The Future of Kidney Transplantation

By Leif Oxburgh and Barry Smith

The facts are straightforward. A kidney transplant is the optimal therapy for renal replacement therapy in ESRD. It is optimal from the point of view of its ability to restore both the health and quality of life of the individual affected and its long-term cost-effectiveness. Dialysis, whether hemo- or peritoneal and whether in-center or at home, is life preserving and necessary, but in the final analysis, it cannot compete with transplantation.

Today, 104,706 people are on the waiting list for a kidney transplant. In 2016, only 19,061 kidney transplants were accomplished. Roughly one-third of these involved living organ donors, and two-thirds involved deceased donors. An eligible person waits a median of 3.6 years for a kidney transplant, with some waiting 8 years or more. Sadly, one-fifth of those on the waiting list die every year (13 die each day) or become too sick or frail to undergo the surgical transplant procedure. Clearly, this is not acceptable.

This article is part of a series arising from a roundtable recently held at The Rogosin Institute. Other articles have explored many of the issues related to increasing living and deceased organ donation and transplantation. Among the concerns addressed were how more kidneys can be made available for transplantation, the use of extended criteria donor kidneys, the incentives and disincentives transplant centers face in using not just the healthiest of the kidney discard rate, and the optimization of the allocation system.

Here, we will look at not only additional ways to increase both living and deceased donation in the future but also, prospects for the repair and rebuilding of whole kidneys, such that the shortage of kidneys for transplantation can be eliminated. We can now envision the possibilities of using an individual’s own stem cells to create a new immunologically matched replacement kidney or editing the genome of banked human stem cells to create a kidney that is a “perfect” immunological match with no requirement for immunosuppression.

Rebuilt or newly built kidneys are an exciting prospect for the treatment of ESRD. Research still has a way to go before such kidneys are available, but the progress is very encouraging. Knowing that, however, are there actions we can take in the meantime to increase the number of available organs to shorten the waiting list time and decrease the mortality and lost opportunities that characterize the situation today? The answer to this question is a definite “yes.”

Previous articles in Kidney News have focused on a multitude of ideas to increase the rate of kidney transplantation (Table 1).

Discarding old assumptions about willingness to donate

An important point is that one potential solution does not fit every situation. For example, a northeastern urban African American community has not been known to have a high rate of living or deceased kidney donation. One might assume that the residents of that community would not be willing to donate. Yet, a community-implemented survey carried out by leaders and volunteers in the Central Brooklyn Health Movement in collaboration with The Rogosin Institute found that 62% of residents were willing to consider giving a kidney as a living donor and a somewhat smaller percentage (56%) were willing to consider giving a kidney as a deceased kidney donor. Although one must be very cautious in interpreting these data (e.g., many of those willing to be living kidney donors would not prove to be medically suitable or might ultimately decide not to follow through), it is also true, as some residents contacted in the survey stated, that they had never been asked the question. These findings indicate that we need to be very careful about the assumptions we make about the willingness to donate organs in any given community.

It is also important that people in the community who are trusted ask the questions about willingness in the “language” of the community. Put another way, different communities need to be asked in ways that are meaningful to them, and their concerns, cultural norms, and modes must be taken into account. In this way, more reliable information can be obtained, and more importantly, the donation of kidneys and other organs can be increased.

These observations lead to other questions about how to best increase organ donation in a given community in a fashion that is sustainable over the long term. The desired changes will not happen all at once. Education about both living and deceased organ donation needs to begin in schools (middle and high schools), and it needs to be carried out where people live, work, play, and worship. The information needs to be provided repeatedly and pervasively in the community, such that it becomes a part of the fabric of the community. The desired message is, “We are a community whose residents care for each other.”

Much of this message can and should be conveyed by community leaders and residents themselves because theirs is the voice that will be listened to in the community. The creation of a culture of organ donation must arise within and be fostered by the community itself. Health professionals have an important role to play in all of this, but it is most often a supportive and reinforcing one that ensures the supply of correct information. The Central Brooklyn Health Movement, mentioned above in relation to the kidney transplantation survey, is a movement of just this sort—a movement for better health of, by, and for the people of eastern New York and Brownsville, Brooklyn, NY—places where the health indices for hypertension, diabetes, and kidney disease, for example, are far higher than they should be and the need for kidneys for transplantation is great.

Advances in newly built kidneys

Even with all these efforts, it is unlikely there will ever be enough living and deceased donor kidneys to meet the need. So how can we address that need? This requires that we consider the prospects for “newly built” kidneys. What are the prospects?

Recent years have seen an explosion of activity in the development of stem cell–based strategies to build new

Table 1. Ideas for increasing the rate of kidney transplantation

<table>
<thead>
<tr>
<th>Idea</th>
<th>Description</th>
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<tbody>
<tr>
<td>A.</td>
<td>Increased communication and publicity designed to draw the public’s attention to the great gift that one human being can give to another in the form of a needed kidney.</td>
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<tr>
<td>B.</td>
<td>Public education about the ease and safety of both living and deceased organ donation and education regarding the value of preemptive kidney transplantation (i.e., done before dialysis must be initiated).</td>
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<td>C.</td>
<td>Adoption of important programs, such as those involving drivers’ licenses, with designation of a presumed willingness to donate an organ after death approaches but with an opt-out provision.</td>
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<td>D.</td>
<td>Legislative approaches to encouraging living donation, making it both economically and emotionally easier for individuals to donate a living kidney, i.e., the current Federal Living Donor Protection Act [H.R.1270] sponsored by Rep. Jerrold Nadler (D-NY) and three recent New York State Assembly bills providing reimbursement for donor expenses, insurance protection, and paid leave.</td>
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<td>E.</td>
<td>The nationwide computer-based best matching of donors and recipients through the National Kidney Registry, creating chains of donors and recipients.</td>
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<td>F.</td>
<td>Encouragement of altruistic kidney donation.</td>
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<td>G.</td>
<td>The use of social media to connect those in need of a kidney with potential donors.</td>
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Kidneys from Very Old Donors Benefit Very Old Recipients

By Bridget M. Kuehn

Older kidney recipients can benefit from organs from older donors. But previous cerebrovascular disease may reduce the survival benefits of these kidney transplants, according to a recent study.

Kidney transplants offer many advantages over dialysis for people with end-stage renal disease (ESRD). But a shortage of donors can make it particularly difficult for older patients to secure a donor organ, said Amado Andrés, MD, transplant coordinator at the Hospital Universitario 12 de Octubre in Madrid, Spain. Kidneys from older donors, which may have reduced function owing to age-related conditions, are a poor bet for younger patients. But in older patients with shorter life expectancies these organs may be sufficient.

“The ideal match for renal transplantation in old and very old recipients are old or very old kidney donors,” Andrés said.

However, the practice is not very common in Spain or other countries because ESRD patients age 70 and up often have serious cardiovascular comorbidities, said Andrés. The Eurotransplant organization has an “old for old” kidney transplant program (Schlierer G, et al. Clin Transplant 2001; 15:100–105). But although the program often uses organs from donors older than 70, it typically transplants them in patients younger than 70, Andrés said. And many countries do not have many older organ donors. Spain, with its very successful deceased donor program, however, has a good supply of older organs, he said.

“In other countries, access to transplantation of recipients older than 70 years is more limited because they require [recipients] to be absent of cardiovascular comorbidity,” he said.

Andrés and his colleagues have begun to extend kidney transplant eligibility to older patients with some cardiovascular morbidity using kidneys from older deceased donors. In their retrospective analysis of 155 kidney transplant recipients age 70 and older, the median donor age was 77 and the median recipient was 75. The 3-year survival rate for recipients was 73.1% and the 5-year survival rate was 67.1%. About 16% of patients died in the first year after transplant. Graft survival, censored for death, was 83.4% at 3 years post-transplant and 80.8% at 5 years post-transplant. The only factor associated with worse survival was a history of cerebrovascular disease (HR 5.12, p=0.27).

A history of diabetes was the only factor associated with graft loss (HR 4.40, p=0.0001).

“Our experience opens the door for the administrations of Western countries to promote organ donation in the elderly [as Spain does],” Andrés said. “It also demonstrates that patients of very advanced age can receive kidney transplants, improving survival and quality of life, without competing with the youngest patients on the waiting list.”

Jon Kobashigawa, MD, director of the Heart Transplant Program at Cedars-Sinai Medical Center in Los Angeles, noted that currently many older organs are not being used in the United States. His program does use older organs for older donors.

“It’s a precious resource that could be used for a good cause and the benefits greatly outweigh the risks,” he said.

He acknowledged that outcomes may not be as good for older transplant patients as for younger ones, but the improvement in quality of life for older recipients is still substantial. One factor that might hold some US programs back from participating in older donor/older recipient transplants is the way the programs are regulated. All US organ transplant programs are overseen by the United Network for Organ Sharing (UNOS) and must meet certain thresholds for recipient and organ survival. Because older organs and older donors may not survive as long it could cause some programs, particular smaller ones, to be flagged by UNOS.

“Regulatory issues do make programs hesitant to take on older donors,” he said.

He said it is not surprising that prior cerebrovascular problems or diabetes were associated with worse outcomes in the study. He noted his program typically reserves the limited organs available for those patients with the lowest risk factors.

“We are taking pains to achieve best outcomes,” he said. Andrews presented results from his study at Kidney Week 2017.