Transplantation in Elderly Patients

Henry B. Randall, MD; Sean Cao, MD; Michael E. deVera, MD

In abdominal organ transplantation, liver and kidney transplantation have become the accepted standard therapeutic options for patients with end-stage liver and kidney diseases. As an increasing number of patients are referred to transplant centers for evaluation, the indications for transplantation continue to expand. Those at the later stages of life are receiving life-saving and life-altering treatment in the form of liver and kidney replacement at an increasing rate. The purpose of this article is to review current data concerning solid organ transplantation in elderly patients and compare their mortality and morbidity with that of a cohort of patients similar in all aspects except age. The results will no doubt elicit debate concerning the equitable distribution of livers, kidneys, hearts, and lungs given a national shortage of available organ donors. These results also hint at another area of intense debate—whether it is ethical to consider healthy family members and friends as donors for this patient population.

Orthotopic liver transplantation, kidney transplantation, and combined kidney and pancreas transplantation have become the standard procedures to replace solid organs damaged by end-stage disease. As clinically important advances have been made in areas such as surgical techniques, intensive care management, perioperative care, and immunosuppression management, the indications for transplantation continue to expand. The number of patients placed on the national waiting list has increased dramatically as has the overall proportion of elderly patients. According to the European Liver Transplantation Registry, the proportion of adult liver recipients older than 60 years increased from 9% in 1990 to more than 16% by 1999. Comparatively, in the United States in 1990, only 3.4% of liver allograft recipients were 65 years and older. However, more than 10.7% of recipients of an allograft liver in the United States in 2000 were older than 65 years.

In a large series, patients older than 60 years who had undergone kidney transplantation were assessed to determine whether receiving a kidney from a donor older than 60 years affected overall results. When this group was examined, patients older than 60 years had overall kidney function comparable with that in patients older than 60 years with a kidney from a donor also older than 60 years. These results elicit an even more provocative issue: Are organs from older donors inferior or marginal when compared with their younger counterparts? Another way to look at this issue is whether marginal organs from marginal donors should be allocated to the oldest patients because these organs will not last as long as others and may not need to, simply because life expectancy is 73 years for men and 79 years for women.

We examined data from the Organ Procurement and Transplant Network (OPTN) for the last 10 years to determine whether it is justifiable to perform transplantation in older patients. Also, further reviews and prospective data analysis may provide the basis for making future recommendations regarding allocation of organs at transplant centers across the United States. Although data from most transplant centers support transplantation in elderly patients, we must con-
tinue to evaluate these data objectively to determine if this is the most prudent use of such a scarce resource.

According to statistics from the United Network for Organ Sharing, the increasing shortage of available organ donors for transplants has led not only to increased median waiting time on the donor list (median >1000 days for kidneys) for elderly patients (those > 60 years) but also to an increase in the mortality rate in patients awaiting transplantation. As of February 2003, more than 80,426 people were awaiting a life-saving or life-altering organ; 53,500 were awaiting a kidney transplant, 16,900 were awaiting a liver transplant, and more than 7660 were awaiting a heart or lung transplant.  

For the purpose of this review, we examined data obtained from 1988 through 2000. Only kidney and liver transplantsations are considered, because intestine and pancreas transplantsations are rarely performed in elderly patients in the United States.

### RESULTS

From 1998 through 2002, 272,572 transplantsations were performed in the United States at all participating transplant centers. All kidney recipients on the US waiting list from 1991 through 2000 (Table 1) included 76,926 patients. The most common diagnoses for which patients received transplants were glomerular disease; diabetes; hypertensive nephrosclerosis; polycystic kidneys; tubular and interstitial diseases; congenital, rare familial, and metabolic disorders; and many other causes that are ill defined or unknown.

Among kidney transplant recipients, 30,234 (39.3%) cadaver allograft recipients were female and 46,692 (60.7%) were male. Among liver transplant recipients, 41.3% of cadaver allograft recipients were female and 58.7% were male. The number of kidney recipients from cadavers increased steadily from 315 (4.3%) in 1991 to 864 (10.7%) in 2000. The number of kidney recipients from living donors increased from 23 (1%) in 1991 to 336 (6.3%) in 2000. Table 2 shows graft and patient survival for all solid organs in all patient groups with follow-up of 3 months, 1 year, 3 years, 5 years, and 10 years. For all cadaver kidney recipients, graft survival was 93.5%, 88.4%, 78.5%, 63.3%, and 36.4% for each period. Similarly, patient survival for each period was 97.3%, 94.0%, 88.4%, 79.9%, and 59.4%. Table 3 shows cadaver and living donor graft and patient survival data in liver transplant recipients. Follow-up is the same: 3 months, 1 year, 3 years, 5 years, and 10 years. Graft survival for cadaver liver transplants was 85.8%, 80.2%, 71.4%, 63.3%, and 45.1%. Patient survival in the same group was 91.1%, 86.4%, 79.5%, 72.4%, and 59.4%. Graft and patient survival for other organs is included for comparison; combined organ transplant data are also included for comparison.

### Table 1. Primary Diagnosis in Kidney Transplant Recipients*

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*Data are the percentage of patients.
Graft survival of kidney transplants from cadavers of those 65 years and older at 3 months, 1 year, 3 years, and 5 years was 1573 grafts (91.2%), 1573 grafts (83.6%), 1278 grafts (69.9%), and 1043 grafts (52.8%), respectively. Survival in living donor kidney transplantation at 3 months, 1 year, 3 years, and 5 years was 545 recipients (95.7%), 545 recipients (92.2%), 333 recipients (82.8%), and 231 recipients (66.3%), respectively. Survival in cadaver kidney transplantation was 1507 recipients (94.4%), 1507 recipients (88.0%), 1229 recipients (74.4%), and 1005 recipients (58.2%). Survival in living donor kidney transplantation was 534 recipients (96.6%), 534 recipients (94.2%), 328 recipients (84.5%), and 225 recipients (76.1%).

Graft survival of cadaver liver transplants for the 4 periods was 628 grafts (84.2%), 628 grafts (74.4%), 573 grafts (69.1%), and 513 grafts (57.1%). Survival in cadaver liver transplantation was 591 recipients (88.2%), 591 recipients (78.8%), 546 recipients (72.0%), and 479 recipients (60.7%). Living donor graft survival was 29 grafts (89.7%) at 3 months, 29 grafts (75.9%) at 1 year, and 3 grafts (66.7%) at 3 years; no data were available for 5-year follow-up. Living donor patient survival was 29 recipients (81.1%) at 3 months and 29 recipients (68.9%) at 1 year; values could not be determined in the 3-year and 5-year categories because of insufficient follow-up. Three patients also received a liver graft, but no 3-year follow-up data were available.

Death in transplant recipients 65 years and older increased steadily from 1991 to 2000. The number of deaths in kidney transplant recipients increased from 116 patients in 1991 to 516 patients in 2000. The rate of deaths per 1000 patient-years at risk increased from 67.9 in 1991 to a high of 91.1 in 2000. For liver transplant recipients, the number of deaths increased from 84 patients in 1991 to 570 patients in 1999 and 520 patients in 2000. The number of deaths increased from 84 patients in 1991 to as many as 7048 in 2000 (Table 3).

The annual death rate in patients awaiting kidney or liver transplantation has increased substantially in patients 65 years and older during the past decade. For patients with kidney failure, the number of patients on the list increased from 1332 in 1991 to as many as 7048 in 2000. The number of deaths increased from 84 patients in 1991 to 570 in 1999 and 520 in 2000. For liver candidates, the number of potential recipients on the waiting list increased from 288 in 1991 to 2241 in 2000. The number of reported deaths in patients waiting for a liver transplant increased yearly from 34 in 1991 to 187 in 2000, with a peak of 217 in 1999. Although the death rate has decreased from 464.7 to 120.4, this number is deceiving because the number added yearly to the waiting list has increased from 1991 to 2000.

**COMMENT**

Similar to other surgical specialties, transplantation has enjoyed an increase in the number of elderly patients seeking organ replacement. Substantial advances in postoperative intensive care management, nutritional studies, cardiac support, and specialized transplantation units collectively have enabled those in the field of transplantation to treat elderly patients.

This patient population presents a unique challenge because of several factors. First and most important, elderly patients tend to have several comorbid factors, such as cardiopulmonary disease and advanced kidney dysfunction, and they tend to be more sedentary than younger healthier patients. We must quickly caution that this is the typical patient population with respect to end-stage liver disease. Patients with kidney failure who are candidates...
for kidney transplantation tend to have more advanced cardiac disease and as a group have more diabetes as the primary disease process. When examining the OPTN data, it is clear that elderly patients also show a trend toward a longer waiting time. To circumvent this problem, patients 65 years and older, as well as transplant centers, have encouraged the family members of elderly potential recipients to become living donors. As the OPTN data show, elderly patients enjoy robust survival in the early stages after transplantation; however, 3-year and 5-year survival data show that the survival curve decreases sharply. Any survival benefit gained at the time of surgery appears to be lost beyond 3 years of follow-up.

Death while on the waiting list is of paramount concern for patients of all ages. In the current analysis, it is evident from the data that as the indications for transplantation continue to grow and the number of patients added to the list increases, so does the mortality rate for patients on the list. Causes for patient removal from the waiting list include performance of transplantation, improvement in medical condition, becoming too sick for transplantation, becoming medically unsuitable, patient refusal of transplantation, or patient death. From 1991 through 2002, the number of patients removed from the waiting list because of death increased from 3700 to 6386. Most of the patients who die on the waiting list are waiting for life-saving organs such as hearts, lungs, and livers. Most patients who die while on the waiting list are aged 35 to 49 years and 50 to 64 years. Patients 65 years and older accounted for 7.0% of the deaths on the US waiting list in 2002. Adults aged 35 to 49 years and 50 to 64 years were 14.6% and 23%, respectively, of the deaths during 2002.

We examined several studies of large series for long-term survival in older recipients of kidney transplants; graft survival in older recipients, when compared with that in cohorts matched for all factors except age, showed no differences in initial graft function. However, differences arise in the number and severity of acute rejection episodes in older control groups. There are several controversies regarding the issue of whether grafts in older patients are lost at a higher rate, as compared with that in younger cohorts. As demonstrated in the OPTN data, 1 outstanding variable is that older patients have a higher rate of mortality, as compared with that in a similar group of younger patients. Most deaths associated with transplant recipients occur in those with a functioning graft at the time of death. Elderly patients are no different in that regard.

As reported in the European Liver Transplant Registry, the 1-year, 5-year, and 10-year survival in more than 3000 liver transplant recipients older than 60 years at the time of transplantation were 64%, 59%, and 49%, respectively. These findings are compared with those in a similar group of 11762 recipients aged 45 to 60 years with survival rates of 69%, 64%, and 55% (P < .001). The United Network for Organ Sharing Scientific Registry database from 1987 to 1997 demonstrated 1-year, 3-year, and 5-year survival rates of 80%, 70%, and 60% in 1412 patients older than 65 years, as compared with survival rates of 88%, 78%, and 73% in 18081 patients aged 25 to 64 years, respectively.

The causes of death in these patients could not be obtained but typically consist of diagnoses such as malignancy, hemorrhage, sepsis, acute and chronic rejection, recurrent diseases, cerebral causes, pulmonary complications, cardiac complications, and multiple organ failure. Causes of death among patients in other age groups tend to be similar, except for the percentage of patients with each diagnosis.

CONCLUSIONS

Given a national shortage of organs suitable for transplantation, indications for transplantation should be carefully considered in all patients regardless of the organ required—liver, kidney, or heart. Although elderly patients should not be completely excluded from transplantation, thoughtful and careful consideration during the evaluation process must be maintained. Anticipated life expectancy has to be compared with expected outcomes from their disease processes, expected waiting times, morbidity and mortality with respect to the diagnosis, type of transplant being sought. Should living donor transplantation be considered if the waiting times are expected to be prohibitive? A multitude of factors must be carefully considered. The process of being listed is routinely a multidisciplinary approach at all centers. Not only is the overall general medical condition of the potential recipient of major concern, but psychosocial factors and financial limitations have also prevented even younger patients from being listed for transplantation. If family support is lacking and elderly patients are expected to spend the rest of their days in nursing care facilities, listing for transplantation should be discouraged.

As the OPTN data show, there is no statistically significant difference in either patient or graft survival in adult recipients older than 60 years. However, data in patients older than 65 years show a clear difference when compared with data in younger patients. The argument that organs from older donors should be given to older recipients also warrants some discussion and evaluation of the OPTN data.

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REFERENCES
