95% CI: 0.97-1.44). However, when comparing to all other ECD recipients aged 50-69, donor age ≥ 70 was associated with a 32% increased risk of graft loss (HR: 1.32; 95% CI: 1.09-1.61).

In spite of the above observations, ECD kidneys provide an important source of organs and improve an elderly candidate's chances of receiving a kidney transplant. The ECD candidates are 41% more likely to receive any kidney transplant than those not ECD-listed[14]. Nevertheless, approximately 50% of kidneys from deceased donors aged ≥ 60 are discarded in the USA[15]. A single-center retrospective analysis of kidneys

transplants allocated under the ESP criterion evaluated outcomes associated with transplantation of deceased donors aged ≥ 75 into recipients aged ≥ 65[16]. Despite a high prevalence of moderate or severe donor atherosclerosis among donors aged ≥ 75 (73%), which is a known risk factor for graft loss[17], there was no difference in creatinine clearance, graft survival, or patient survival at five years between ESP recipients of donor age ≥ 75, ESP recipients of donor age 65-74, or recipients of younger kidneys (15-63 years old) allocated under the ETKAS[16]. These observations highlight the need for better assessment tools of donor quality and suggest that some donor organs that are typically discarded may be used in the elderly population with favorable results.

Immunosuppression and Acute Rejection

Infectious complications are a significant concern in the management of elderly kidney recipients. Older patients are more susceptible to infection-related mortality than younger patients[18] and there is an exponential increase in the risk of infectious death with advancing recipient age in kidney transplantation[19]. Judicious use of immunosuppression is therefore critical to the management of the elderly kidney transplant recipient.

Despite the above concerns, we observed no difference in the use of lymphocyte-depleting antibody induction agents among recipients aged ≥ 80 and those aged 60-69 and 70-79, nor were any differences observed in the proportion of infection-related deaths among the three groups[11]. In the ESP experience, a greater proportion of ESP recipients received antibody induction than younger recipients allocated kidneys through ETKAS[8]. Similar to the Eurotransplant region, the use of lymphocyte-depleting antibody induction agents in the USA has increased in recent years and is now more commonly used than interleukin-2 receptor antagonists (IL-2RA) among elderly recipients aged ≥ 60[20].

Anti-thymocyte globulin (ATG) induction is associated with a lower risk of acute rejection compared to IL-2RA in elderly recipients aged ≥ 60[20]. This association holds true in subgroup analyses, when recipients aged ≥ 60 were stratified according to immunologic risk, defined on the basis of recipient (panel reactive antibody ≥ 20%, black race, or retransplantation) and donor factors (ECD, donor after cardiac death, or cold ischemia time > 24 hours). In all combinations of recipient and donor risk (high recipient/high donor risk; high recipient/low donor risk; low recipient/high donor risk; and low recipient/low donor risk), the use of ATG was associated with a lower risk of acute rejection over the first posttransplant year than IL-2RA. Additionally, the use of ATG induction was associated with a lower risk of death-censored graft loss compared to IL-2RA among high-risk recipients of a high-risk donor. This association was lost after adjustment for acute rejection in a multivariate Cox regression model, suggesting that increased graft loss associated with IL-2RA may be related, at least in part, to acute rejection episodes. These observations are supported by a previous report indicating that acute rejection episodes may be more deleterious to graft survival in older recipients than in younger recipients[21].

Despite the risks of infection and malignancy associated with the use of ATG[22,23], ATG was not associated with an increased risk of death compared to IL-2RA among recipients aged ≥ 60. However, alemtuzumab induction was associated with an increased risk of death compared to ATG in high-risk recipients of a high-risk donor and low-risk recipients of a high-risk donor and an

increased risk of death-censored graft loss in all recipient/donor risk subgroups, with the exception of high recipient/low donor risk[20]. Although these observations are associative and do not prove causality, the above data cast some degree of uncertainty on the benefit of alemtuzumab induction in elderly recipients.

In summary, although elderly transplant recipients tend to exhibit an attenuated immune response[18,24], the above data underscore that the importance of adequate immunosuppression and risks of acute rejection in the elderly should not be underestimated.

Conclusions

Whereas kidney transplantation in octogenarians was once unthinkable, more patients aged ≥ 80 have been transplanted in recent years. Yet, kidney transplantation is still limited to a select few octogenarians. The relative benefit of kidney transplantation among individuals in their ninth decade of life is unclear, although data regarding their intermediate-term outcomes are encouraging. At present, the conclusions that can be made about kidney transplantation among individuals in their ninth decade of life must be extrapolated from data regarding younger elderly recipients. The existing literature variably defines “elderly”, although many studies characterize elderly recipients as those aged ≥ 60. It is likely that octogenarians have qualitative differences in regards to functional status, life expectancy, and immunosuppressive vulnerability compared to recipients in their 60s or 70s. Is the transplant community ready to extend kidney transplantation to octogenarians on a wider scale? Until a greater body of data exists to validate the early experience with kidney transplantation in octogenarians, it is likely that receiving a kidney transplant in the ninth decade of life will remain uncommon.

References

1. U.S. Renal Data System, USRDS 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2010.
2. Santoro A, Mancini E. Hemodialysis and the elderly patient: complications and concerns. J Nephrol. 2010;23 (Suppl 15):S80-9.
3. Segev DL, Kucirka LM, Oberai PC, et al. Age and comorbidities are effect modifiers of gender disparities in renal transplantation. J Am Soc Nephrol. 2009;20:621-8. ***Illustrates that age is an effect modifier of gender disparities in access to transplantation, such that decreased access affects older (specifically > 55 years old) and not younger women (≤ 55).*
4. Stevens KK, Woo YM, Clancy M, McClure JD, Fox JG, Geddes CC. Deceased donor transplantation in the elderly--are we creating false hope? Nephrol Dial Transplant. 2011;26:2382-6. ***Single center study that reflects waitlisting and transplantation rates of elderly patients ≥ 75 in the United Kingdom.*
5. Wolfe RA, Ashby VB, Milford EL, et al. Differences in access to cadaveric renal transplantation in the United States. Am J Kidney Dis. 2000;36:1025-33.
6. Schaeffner ES, Rose C, Gill JS. Access to kidney transplantation among the elderly in the United States: a glass half full, not half empty. Clin J Am Soc Nephrol. 2010;5:2109-14. ***Assesses how the likelihood of transplantation from any donor source in the USA has changed for an incident ESRD patient from 1995 to 2006.*
7. Schold J, Srinivas TR, Sehgal AR, Meier-Kriesche HU. Half of kidney transplant candidates who are older than 60 years now placed on the waiting list will die before receiving a deceased-donor transplant. Clin J Am Soc Nephrol. 2009;4:1239-45. ***Assesses waitlist mortality and transplantation rates among elderly candidates older than 60 who were waitlisted in the USA from 1995 to 2007.*
8. Frei U, Noeldeke J, Machold-Fabrizii V, et al. Prospective age-matching in elderly kidney transplant recipients--a 5-year analysis of the Eurotransplant Senior Program. Am J Transplant. 2008;8:50-7. ***Reports long-term patient and graft outcomes associated with the Eurotransplant Senior Program.*
9. Merion RM, Ashby VB, Wolfe RA, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. JAMA. 2005;294:2726-33. ***Important study assessing which patients would derive survival benefit from accepting an expanded criteria donor kidney earlier versus waiting for a standard criteria donor kidney.*
10. Schold JD, Meier-Kriesche HU. Which renal transplant candidates should accept marginal kidneys in exchange for a shorter waiting time on dialysis? Clin J Am Soc Nephrol. 2006;1:532-8.
11. Huang E, Poommipanit N, Sampaio MS, et al. Intermediate-term outcomes associated with kidney transplantation in recipients 80 years and older: an analysis of the OPTN/UNOS database. Transplantation. 2010;90:974-9. ***Reports two-year patient and graft outcomes associated with kidney transplantation in recipients ≥ 80 years old.*
12. Gill J, Bunnapradist S, Danovitch GM, Gjertson D, Gill JS, Cecka M. et al. Outcomes of kidney transplantation from older living donors to older recipients. Am J Kidney Dis. 2008;52:541-52.
13. Chavalitdhamrong D, Gill J, Takemoto S, et al. Patient and graft outcomes from deceased kidney donors age 70 years and older: an analysis of the Organ Procurement Transplant Network/United Network of Organ Sharing database. Transplantation. 2008;85:1573-9.

14. Sung RS, Guidinger MK, Leichtman AB, et al. Impact of the expanded criteria donor allocation system on candidates for and recipients of expanded criteria donor kidneys. Transplantation. 2007;84:1138-44.
15. Rosengard BR, Feng S, Alfrey EJ, et al. Report of the Crystal City meeting to maximize the use of organs recovered from the cadaver donor. Am J Transplant. 2002;2:701-11.
16. Giessing M, Fuller TF, Friedersdorff F, et al. Outcomes of transplanting deceased-donor kidneys between elderly donors and recipients. J Am Soc Nephrol. 2009;20:37-40. ***Assesses graft outcomes of a small number of kidneys from deceased donors ≥ 75 allocated under the Eurotransplant Senior Program.*
17. Kahu J, Kyllonen L, Raisanen-Sokolowski A, Salmela K. Donor risk score and baseline biopsy CADI value predict kidney graft outcome. Clin Transplant. 2011;25:E276-83.
18. Meier-Kriesche HU, Ojo A, Hanson J, et al. Increased immunosuppressive vulnerability in elderly renal transplant recipients. Transplantation. 2000;69:885-9.
19. Meier-Kriesche HU, Ojo AO, Hanson JA, Kaplan B. Exponentially increased risk of infectious death in older renal transplant recipients. Kidney Int. 2001;59:1539-43.
20. Gill J, Sampaio M, Gill JS, et al. Induction immunosuppressive therapy in the elderly kidney transplant recipient in the United States. Clin J Am Soc Nephrol. 2011;6:1168-78.
21. Meier-Kriesche HU, Srinivas TR, Kaplan B. Interaction between acute rejection and recipient age on long-term renal allograft survival. Transplant Proc. 2001;33:3425-6.
22. Brennan DC, Daller JA, Lake KD, Cibrik D, Del Castillo D. Rabbit antithymocyte globulin versus basiliximab in renal transplantation. N Engl J Med. 2006;355:1967-77.
23. Hoegh-Petersen M, Goodyear D, Geddes MN, et al. High incidence of post transplant lymphoproliferative disorder after antithymocyte globulin-based conditioning and ineffective prediction by day 28 EBV-specific T lymphocyte counts. Bone Marrow Transplant. 2011;46:1104-12.
24. Wu C, Shapiro R, Tan H, et al. Kidney transplantation in elderly people: the influence of recipient comorbidity and living kidney donors. J Am Geriatr Soc. 2008;56:231-8.