The kidney transplant waiting list

Gabriel Danovitch, MD

UpToDate performs a continuous review of over 375 journals and other resources. Updates are added as important new information is published. The literature review for version 15.1 is current through December 2006; this topic was last changed on August 16, 2006. The next version of UpToDate (15.2) will be released in June 2007.

INTRODUCTION — Over 70,000 patients are currently registered on the kidney transplant waiting list at the United Network for Organ Sharing (UNOS) in the United States [1]. Registration on this list by individual transplant programs is required before a patient can be allocated a deceased donor organ.

This topic review will discuss the composition of and access to the kidney transplant waitlist, as well as the management of patients while they await allocation of a kidney. Additional information is available elsewhere [1-3], and on the UNOS website, which can be found at the web address: www.UNOS.org

The details of the allocation algorithm for deceased donor kidneys and issues related to the evaluation of the kidney transplant candidate, including the possible presence of coronary disease, are discussed separately. (See "Evaluation of the potential renal transplant recipient" and see "Coronary heart disease in end-stage renal failure" and see "Organ sharing in kidney transplantation").

DEMOGRAPHICS — The kidney transplant waiting list in the United States is expanding inexorably at a rate of 3000 to 4000 patients each year [2]. If present growth rates continue, the list will consist of approximately 80,000 registrants by the year 2010. The rate of expansion of the list reflects the number of new registrants (approximately 25,000 each year) minus the number of patients who are transplanted from living and deceased donors (approximately 16,000 each year) and the number of patients who die while awaiting a transplant or who are removed from the list for other reasons.

Age — The waiting list in the United States consists of an increasing absolute number and relative proportion of older patients. In the years between 1994 to 2003, there was a five-fold increase in the number of candidates over the age of 65 years and a two-fold increase in their percent representation on the list (show figure 1) [2].

By comparison, the proportion of younger candidates decreased over this time period:

- Those between 18 and 34 years of age represented 22 and 14 percent of the list in 1994 and 2003, respectively

- Those between 35 and 50 years represented 40 and 31 percent of the list in 1994 and 2003, respectively.

The steady rise in both the absolute number and percentage of older patients newly registered and on the list means that, with the current allocation algorithm, younger adults are competing for kidneys with increasingly larger numbers of older patients. (See "Renal transplantation and the elderly").
Ethnicity — The ratio of Caucasian to African-American listed registrants has remained unchanged over the last decade [2]. African-Americans account for approximately 35 percent of listed registrants; this is similar to their representation in the chronic dialysis population and is approximately three fold higher than their frequency in the general population. African-Americans account for approximately 30 percent of new registrants. The higher percentage of African-Americans on the list compared to those newly listed (35 versus 30 percent) is accounted for by their slower rate of transplantation.

The situation is reversed for Caucasians (54 and 63 percent of the existing list and newly listed registrants, respectively) [2]. This reflects their higher rate of transplantation. As of 2003, 17 percent of both listed registrants and new registrants were Hispanic or Latino.

Gender and blood group — Representation of males remains approximately 15 percent greater than females [2]. Blood group O registrants consistently comprise more than 50 percent of the list.

Renal diagnosis — The relative proportion of waitlisted registrants with a specific primary renal diagnosis does not parallel the proportion of patients receiving chronic dialysis with the same primary diagnosis [2]:

- Patients designated as diabetic or hypertensive account for 40 and 28 percent of the dialysis population, but only 26 and 19 percent of waitlisted registrants.

- By comparison, patients designated as suffering from glomerular diseases and autosomal dominant polycystic kidney disease (PKD) account for 12 and 3 percent of the chronic dialysis population and for 22 and 6 percent of waitlisted registrants, respectively.

These discrepancies exist because hypertension and diabetes are more likely to be diagnosed in older patients with comorbid conditions that may exclude them from transplantation. Patients with glomerular diseases and PKD are likely to be younger with fewer comorbidities that preclude transplantation.

WAITING TIME — Patients currently remain on the waitlist for increasingly prolonged periods. As of 2004, the median time to transplant (indicating the number of days by which 50 percent of the patients have been transplanted) was 1176 days (3.2 years) and approximately 10 percent of patients had been waiting for more than five years [3].

One reason for this prolonged wait may be related to how waiting time is currently accrued when a patient is placed on the "inactive list." The term "inactive" is used to describe registrants who are placed on the list but are subsequently reported to the United Network for Organ Sharing (UNOS) as being temporarily unsuitable for transplant and not offered kidneys.

The current policy concerning inactive patients differs from the previous approach. In the past, these registrants did not accrue waiting time on the list one month after their inactive status was reported to UNOS. This policy has been changed to permit accrual of waiting time while on inactive status. As a result, 21 percent of registrants were defined as being "inactive" in 2004 compared to 10 to 12 percent in the mid-1990s [3].
The time to transplant also varies among blood types. Blood group O and B patients wait the longest: approximately two to three times as long as blood group A and four times as long as blood group AB.

Although the time to transplant has been increasing steadily in all ethnic groups, the increase has been greatest among African-Americans who, as of 1999, waited more than twice as long as Caucasians. Waiting time for Asian patients was approximately 85 percent greater than for Caucasians.

In the future, these differences may be reduced by changes made in the allocation algorithm to de-emphasize the importance of HLA typing. However, much of this difference is immutable and is related to geographical differences in allocation and the relatively greater percentage of African-American registrants who are blood group O.

The waiting time for non-resident aliens does not differ from that of United States citizens.

Previously transplanted and presensitized patients — Presensitization describes the development of antibodies against histocompatibility antigens as a result of blood transfusion, pregnancy, and prior failed transplants. These antibodies, termed panel reactive antibodies (PRA), are detected by incubating the patient's serum with a panel of antigens developed from the general population.

Patients with high levels of PRA have difficulty achieving a negative crossmatch and wait approximately twice as long for a transplant as those with a low PRA. As a group, previously transplanted patients wait approximately twice as long as those awaiting a first transplant. However, for previously transplanted registrants with a low PRA, there is little difference in the time to transplant.

Issues surrounding attempts to lower HLA antibody levels in patients with very high PRA levels are discussed separately. (See "HLA and ABO sensitization and desensitization in renal transplantation").

DEATH ON THE WAITING LIST — Overall mortality on the waiting list is approximately 6 percent per year, with a higher estimate of 10 percent per year for diabetic patients [3,4]. The death rate increases with age. For the years 2000 to 2003, the death rate was approximately 30 deaths per 1,000 patient years at risk for patients aged 18 to 34 years, which increased progressively to 100 deaths per 1,000 patient years at risk for patients ages greater than 65 years [3]. Thus, a patient over the age of 60 years who will need to wait five years for a kidney has an approximately 50 percent chance of dying before a kidney becomes available.

This mortality rate on the waitlist is approximately two-fold higher than in patients on the list who receive a kidney from a living donor or a standard criteria deceased donor. For the recipient of an expanded (or extended) criteria donor (ECD) kidney (which is a lesser quality kidney), the mortality rate reduction is approximately one-third less. (See "Organ sharing in kidney transplantation").

Expanded donor kidneys — Patients who agree to be placed on the list waiting for an ECD kidney are also eligible to receive standard donor kidneys. As a result, it may be difficult for patients to decide whether to accept an ECD kidney and have a decreased time on the waitlist or to stay a longer time on the waitlist and eventually receive a standard criteria deceased donor kidney. This dilemma is most typically faced by older patients. Expressed simply the question is: is it better to
accept an ECD kidney after a short wait or a standard criteria donor kidney after a longer wait?

The answer to this question depends to a large extent on patient age and also on the anticipated waiting time for a deceased donor kidney in their graphical area. Quality of life with maintenance dialysis is a highly subjective factor that individual patients and their advocates should take into account in their decision-making process.

Based upon patient age, there may be a survival advantage or disadvantage to waiting longer for a living donor or standard criteria deceased donor kidney compared with a shorter wait for an ECD kidney. This was shown in a study of all adult renal transplant candidates and recipients in the United States in the period from 1995 to 2004 [5]. The following findings were noted:

• For patients aged 18 to 39 years, there was a longer life expectancy with receiving a living donor (27.6 years) or standard criteria donor (26.4 years) kidney after four years of dialysis versus an extended criteria donor kidney (17.6 years) after two years of dialysis.

• By comparison, for patients greater than 65 years of age, life expectancy was slightly higher with an extended criteria donor (ECD) kidney (5.6 years) after two years of dialysis versus a standard (5.3 years) or living donor (5.5 years) kidney after four years of dialysis.

Hence, for younger patients it is generally worth waiting for a higher quality kidney, whereas for older patients the extra wait is not in their interest. However, if older patients are fortunate to live in a geographical area of the US where waiting times are relatively short then it may be in their interest to wait somewhat longer for the higher quality organ.

The complexity of this decision process requires that older patients be given ample opportunity to make an informed decision with which they are comfortable.

Overall, patients of all ages and diagnoses who are on the waiting list benefit from the reduced relative mortality of transplantation, including those who require a prolonged wait for a kidney. Patients with a lower life expectancy can anticipate a lesser absolute gain in life-years from transplantation. (See "Patient survival after renal transplantation", for a detailed discussion of these issues).

ACCESS TO THE WAITING LIST — Deceased donor transplantation requires access to the waiting list, which in turn requires access to a transplant center. Optimal outcomes occur when kidney transplantation is performed as early as possible after the development of advanced chronic kidney disease (CKD), preferably before dialysis is required (preemptive transplantation). Unfortunately, most CKD patients do not see a nephrologist until late in the disease course. Thus, because of the prolonged wait for a kidney, preemptive transplantation from a deceased donor is only an option for a small proportion of CKD patients. (See "Dialysis issues prior to and after renal transplantation").

A number of variables have been reported to inhibit timely referral to transplantation. These include [2]:

• Lower level of educational attainment
• Lower socioeconomic status
• Non-English-speaking background
• Minority race
• Female gender
• Dialysis in for profit or isolated dialysis units
• Certain medical diagnoses, such as diabetes mellitus
• Obesity

(See "Evaluation of the potential renal transplant recipient")

To minimize delays, patient and professional education about the benefits of early referral for transplantation is critical. For predialysis patients, early referral provides an opportunity to determine if a living donor is available and if the donor work-up can be completed expeditiously. This may facilitate the performance of preemptive transplantation and avoid access placement. (See "Evaluation of the potential renal transplant donor").

Early referral and listing also exposes patients to the possibility of being offered a zero-mismatch deceased donor kidney. These kidneys are allocated independent of waiting time. (See "Organ sharing in kidney transplantation").

UNPREDICTABILITY OF ALLOCATION — Deceased donor transplantation is unique among surgical procedures in that it is an urgent procedure performed in an elective population. Because of the inclusion of histocompatibility matching in the allocation algorithm, it has not been possible to accurately determine when a given patient will be called for transplantation.

This unpredictability has presented transplant programs with the formidable challenge of attempting to ensure that large numbers of patients, most of whom are not under their direct care, are medically cleared for transplant at all times. It has also been difficult for patients and their caregivers to know when a kidney is likely to be offered.

Over the last few years, the following changes in the kidney allocation algorithm have somewhat alleviated this unpredictability:

• Extended criteria donor kidneys are allocated based upon waiting time alone. It is therefore possible to predictably determine, for each blood group, the first person on the waiting list.

• Standard criteria donor kidneys are allocated based upon waiting time (one point per year) and HLA DR matching (maximum of two points, which is equivalent to two years of waiting). As a result, patients within the top two years of the waiting list for each blood group most commonly receive these kidneys.

(See "Organ sharing in kidney transplantation", for an additional discussion of these issues).

HEALTH MAINTENANCE

Preventive health measures — Patients on the active transplant list can be called for a transplant at any time. As a result, every effort must be made to optimize their health according to best practices and published clinical practice guidelines. In parallel, dialysis units, nephrologists, and the patients themselves must keep transplant programs appraised of major developments in the patient's health that could be relevant to their transplant candidacy and post-transplant management.
Cardiovascular testing — Because of the prevalence of clinically silent coronary heart disease and increased incidence of adverse cardiovascular events in renal transplant recipients, cardiovascular evaluation is a critical part of the assessment of all transplant candidates. Diabetic patients are at particular risk of an adverse event. (See "Evaluation of the potential renal transplant recipient" and see "Coronary heart disease in end-stage renal failure", for detailed discussions concerning the cardiovascular evaluation of the patient with end stage renal failure).

Once the patient is placed on the transplant list after undergoing an initial cardiovascular evaluation, continued cardiovascular surveillance is required for many patients, particularly those deemed high-risk. In such patients, the cardiovascular status may deteriorate during the prolonged wait for a kidney. There is, however, no firm consensus as to who should be tested, at what interval, and with what modality. This decision is made in part by estimation of patient risk.

A high-risk patient is defined as an individual with more than a 20 percent risk of a cardiovascular event in the next 10 years based upon the Framingham risk score. In comparison, patients with less than a 10 percent risk of a cardiovascular event in the next 10 years are considered to be at low risk.

A review of how one estimates cardiovascular risk in an individual in the general population, including the Framingham risk score, and of the different noninvasive and invasive tests that may be utilized in this evaluation are presented separately. (See "Estimation of cardiovascular risk in an individual patient without known cardiovascular disease" and see "Evaluation of the potential renal transplant recipient" and see "Coronary heart disease in end-stage renal failure", and see "Myocardial dysfunction in end-stage renal disease").

The following represents general recommendations for the timing of reevaluations in patients on the transplant waiting list that were adopted by many transplant programs based upon a National Conference Report published in 2003 [2]; these recommendations are consistent with the 2005 K/DOQI guidelines for coronary artery disease in dialysis patients [7]:

- If the initial cardiac evaluation was negative for cardiac disease, then:
  - Annual reevaluation if the patient is diabetic.
  - Every two-year reevaluation if the patient is high risk but not diabetic.
  - Every three year reevaluation if the patient is low risk.

- If the initial cardiac evaluation was positive for cardiac disease, then:
  - Annual reevaluation if there was no history of a prior revascularization procedure or if there was a history of prior percutaneous coronary intervention.
  - Every three year reevaluation then annual reevaluation for the patient who has had coronary artery bypass that successfully revascularized all target vessels. Annual reevaluation is recommended if the surgery was incomplete.
  - Annual echocardiogram if there is asymptomatic moderate or worse aortic stenosis

(See "K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients: IV. Section 1: Guidelines 1 and 2", for details concerning the K/DOQI guidelines for this issue)
This approach can be onerous and the recommendations were made before the kidney transplant waiting list was made more "predictable." With the current allocation algorithm, it may be more practical to emphasize cardiac surveillance of those patients within the top two years of the top of the list.

The recommendations from the 2003 National Conference were based on the use of noninvasive assessment of coronary heart disease because of the desire to avoid widespread use of coronary angiography. However, the utility of such noninvasive testing in patients with chronic kidney disease has been questioned because it is less reliable in detecting silent myocardial ischemia, and in predicting the occurrence of cardiac events post-transplant \cite{8,9}. In addition, the incidence of ischemic heart disease events in low-risk transplant candidates (<10 percent coronary risk at 10 years) who are not screened appears to be very low \cite{10}.

As a result, surveillance cardiac testing in waitlisted patients based upon ongoing clinical assessment of cardiac risk rather than the recommended practice of periodic screening may result in fewer investigations without an associated increased frequency of cardiac events.

For these reasons, the practitioner is advised to view current guidelines as recommendations rather than as strict rules and to combine them with clinical judgement. In addition, excessive reliance on noninvasive tests that are not sufficiently accurate to exclude significant coronary heart disease in high-risk candidates may engender a false sense of security \cite{11}.

**Physical activity** — Although the benefits of increased physical activity on all-cause and cardiovascular mortality have been well established in the general population, prospective studies in patients with chronic kidney disease are lacking. However, mortality risks have been reported to be greatest for patients with severe limitations in either moderate or vigorous physical activity and lowest for patients who exercise regularly \cite{12,13}. These data support the view that patients should be encouraged to engage in frequent physical activity while waiting for a transplant. (See "Physical activity in end-stage renal disease and renal transplantation", for a detailed discussion of this issue").

**SUMMARY**

- The kidney transplant waiting list in the United States continues to grow, particularly with respect to the proportion of older individuals. Over the last decade, the proportion of older candidate groups aged over 50 years increased, while the proportion of younger candidates decreased. The ratio of Caucasian to African-American listed registrants has remained unchanged over the last decade (See "Demographics" above).

- Patients currently remain on the waitlist for increasingly prolonged periods. This may in part reflect the increasing number of patients placed on the inactive list. The time to transplant varies by blood type, ethnic group, and panel reactive antibody levels. (See "Waiting time" above).

- Overall mortality on the waiting list is approximately 6 percent per year, with a higher estimated rate for diabetics and older individuals. (See "Death on the waiting list" above).

- Deceased donor transplantation requires access to the waiting list, which in turn requires access to a transplant center. A number of variables may inhibit timely referral to transplantation. (See "Access to the waiting list" above).
Because of the inclusion of histocompatibility matching in the allocation algorithm, the allocation of deceased donors is inherently unpredictable. However, changes in the kidney allocation algorithm over the last few years have somewhat alleviated this unpredictability. (See "Unpredictability of allocation" above).

Since patients on the active transplant list can be called for a transplant at any time, every effort must be made to optimize their health according to best practices and published clinical practice guidelines. There is widespread agreement that continued cardiovascular surveillance is required for many patients, particularly those deemed "high-risk" (greater than a 20 percent risk of a cardiovascular event in the next 10 years), since their cardiovascular status may deteriorate during the prolonged wait for a kidney. Patients should also be encouraged to engage in frequent physical activity while waiting for a transplant. (See "Health maintenance" above).

Use of UpToDate is subject to the Subscription and License Agreement.

REFERENCES

Kidney waiting list by age. Figure showing percentage on the United States kidney waiting list by age group during the period 1994 to 2003. As shown, the proportion of older candidate groups aged over 50 years increased during these years, while the proportion of younger candidates decreased. Reproduced with permission from: Danovitch, GM, Cohen, DJ, Weir, MR, et al. Am J Transplant 2005:5:904. Copyright © 2005.