Management of the Waiting List for Cadaveric Kidney Transplants: Report of a Survey and Recommendations by the Clinical Practice Guidelines Committee of the American Society of Transplantation

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Abstract. The Clinical Practice Guidelines Committee of the American Society of Transplantation developed a survey to review the policies of kidney transplant programs in the United States with respect to the management of the steadily expanding waiting list for cadaveric kidneys. The survey was sent to 287 centers, and 192 (67%) responded. The survey indicated that regular follow-up monitoring, most frequently on an annual basis, is required by the majority (71%) of programs. Patients considered to be at high risk and candidates for combined kidney-pancreas transplantation may be monitored more frequently. Annual screening for coronary artery disease is typically required for asymptomatic patients considered to be at high risk for covert disease. Noninvasive techniques are typically used, and a designated cardiologist is usually available to the transplant program. The dialysis nephrologist or the potential transplant recipient is expected to inform the transplant program of intercurrent events that may affect transplant candidacy. Standard health maintenance screening is required, together with the routine updating of serologic and other blood tests that may be relevant to the posttransplant course. Smaller transplant programs (<100 patients on the waiting list) are more likely to maintain closer contact with the wait-listed patients and to attempt to influence their treatment during dialysis and are less likely to cancel transplants because of unanticipated pretransplant medical problems. The work load necessitated by the follow-up monitoring of wait-listed patients was assessed and, in the absence of specific evidence-based information, a series of recommendations were developed to reflect current standards of practice and to suggest future research initiatives.

In May 2001, nearly 50,000 patients were enrolled on the United Network for Organ Sharing (UNOS) waiting list for cadaveric kidney transplants (1). Approximately 9000 patients each year receive cadaveric transplants, and patients typically wait several years before receiving a kidney. In the coming years, despite anticipated advances in immunosuppressive therapy and transplant immunobiology, the waiting list and waiting times will inevitably lengthen, as the demand for kidneys continues to exceed the supply. The UNOS kidney waiting list is currently increasing at a rate of 20%/yr and will include between 100,000 and 150,000 patients by the year 2010. In the absence of dramatic increases in the availability of organs, waiting times of a decade or more may become routine.

The Clinical Practice Guidelines Committee of the American Society of Transplantation (AST) has published detailed guidelines for the evaluation of candidates for kidney transplantation (2). These guidelines refer to the wide range of medical issues that must be addressed when patients wish to be considered as transplant candidates. It is clear, however, that the health status of transplant candidates, the great majority of whom are undergoing chronic dialysis, may deteriorate with time and the medical, psychosocial, and demographic aspects of their care may change during prolonged waiting periods. The kidney transplant waiting list is a dangerous place to be. The overall annual death rate for wait-listed patients has been estimated to be 6.3%/yr, and rates are ≥10%/yr for diabetic patients or patients ≥65 yr of age (3). Therefore, even a nondiabetic patient who can expect to be on the list for 5 yr has a >30% chance of dying before a kidney becomes available. Moreover, the length of time a patient spends on the waiting list has been demonstrated to be an independent determinant of
the long-term posttransplant prognosis (4). This effect is likely to be attributable, at least in part, to the so-called “atherogenic” nature of chronic renal failure and dialysis treatment, which may cause deterioration in the cardiovascular status of all potential transplant recipients and of diabetic patients in particular (5).

The challenges facing transplant programs are considerable. Cadaveric transplantation is unique in medical care, in that it is an urgent medical procedure performed in an elective population. Patients on the transplant list are known to the transplant programs but typically are not under their direct care before the transplantation procedure. For reasons noted above, patients may be urgently called for a transplant months or, more likely, years after their first evaluation. During that period, significant new medical issues might have arisen among the potential recipients, which might unfavorably affect their postoperative course. If the transplant program is not aware of these issues, then they may lead to cancellation of the procedure, and the inevitable prolongation of cold ischemic injury to the transplant might impair its function in the eventual recipient (6). If, however, a decision is made to proceed with the transplant despite unanticipated medical problems, then the patient may be placed at unnecessary risk. If the transplant is canceled, then the originally designated recipient may undergo another prolonged wait until he or she is called again.

There are currently no formal policies defining the manner in which transplant programs address these problems, and the medical evidence on which to base such policies is limited. For this reason, the Clinical Practice Guidelines Committee of the AST undertook to survey the policies of transplant programs in the United States. The survey was prepared and analyzed to assess standards of practice, to provide recommendations for improvement in which transplant programs address these problems, and the availability of pancreas transplantation. The questionnaire was sent to 287 individual centers and was program size, as assessed by the number of patients on the waiting list. Thirty-two percent of programs were considered small, with <100 patients awaiting renal transplantation, 53% included 100 to 500 patients, 11% included 500 to 1000 patients, and 4% included >1000 patients awaiting transplantation. The small programs tended to be privately based (P < 0.001) and were less likely to provide pancreas transplantation than were larger programs (P < 0.001).

The survey revealed that regular contact between the transplant center and all of its potential transplant recipients was maintained by 71% of the programs. An additional 11% of the programs maintained regular contact only with patients considered to be at high medical risk. For the remaining programs, there was no consistent pattern of contact with the transplant center. The small programs were more likely to maintain regular contact with all of their patients (87% of programs with <100 patients, 64% of programs with 100 to 1000 patients, and 43% of programs with >1000 patients; P < 0.001 for comparison of small centers with larger centers) (Figure 1). A variety of techniques were used to maintain contact. Approximately one-half of the programs scheduled routine patient clinic visits, and one-half maintained contact by telephone. Twenty-seven percent of programs indicated that they arrange visits by transplant program staff members to dialysis centers, 27% of programs request that the patients initiate contact with the program, 14% of programs use a mailed questionnaire, and 19% of programs indicated that they use a variety of other techniques, such as contact between the transplant program and dialysis staff members or nephrologists. The frequency of contact also varied. Nearly one-half of the programs contacted their patients on an annual basis, 23% contacted patients every 6 mo, and 7% contacted patients every 2 yr. Seven percent of programs specifically indicated that they contacted their patients at least quarterly. Thirty-four percent of programs indicated that contact with patients considered to be at high risk was more frequent.

The responsibility for informing the transplant program of intercurrent medical events that could be relevant to the transplant status of patients was left to the dialysis nephrologist by 73% of programs. One-half of the programs expected the patients to inform the transplant center, and 17% of programs indicated that they had no fixed policy. After listing of patients for transplantation, 34% of transplant programs consistently attempted to influence the care of the patients on the waiting list; 36% of programs indicated that they did so inconsistently. Smaller programs were more likely to attempt to influence management than were larger programs (46% for the smallest programs and 12% for programs with >500 wait-listed patients, P < 0.001) (Figure 1).

The survey specifically addressed concerns regarding the
Table 1. Survey questions and responses

1. With respect to the person answering this survey, are you a...?
   a. Transplant physician (26%)
   b. Transplant surgeon (53%)
   c. Transplant coordinator (21%)

2. Is your kidney transplant program...?
   a. In a private hospital (48%)
   b. In a university hospital (52%)
   c. Do you have a pancreas program (21%)

3. Does your program offer pancreas transplantation?
   a. Yes (59%)
   b. No (41%)

4. Approximately how many patients are on your kidney transplant waiting list?
   a. <100 (32%)
   b. 100 to 500 (53%)
   c. 500 to 1000 (11%)
   d. >1000 (4%)

5. Do you maintain regular contact with transplant candidates once they are listed, for purposes of demographic updates, availability of living donors, and new medical or social problems?
   a. Not consistently (18%)
   b. Yes, all patients (71%)
   c. Yes, only certain patient groups (e.g., diabetics/CAD/age) (11%)

6. How do you maintain contact with your patients once they are listed?
   a. No systematic attempt is made to maintain contact (7%)
   b. By routine scheduled patient visits to the transplant program (50%)
   c. By telephone contact from the transplant program to the patients (49%)
   d. By patient-initiated contact with the transplant program (27%)
   e. By visits to dialysis centers by transplant program staff (27%)
   f. By mailed-in questionnaire (14%)
   g. Other (19%)

7. How often do you maintain contact with listed patients?
   a. Every 6 mo (23%)
   b. Annually (50%)
   c. Biannually (4%)
   d. More frequently for high-risk patients (34%)
   e. No consistent policy (15%)
   f. Other (10%)

8. Who is responsible for informing the transplant program of intercurrent events that could be relevant to transplant status (e.g., cardiac events/peritonitis/foot ulcer/noncompliance)?
   a. No fixed policy (17%)
   b. Dialysis nephrologist is requested to call program (73%)
   c. Patient or family is expected to call program (50%)
   d. Other (13%)

9. Does your transplant program attempt to influence the management of wait-listed patients who are under the care of local nephrologists, with respect to issues that could be relevant to the long-term posttransplant course (e.g., blood pressure control, CAD risk factors, or obesity)?
   a. Consistently yes (34%)
   b. Inconsistently yes (38%)
   c. Rarely (27%)
   d. Other (2%)

10. While awaiting a transplant and in the absence of a documented or suspected cardiac event, is invasive or noninvasive testing to rule out or monitor CAD performed or requested on a regular basis?
    a. No routine testing or retesting (18%)
    b. Yes, in all patients (8%)
    c. Yes, in patients with documented CAD (53%)
    d. Yes, in diabetics (59%)
    e. Yes, in other high-risk groups (age, obesity) (52%)
    f. Other (7%)
changing cardiac risk status of wait-listed patients and the techniques used to detect such changes in the absence of documented or suspected clinical events. Only 8% of programs routinely engaged in cardiac screening for all of their wait-listed patients; however, the majority of programs routinely screened patients deemed to be at high cardiac risk. Fifty-nine percent of programs screened their diabetic patients, 53% screened their patients with documented coronary artery disease, and 59% screened their diabetic patients. The percent responses are noted in parentheses after the questions. Percentages may add up to >100% because some responders may have indicated more than one option. CAD, coronary artery disease; PSA, prostate-specific antigen.
ease (CAD), and 52% screened their patients considered to be at high cardiac risk for other reasons, such as obesity or
advanced age. Only 18% of programs did not routinely request
cardiac screening for any patient group. The majority of cen-
ters (79%) screened their patients on an annual basis, although
there was considerable variation in the methods used. Nuclear
perfusion scanning was used most frequently (40%), followed
by exercise thallium scanning (33%), dobutamine echocardio-
graphy (31%), and coronary angiography (15%). Six pro-
grams specifically indicated that they used coronary angiogra-
phy more frequently for potential recipients of pancreas
transplants. A designated cardiologist or group of cardiologists
was assigned to the care of patients awaiting transplantation by
56% of transplant programs.

Standard cancer prevention recommendations are available
for the general population, and we polled the transplant pro-
grams regarding their insistence that their wait-listed patients
abide by those recommendations. Sixty-nine percent indicated
that they did, and an additional 20% left the decision to the
dialysis nephrologist. Smaller programs were more likely to be
consistent than larger programs (72% of programs with <500
patients and 54% of programs with >500 patients, P < 0.05)
(Figure 1). Periodic serologic testing for viral hepatitis was
required by 80% of the programs, and screening for other
infectious diseases was required by 52%. Regular prostate-
specific antigen testing of older male patients was required by
79% of programs.

Cancellation of a cadaveric transplant, because of unantici-
pated medical problems, after the patient had been called into
the transplant center seemed to be a relatively infrequent event.
Sixty-one percent of programs indicated that such events af-
fected <2% of the patients called for transplantation (80% of
small programs, P < 0.001 for comparison with larger pro-
grams) (Figure 1). 26% of programs indicated that such events
affected 2 to 5% of transplants, 10% indicated that such events
affected 5 to 10% of transplants, and seven programs indicated
such events affected >10% of transplants. The frequency of
removal of a patient from the waiting list because of medical or
psychologic problems varied considerably among programs.
Thirty-six percent of programs indicated that 5 to 10% of their
patients were removed, 33% indicated that 2 to 5% of their
patients were removed, 18% indicated that 10 to 20% of their
patients were removed, and 11% indicated that removal was
rare (<2%), but 4% of programs reported that >20% of their
patients were removed.

With respect to the use of so-called “marginal kidneys,”
81% of the centers indicated that they informed their patients
regarding the features of these kidneys at the time of trans-
plantation and consulted with the patient’s nephrologist before
such transplants in approximately 60% of cases. Forty percent
of programs indicated that the potential allocation of a mar-
ginal kidney was discussed at the time patients were placed on
the waiting list, and 12% of programs maintained a separate
recipient list for marginal kidneys.

Discussion

Our survey indicates that the necessity for routine follow-up
monitoring of patients awaiting kidney transplantation is
broadly recognized by transplant programs in the United
States. From the survey, it is possible to construct a profile of
a typical program. Annual follow-up assessment, via either
routinely scheduled appointments or program-initiated tele-
phone contacts, is required. Patients considered to be at high
risk and candidates for combined kidney-pancreas transplanta-
tion may be monitored more frequently. Annual screening for
CAD is required for asymptomatic patients deemed to be at
high risk because of previously documented CAD, diabetes
mellitus, advanced age, or obesity. Noninvasive techniques are
typically used, and a designated cardiologist is usually avail-
able to the transplant program. The dialysis nephrologist or
the potential transplant recipient is expected to inform the trans-
plant program of intercurrent events that may affect transplant
candidacy. Standard health maintenance screening is required,
together with the routine updating of serologic and other blood
test results that may be relevant to the posttransplant course.

Our survey confirms the widely recognized concerns, ex-
pressed by kidney transplant programs, regarding the preva-
ience and progression of CAD (7). Kidney transplantation does
not take place in a clinical vacuum. All transplant candidates
experience end-stage renal disease (ESRD) and its conse-
quences and are exposed to excess cardiovascular risk. The
phrase “the epidemic of cardiovascular disease” has been used
to describe the magnitude of the threat of cardiovascular events
among patients with ESRD, which is up to 100-fold greater
than that in the general population (8). Preoperative assessment of cardiac disease among renal transplant candidates presents particular difficulties, because diagnostic studies are less reliable than among patients without ESRD and revascularization techniques do not provide equivalent long-term results (2,9). In addition, the cardiovascular risk status of transplant candidates is not constant and tends to deteriorate with time (7,10). Such deterioration is often asymptomatic, so that cardiovascular assessments that initially provide clearance for surgery may require serial updates as patients wait years for a kidney to be offered to them. Left ventricular function deteriorates among dialysis patients, particularly in the first year (10). Valvular disease, especially aortic stenosis, may progress markedly over the years among patients on the waiting list and may preclude transplantation before aortic valve replacement (11). Concern regarding clinically unrecognized CAD progression was reflected in our survey by the fact that 79% of transplant programs reported that screening for CAD was repeated on an annual basis among patients without symptoms.

Transplant programs use a variety of techniques to screen for covert CAD. In our survey, programs seemed to be evenly divided with respect to their preferences for exercise stress testing enhanced by nuclear imaging or chemical stress testing with either nuclear imaging or echocardiography. Only a minority of programs routinely used angiography. Unfortunately, the literature provides ample documentation that noninvasive screening tests for CAD among asymptomatic patients with ESRD are of limited value because of low sensitivity (12). Dipyridamole single-photon emission computed tomographic thallium imaging has not been proven to be a useful screening test for angiographically significant CAD (sensitivity, 37%; specificity, 73%) and does not predict cardiac prognoses among patients with ESRD (13). Dobutamine stress echocardiography is a useful but imperfect screening test for angiographically significant CAD among renal transplant candidates (sensitivity, 75%; specificity, 71%, compared with quantitative coronary angiographic assessment of >70% stenosis) (14). Dobutamine stress echocardiography also provides a noninvasive method of long-term, repeated follow-up monitoring, although the required frequency of follow-up assessments with this method or any other noninvasive screening method has not been determined. Coronary artery calcification is common and progressive among young adults with ESRD who are undergoing dialysis (15). Noninvasive serial measurement of coronary artery calcification scores may become a useful technique for longitudinal assessment of coronary risk among patients with ESRD. We emphasize that these comments refer to asymptomatic wait-listed patients. The development of new overt cardiac symptoms while the patient is on the waiting list clearly requires urgent cardiologic evaluation, with reassessment of the patient’s suitability for transplantation.

Our survey indicates some lack of uniformity regarding the manner in which transplant programs are kept apprised of changes in patient health status that may be relevant to the transplant course. The majority of transplant programs indicated that they expect the dialysis nephrologist to keep the transplant program informed regarding “transplant-relevant” events, one-half of the programs expect the patients to do so, and 17% of the programs have no fixed policy. Most transplant programs do not seem to play an active role in the treatment of wait-listed dialysis patients. Dialysis nephrologists are clearly primarily responsible for the health of their patients as long as the patients are dialysis dependent. Transplant programs, however, must ensure the readiness of each patient for major surgery and must be concerned regarding the effects of the prolonged wait for a kidney on the long-term outcome of the transplant endeavor. Ideally, dialysis nephrologists and transplant teams should work in concert to enhance the long-term health of patients, whether they remain on dialysis or receive a transplant. Dialysis nephrologists and patients should be acutely aware that a call from the transplant program could come at any time, and they should keep the transplant program informed, in a timely manner, of medical and other events that may be relevant to transplant candidacy.

Our survey indicates that the removal of patients from the waiting list because of deterioration of their medical condition is a frequent occurrence. UNOS regulations allow a patient whose condition has deteriorated and who is not a candidate for transplantation to remain on the list but not to accrue “waiting points” (so-called “status 7”). The survey did not specifically ask whether the condition of patients removed from the list by the transplant program was automatically reported to UNOS (i.e., patients designated as status 7). There are currently no consistent guidelines for removing patients from the waiting list or placing them “on hold” and formally reporting this information to UNOS. In the absence of such guidelines, kidneys may be initially allocated to patients who are not deemed candidates, and delays in the eventual placement of the organ are inevitable.

The work load and expense generated by the broadly accepted necessity to constantly update the medical and demographic relevance of the waiting list in the manner reported by most transplant programs that responded to our survey are enormous and will inevitably increase as waiting times are prolonged. Repeated cardiac imaging alone may cost many thousands of dollars. A transplant program with 500 patients on its list that deems it necessary to update the list annually would require approximately 40 patient contacts/mo, and patients judged to be at high cardiac risk would require multiple imaging studies during long waiting periods. Special clinics and adequate medical and transplant nurse coordinator staffing might be required to handle the medical and bureaucratic work load that adequate follow-up monitoring of wait-listed patients inevitably requires. In this respect, it is interesting that, as noted in our survey, larger programs were less likely to maintain consistent contact with their patients than were smaller programs, were less likely to attempt to influence the treatment of patients on the list, and were less likely to insist on routine screening recommendations. We surmise that these differences between smaller and larger programs reflect the amount of work these endeavors require. The consequences of not maintaining contact include an increased likelihood that a patient cannot be located because of demographic changes, an increased frequency of the designated recipient being sent home
because of unanticipated medical problems (which was less frequent in the smallest programs) (Figure 1), and increased perioperative morbidity and mortality rates if such problems go unrecognized.

The manner in which the waiting list is managed is related to the way in which cadaveric kidneys are distributed. The current UNOS-approved algorithm for the allocation of cadaveric kidneys provides points, within each blood-group category, for the time spent waiting for a transplant and for the degree of HLA histocompatibility, with most of the points in the early years of waiting coming from HLA matching. The algorithm is applied in each of the UNOS geographic regions, with the exception of fully matched or “no-mismatched” kidneys, which are shared nationally. This system is thus a hybrid one, designed to take into account both the long-term graft survival rate advantages associated with closer degrees of matching and the length of time patients spend waiting for a transplant. With such a system, it is almost impossible to anticipate when any given patient will be called to receive a kidney. There is really no “top of the list”; patients must thus be prepared for their fateful telephone call at all times, and a system must be in place to ensure their medical, emotional, and demographic preparedness.

An alternative distribution system, based primarily on waiting time, is in place in some regions. In this system, patients are placed on the waiting list after applying to a transplant program and undergoing screening or more extensive evaluation. Because waiting time is the primary determinant of distribution, it is possible to anticipate with some degree of accuracy when a kidney will become available. Patients can be reevaluated or evaluated more thoroughly within weeks or months of their anticipated call. The need to ensure preparedness at all times is less pressing than with the standard distribution algorithm, although patients may still be called for a fully matched or no-mismatched kidney at any time and ideally would always be prepared for such a call.

Our survey addresses the waiting list from the viewpoint of the transplant programs, rather than the patients themselves. Attempts to design more efficient and effective follow-up mechanisms should take into account patient needs. After the patient’s initial contact with the transplant program at the time of the first evaluation, the transplant program and its staff may seem increasingly remote as the years spent waiting for a kidney elapse. Regular contact with the transplant program can serve to reinforce transplant-related educational needs, may serve to diminish the patient’s sense of hopelessness, and may provide an opportunity to evaluate the availability of suitable living donors.

Although our survey was designed to address the practical aspects of management of the transplant waiting list, we took the opportunity to review the policies of transplant programs with respect to so-called marginal kidneys. The transplant donor pool is inexorably aging (16) and, as a result, patients may be offered kidneys with features that may impair their long-term utility (17). Ironically, these kidneys, which are more susceptible to cold ischemic injury (18) and subsequent delayed graft function, tend to be transplanted with cold ischemia times that are prolonged because of delays in placement (6). As indicated in this survey, the majority of transplant programs informed their patients regarding the features of these organs but chose to do so at the time they became available. A minority of programs prepared a separate list for marginal kidneys. Such a list of previously informed and educated wait-listed patients could facilitate and expedite the placement of these organs and could thus improve their function.

In conclusion, we note that the practice profile for waiting list management that we have outlined is not based on specific evidence. The widespread policy of maintaining annual contact with wait-listed patients for the purpose of updating their medical and demographic status is rational. As the waiting time for transplantation inevitably lengthens, however, and the number of waiting patients steadily increases, more of the resources of transplant programs will be used for list maintenance, rather than transplantation itself. The purpose of our survey was to review the practices of transplant programs and bring attention to the program and patient needs during the prolonged waiting period. We avoid making specific proposals regarding how individual programs should address these problems, because local requirements and responses will inevitably differ and scientific evidence to support specific proposals is limited. However, the following general recommendations can be made. (1) Each transplant program should develop a consistent organized system for maintaining ongoing contact with its wait-listed patients. (2) Each transplant program should develop clear lines of communication with nephrologists and dialysis staff members. (3) Transplant programs should clearly describe to wait-listed patients, their nephrologists, and dialysis staff members precisely what is required of them during the waiting period. (4) Patients considered to be at high risk for cardiac events should undergo repeated imaging studies, to rule out covert progression of CAD during the waiting period. Evidence for progression should trigger cardiologic assessment. (5) The definition of “high risk” must be carefully studied and validated in prospective trials, to avoid the increased cost and inconvenience of repeated testing. (6) Prospective trials should be planned and implemented to assess the usefulness of noninvasive cardiac imaging for wait-listed patients and to determine the optimal and minimal requirements for imaging repetition. (7) Uniform criteria should be developed for placing wait-listed patients on hold or removing them from the active transplant list. Such a policy would serve to avoid the allocation of kidneys to patients who are not medically ready for transplantation at the time a kidney becomes available for them. (8) Meticulous attention should be paid to the health of patients considered candidates for transplantation (in particular, their cardiac risk factors), to optimize the eventual health benefits of transplantation. (9) The cost implications and medical, nursing, and administrative requirements for repeated patient evaluations and cardiac testing must be taken into account by government agencies, third-party insurers, and hospital administrations. (10) The design of algorithms for the allocation of cadaveric organs should take into account their effects on patient treatment during the waiting period. (11) The
issue of acceptance of marginal kidneys by patients at the time of their placement on the waiting list, to facilitate the rapid appropriate placement of these organs, should be considered.

References