Involving Patients in the Cadaveric Kidney Transplant Allocation Process: A Decision-theoretic Perspective

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The United Network for Organ Sharing system of allocating cadaveric kidneys for transplantation permits only minimal involvement of patients in the selection process. The system ignores potential variations in the importance that patients may attach to outcomes associated with the transplant decision. For instance, some patients may prefer only kidneys that will give them a very favorable chance to achieve a successful transplant. We designed a decision model in which patients are surveyed about their preferences for health states that in turn affect decisions about the type of donor kidneys that would be acceptable for transplantation. Our analyses show that patients with favorable transplant characteristics (e.g., young age, good health, good immunologic match between the donor kidney and the recipient) or who expect a minimal improvement in quality of life after successful transplantation can afford to be selective when considering which kidneys to accept for transplantation. Involving patients in selecting the optimal donor-kidney should improve patients' quality and duration of life with end-stage renal disease, and thereby improve the overall efficiency of the U.S. kidney transplantation program. (Kidney Dialysis; Kidney Transplantation; Decision Analysis; Action-Timing Problems)

1. Introduction

The demand far exceeds the supply of cadaveric donor kidneys for transplantation into patients with end-stage renal disease (ESRD) in the United States. More than 20,000 persons are listed each year as waiting for kidney transplants, but less than 9000 renal transplants were performed in 1992 (USRDS 1993). Despite aggressive efforts to increase the number of donor kidneys, the supply almost certainly will not meet the demand within the next decade (Ellison 1993). In the setting of an increasingly serious imbalance between demand and supply of donor kidneys, the United Network for Organ Sharing (UNOS) established a Point System to guide the allocations of donor kidneys (Starzl et al. 1987). The Point System calculates points for each patient waiting for transplantation considering such factors as age of the patient, duration of waiting for transplantation, and markers that predict rejection of the kidney, such as quality of immunologic matching and sensitization to foreign antigens. According to the Point System, when a donor kidney becomes available, the patient with the most points is allocated the kidney (GAO 1993). Any patient located in the United States with a near perfect immunologic match (i.e., 0-antigen mismatch) and compatible blood type has priority for a transplant over other patients on the waiting list. With the current system, the transplant team effectively selects a patient for the available kidney.

Several recent studies of kidney transplantation in the United States suggest there are many inequities and inefficiencies in the current donor-kidney allocation system. Waiting times for minorities, women,
and persons in lower socioeconomic strata are disproportionately longer than for other patient groups (Held et al. 1988; Gjertson 1991a, 1991b, 1993; Kasiskie et al. 1991; Sanfilippo 1991; Ayres et al. 1993). In a recent review of the UNOS Point System, Gaston and colleagues argue that much of the inequity in the waiting times could be alleviated by placing less emphasis on achieving high-level immunologic matching between the donor kidney and the recipient (Gjertson 1991a, 1991b, 1993). We believe also the UNOS Point System fails to consider variations in patient preferences for different health outcomes associated with alternative treatments for ESRD. Some patients may find the nontransplantation treatment options (i.e., dialysis) sufficiently tolerable that they would be willing to wait longer for a donor kidney that has a high probability of successful transplantation. Conversely, other patients may find the dialysis treatment so intolerable as to accept a donor kidney that has a low probability of successful transplantation.

Because decision theory explicitly considers the importance that patients attach to outcomes of the decision, we designed a model for deciding which kidneys would maximize a patient's duration and quality of life. In the model, the patient is involved in the process of deciding which kidneys would be acceptable or unacceptable for transplantation. We illustrate the decision model of four representative patients awaiting kidney transplantation.

This paper is organized as follows. Section 2 provides background information on the management of patients with end-stage renal disease. Section 3 describes the method for deciding which donor kidneys would be acceptable for transplantation and §4 illustrates this method for four representative patients. We discuss the implications of using this method in §5 and describe the mathematics that underlie the method in §6.

2. Background of End-stage Renal Disease

More than 40,000 persons per year in the United States develop insufficiency of kidney function to such an extent that they are unable to remove fluid, electrolytes, and biologic waste products (USRDS 1993). Without treatment, these patients would die within weeks to months from any number of complications, including excessive accumulation of fluid in the lungs, arrest of the normal heart rhythm, seizures, or coma. The primary forms of treatment for removing potentially toxic biologic waste products are hemodialysis (dialysis through direct cleansing of the blood), peritoneal dialysis (dialysis through the small vessels surrounding the gut), and kidney transplantation. Each of these options are imperfect solutions to ESRD. Dialysis is a significant inconvenience to most patients because of the extensive time needed for treatments—at least 9 to 12 hours per week. Further, patients treated with dialysis on average experience a significantly lower level of function or quality of life than persons without kidney disease.

If successful, kidney transplantation offers patients the opportunity to be free of the inconveniences of dialysis treatments and patients often report a quality of life that is comparable to persons without kidney disease. The limitations of transplantation are the immediate risks of surgery and the later risks of the potent immunosuppressive drugs needed to reduce the risk of rejection of the donor kidney—or graft—such as life-threatening infections and some forms of blood and skin cancers. The best chance at limiting the risk of transplant rejection is achieved by transplanting the kidney of a living-related donor. But the number of living-related donor transplants is small in the United States, such that more than 70 percent of donor kidneys are obtained from cadavers.

Physicians are required by law to inform each patient at the beginning of ESRD of the three treatment options for ESRD. Because of the poor availability of donor kidneys, more than 90 percent of patients begin one of the two dialysis options. For those patients who desire a transplant, they are referred to a local transplant facility to be placed on the transplant-waiting list. Waiting times on the transplant list vary on average between 20 and 35 months depending on patient health and demographic characteristics (USRDS 1993). For example, patients with A blood type experience shorter waiting times because of the greater availability of A donor kidneys (Held et al. 1988).
Based on criteria established by the UNOS Point System, when a donor kidney becomes available, the transplant team selects a patient from the waiting list to receive the donor kidney.

Among the most important selection criteria for the UNOS Point System is the degree of immunologic match between the donor kidney and the patient (Table 1). Almost every cell of the body contains proteins called Human Leukocyte Antigens (HLA). Leukocytes are white blood cells that play a vital function in recognizing and reacting to proteins that are not commonly found in the body (Danovitch 1992). For example, white blood cells are essential for combating infections. In the setting of organ transplantation, however, white blood cells are stimulated to recognize the grafted organ as foreign and release substances that damage the kidney and that ultimately will lead to rejection of the graft and the patient needing to return to dialysis. In the first year after transplantation, about 15 percent of patients reject the grafted organ and resume dialysis. HLA antigens play a key role in the white blood cells’ recognition of foreign antigens. The two primary means for limiting the reaction against the graft are to match as closely as possible HLA antigens between the donor kidney and recipient and to have the patient take immuno-suppressive medications. The three major types of HLA antigen used in the UNOS Point System are A, B, and DR.

At the time that a donor is identified—usually a traumatic death in a person under age 45—the donor kidney is harvested and transported as quickly as possible in a preservative solution to limit damage that occurs to tissue that is not constantly perfused with blood. The referring dialysis physician also is notified about the availability of the kidney and asked if the patient is medically suitable still for transplantation. Some patients may not be suitable because they have been hospitalized, have a recent illness that precludes immediate transplantation, or have decided they no longer desire a transplant. The patient is called to come to the transplant facility and the transplant is performed as soon as possible, usually within 24 hours.

### Table 1: United Network for Organ Sharing Point System

<table>
<thead>
<tr>
<th>HLA Matching</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>0—A, B, DR mismatch</td>
<td>10</td>
</tr>
<tr>
<td>0—B, DR mismatch</td>
<td>7</td>
</tr>
<tr>
<td>0—A, 8 mismatch</td>
<td>6</td>
</tr>
<tr>
<td>1—B, DR mismatch</td>
<td>3</td>
</tr>
<tr>
<td>2—B, DR mismatch</td>
<td>2</td>
</tr>
<tr>
<td>3—B, DR mismatch</td>
<td>1</td>
</tr>
<tr>
<td>Waiting time</td>
<td></td>
</tr>
<tr>
<td>Patient with longest waiting period</td>
<td>1</td>
</tr>
<tr>
<td>(proportionate points for shorter periods)</td>
<td>0.5</td>
</tr>
<tr>
<td>Each year on the waiting list</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Children</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 0–5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Age 6–10</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

| Prenatalization (i.e., PRA > 80%) | 4 |

*PRA = panel reactive antibodies.

3. **Methods**

The current system of allocating kidneys provides the patient little opportunity to be involved in deciding which donor kidneys would be acceptable for his or her circumstances. Decisions are made instead by the transplant team in conjunction with criteria of the UNOS Point System. As a result, some patients may receive kidneys that they would have preferred not to receive and that would have been acceptable to other patients on the waiting list. Conversely, some patients may be denied kidneys that they would have found acceptable. In the experience of one of us (I.C.H), patients have chosen not to be placed on the transplant waiting list because of concerns about receiving a donor kidney with an unacceptably high risk of rejection or where the risks of immunosuppressive drug side-effects are high.

In our framework, the patient contributes to the decision about which types of kidneys would be acceptable to him or her for transplantation. We based our model on the principles of other models in which the decision maker judges when the characteristics, or qualities, of an option are sufficiently good to justify making a decision (Navarro 1987, Howard 1989). For example, the stock broker judges whether the price of a stock is sufficiently high to justify the buying or
selling of that stock. In this decision, the stock broker must consider his or her expectation of future stock prices. Similarly, an employer judges the qualifications of job applicants to decide whether to hire among the available pool of applicants or to continue to interview job applicants in the hopes of finding a more qualified candidate.

The problem patients face is to judge the quality of donor kidneys that would be acceptable to them for transplantation. In this instance, we chose the expected 1-year graft (transplanted kidney) survival rate as the criterion for judging the acceptability of a donor kidney because, from the perspective of patients and clinicians, 1-year graft survival is an important outcome of transplantation. As describe in more detail in §6.1, the expectation of 1-year graft survival can be estimated for any donor kidney-patient pair using published regression models (Gjertson 1991b). For each patient, we derive his or her \textit{minimum acceptable} expected 1-year graft survival rate, which we denote as $d^*$, such that if the expected 1-year graft survival rate for donor kidney is assessed to be higher than this minimum, the patient would be willing to accept the donor kidney for transplantation.

3.1. Selecting Acceptable Donor Kidneys

We estimated the patient- and donor-kidney-specific expectation of 1-year graft survival using a published regression model of the UCLA Transplant Registry (Gjertson 1991b). In an analysis of more than 30,000 kidney transplants done in the United States between 1985 and 1989, Gjertson estimated in a logistic-regression model the effect of patient and donor-kidney characteristics on 1-year graft survival (Gjertson 1991b). Patient characteristics included age, gender, race/ethnic background, original cause of ESRD, response to antigens that are foreign to the patient’s normal body proteins (panel reactive antibodies), and the facility where the transplantation was performed. Donor-kidney characteristics included donor age, gender, race/ethnic background, duration the donor kidney was not perfused by blood (called cold-ischemia time), and the degree of matching of HLA markers (Gjertson 1991b).

Just as the stock broker must predict the price of future stocks to decide whether to buy or sell stock now, the patient must predict the expected 1-year graft survival rates of future donor kidneys to decide whether to be considered eligible for a donor kidney now. The UCLA Transplant Registry published data also on the number of donor kidneys with each characteristic—e.g., the number of donor kidneys by race and gender. We thereby estimated the distribution, using a beta distribution, of 1-year graft survival that the patient may expect to observe in a given month (see Appendix, §6.2). We chose a beta distribution because it fit the data well and the beta distribution describes values bounded between 0 and 1, like graft-survival rates.

We modeled a representative patient’s quality-adjusted life expectancy from the moment he or she became eligible for transplantation. We assumed the patient in any month may experience one of five health states: alive on dialysis waiting for transplant ($S_1$); not eligible for transplantation ($S_2$); received a functioning renal transplant ($S_3$); transplant failed ($S_4$); and death ($S_5$). We modeled monthly transition rates among these health states as a Markov chain (see Figure 1). We used monthly transition rates, instead of daily transition rates, because the available data are not sufficiently precise to calculate daily transitions. However, the model could be generalized to use daily transition rates if such data were available. In practice, patients may move from $S_1$ to $S_2$ and back to $S_1$ or other states in the same month; however, these

![Illustration of the Markov Process (e.g., Transitions Among Outcomes) Used in the Model. Each State is Represented by a Circle. Transitions Between States Are Shown by the Arrows.](image-url)
Table 2 Four Representative Profiles of Patient Health and Demographic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65</td>
<td>45</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Gender</td>
<td>male</td>
<td>female</td>
<td>male</td>
<td>female</td>
</tr>
<tr>
<td>Ethnic group</td>
<td>white</td>
<td>white</td>
<td>black</td>
<td>white</td>
</tr>
<tr>
<td>ABO blood type</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PRA level (%)(^a)</td>
<td>20</td>
<td>0</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Renal diagnosis</td>
<td>diabetes</td>
<td>nephrosclerosis</td>
<td>diabetic</td>
<td>diabetic</td>
</tr>
<tr>
<td>Prior transfusions (#)</td>
<td>no</td>
<td>yes (&gt;3)</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Prior grafts (#)</td>
<td>yes (1)</td>
<td>no</td>
<td>yes (1)</td>
<td>yes (1)</td>
</tr>
</tbody>
</table>

\(^a\) Panel reactive antibodies.

events are so rare that little precision is lost by using monthly transition rates.

In any state, the patient is assumed to be able to assign a quality-of-life score (QOL,) to that state \(i\). In practice, each patient could be surveyed at the time of the first evaluation for eligibility of transplantation. We assumed that 0 represents death, 1 represents the quality of life of the highest attainable health state, and other health states had scores between 0 and 1. If the quality-of-life scores were equal to 1 for each health state, then quality-adjusted life expectancy would equal life expectancy. We also considered the adverse effect on quality of life of immunosuppressive drug side effects (Danovitch 1992). The approach taken here assumes that the various elements of a health state are incorporated into one aggregate health state. For example, the quality of life of dialysis is a function of the patient’s attitudes toward intradialytic symptoms, the inconvenience of longer dialysis sessions, and the risk of complications, such as hospitalizations or uremic symptoms. Similarly, the quality of life with transplant is a function of the patient’s attitude toward the risks of surgery, the inconvenience and risks of taking immunosuppressive medications, and the chance to avoid the inconveniences of dialysis. It is possible, in theory, to survey patients about each of these attributes to create a patient-specific multiattribute utility function that expresses the patient’s quality of life in these states (Keeney and Raiffa 1976); however, routinely conducting such surveys in clinical practice would be difficult. Moreover, to make this decision, it is of less importance to know precisely how patients would aggregate the various attributes that comprise a health state. We therefore chose to design the model using global, or holistic, descriptions of health states (Keeney and Raiffa 1976). To account for perception that future life years may not be as valued as current life years, we discounted future time periods at a fixed monthly rate \((1 - \alpha)\) (Lipscomb 1989).

In each health-treatment state, it is possible to write a mathematical expression describing the patient’s quality-adjusted life expectancy once they visit that state. These mathematical expressions are described in §6.3 of the Appendix. From state 1, the patient’s quality-adjusted life expectancy is a function of (1) expected quality-adjusted life expectancy if a donor kidney were to become available that the patient would permit to be transplanted, (2) the expected quality-adjusted life expectancy if a donor kidney became available that the patient would not permit to be transplanted, and (3) the quality of life with dialysis in that month. If the patient sets a high standard for judging donor kidneys as acceptable, then they would reduce their probability of being transplanted in any given month. However, once they were transplanted, they would have a higher probability of 1-year graft survival. The model balances these concerns taking into consideration also the patient’s attitudes about the quality of life in these various states.
Table 3  Assigned Quality-of-Life Assessments

| Patient | S₁ | S₂ | S₃ | S₄ | S₅ | Imm
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.65</td>
<td>0.60</td>
<td>0.90</td>
<td>0.60</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>2</td>
<td>0.65</td>
<td>0.60</td>
<td>0.90</td>
<td>0.60</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>3</td>
<td>0.65</td>
<td>0.60</td>
<td>0.90</td>
<td>0.60</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>4</td>
<td>0.65</td>
<td>0.60</td>
<td>0.90</td>
<td>0.60</td>
<td>0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

S₁ = alive on hemodialysis with option for transplantation; S₂ = alive on hemodialysis with no option for transplantation (e.g., acute or chronic illness that precludes transplant); S₃ = successful transplantation; S₄ = failed transplantation; S₅ = death; Imm = side effects of immunologic drugs.

It calculates the minimum 1-year graft survival rate that, used as the criterion for judging the acceptability of donor kidneys for transplantation, would maximize the patient's quality-adjusted life expectancy from state 1.

4. Illustration

We illustrate the framework for four representative patients awaiting kidney transplantation. Depending on their medical status, preferences, and state of information, the minimum acceptable 1-year graft survival is estimated for each patient.

4.1. Representative Patient Types

Table 2 shows the patients' demographic and health characteristics. Patient 1 has characteristics of a significant fraction of patients undergoing hemodialysis, such as age 60 or more, diabetes, and type O blood type. Patient 2 is more typical of patients who receive a transplant, such as age 50 or less, no diabetes, and never previously transplanted. Patient 3 differs from Patient 1 only by race (black vs. white), which is an important consideration because of the different distribution of HLA antigens by race that affect the likelihood of finding donor kidneys with low numbers of mismatches. This race difference in expected mismatch rates is reflected in our model in the estimate of the distribution of expected 1-year graft survival rates. Patient 4 differs from Patient 1 only by gender. We set the annual discount rate equal to 5 percent (Lipscomb 1989), i.e., \( \alpha \) equal to 0.996 (≈ \( (1 - 0.05)^{11/12} \)).

4.2. Data Sources

We assigned transition probabilities based on published data on graft- and patient-survival rates in the United States (Gjertson, 1991, 1993; USRDS 1993). To contrast only the effects of differences in 1-year graft-survival rates among Patients 1, 3, and 4, we assumed identical transition rates (Figure 2). Because of Patient 2's younger age, we assigned her lower rates of transition into state 5 (death) than the other patients. As described before, graft-survival rates were calculated based on a regression model published by Gjertson (Gjertson, 1991, 1993).

In the base-case analysis, we assigned for each patient the same quality-of-life ratings to each of the five health states (Table 3). We alter these assumptions (see §4.4, Sensitivity Analyses) to determine how quality-of-life ratings affect the minimum criterion for selecting donor kidneys. Based on published reports of patients' experiences with end-stage renal disease (Sackett and Torrance, 1978, Hornberger 1993), we assigned quality-of-life ratings that approximate the average ratings of patients surveyed in the literature.

4.3. Results

The minimum 1-year graft survival rate, \( d^* \), differed significantly among the four patients: 69.9% for Patient 1, 87.3% for Patient 2, 66.2% for Patient 3, and 72.2% for...
Patient 4 (Table 4). The quality-adjusted life expectancy also differed significantly among the four patients: 63.3 months for Patient 1, 70.0 months for Patient 2, 60.9 months for Patient 3, and 64.8 months for Patient 4.

For each of these four representative patients, it is possible to separate the patient-specific from the donor-kidney-specific contribution to the minimum 1-year graft survival rate, $d^*$. For example, some patients may have lower $d^*$ because their personal characteristics make it difficult for them to be selective about the types of kidneys they can accept. Using a logistic model, we calculated the overall weighting score, $w^*$, that corresponds to $d^*$, where

$$d^* = \frac{1}{1 + e^{-w^*}}. \quad (1)$$

We also calculated for each of the four representative patients their patient-specific scores, $w$, by summing the Gjertson model’s regression coefficients for each of the patients’ characteristics. Their donor-kidney-specific scores, $w$, then were calculated by subtracting $w$ from $w^*$. Larger weighting scores imply a more favorable probability of successful transplantation at 1 year. $w$ was 0.748 for Patient 1, 1.480 for Patient 2, 0.514 for Patient 3, and 0.906 for Patient 4 (Table 4). For example, Patient 2 can be more selective—i.e., have a higher minimum acceptable 1-year graft survival—than Patient 1, in part because of her more favorable transplant characteristics (young age, low PRA, never transplanted).

We compared the results of our preference-based framework with what might be expected when using the UNOS Point System for four representative donor kidneys (Table 5). With our framework, Patients 1, 3, and 4 would accept three of the donor kidneys (Cases 1, 3, and 4) and Patient 2 would accept only one of the kidneys (Case 1). Even though the expected 1-year graft survival for Case 3 is greater for Patient 2 (86.3%) than for Patient 1 (75.2%), Patient 1 would accept this kidney while Patient 2 would reject it. These results occurred because Patient 2 has stricter criteria for selecting kidneys than Patient 1. With the UNOS Point System, all patients could be transplanted with any one of the four kidneys if the patients had waited long enough (e.g., more than 3.5 years on the waiting list, which approximates the average waiting time for blacks in the United States) (USRDS 1993). Hence, patients could be transplanted with unacceptable kidneys, which then would be unavailable to other patients who would have found them acceptable for transplantation.

### 4.4. Sensitivity Analyses

We changed each of the variables in the model to assess the effect of these changes on $d^*$ (Table 6). The important variables affecting $d^*$ were: quality of life assessment after the failed transplant (QOL), immunosuppressive side effect (Imm), probability of death while undergoing dialysis ($P_{13}$), probability of death after failed transplant ($P_{15}$), time preference ($\alpha$), and the probability of being eligible for retransplantation ($\delta$). Among them, the probability of death while undergoing dialysis ($P_{13}$) most affected the value of $d^*$. It is notable that a 3% absolute reduction in patient survival on dialysis ($P_{13}$) would give an approximate 8% absolute reduction in the value of $d^*$. Patients with a higher relative risk of death on dialysis should, thereby, be less selective in choosing among donor kidneys.

### 5. Discussion

Before a patient can be selected to receive an available donor kidney, it is necessary to decide which patients should be considered eligible for that kidney. Choosing the set of eligible patients with the current UNOS Point System typically ignores how patients’ preferences may determine their willingness to be transplanted with some kidneys. Moreover, the UNOS Point System,
which was based on expert judgment (Starzl, Hakala et al. 1987), is insufficiently flexible to take full advantage of the latest published data on patient outcomes.

We designed and illustrated a method to improve the allocation of cadaveric donor kidneys that considers the importance patients attach to health outcomes and uses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base Case</th>
<th>Range</th>
<th>Absolute Change of $d^*$ (in % units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{OOL}_4$</td>
<td>0.6</td>
<td>0.0-0.9</td>
<td>Patient 1: -3.1, Patient 2: -1.4, Patient 3: -3.3, Patient 4: -3.0</td>
</tr>
<tr>
<td>$\text{Imm}$</td>
<td>0.2</td>
<td>0.0-0.5</td>
<td>Patient 1: 3.1, Patient 2: 2.4, Patient 3: 3.0, Patient 4: 3.3</td>
</tr>
<tr>
<td>$p_{15}$</td>
<td>0.04</td>
<td>0.01-0.05</td>
<td>Patient 1: -8.5, Patient 2: -8.7, Patient 3: -8.6, Patient 4: -8.4</td>
</tr>
<tr>
<td>$p_{65}$</td>
<td>0.04</td>
<td>0.01-0.06</td>
<td>Patient 1: 4.7, Patient 2: 2.2, Patient 3: 5.0, Patient 4: 4.5</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>0.996</td>
<td>0.97-1.0</td>
<td>Patient 1: 3.2, Patient 2: 3.9, Patient 3: 3.3, Patient 4: 3.1</td>
</tr>
<tr>
<td>$\delta$</td>
<td>0.3</td>
<td>0.0-0.5</td>
<td>Patient 1: -3.9, Patient 2: -1.8, Patient 3: -3.9, Patient 4: -4.0</td>
</tr>
</tbody>
</table>

$^a$ A positive value implies that an increase in variable through its range led to an increase in $d^*$ and a negative value implies an increase in the variable through its range led to a decrease in $d^*$.

$^b$ Value used in base case analyses.

$^c$ Range over which variables were assessed.
the published data on transplant outcomes. Using this system, patients might be found who are willing to wait longer to assure being transplanted with a very desirable kidney and thereby allow other patients to be transplanted sooner. Once a donor kidney becomes available, its characteristics could be observed to identify its type, such as described by Gjertson (Gjertson 1991a, 1991b, 1993). Our results suggest that patients might vary significantly in the criteria they would use to accept a donor kidney for transplantation. As the sensitivity analyses showed, some patients may be less selective in the donor kidneys they would accept because they rate the quality of life of hemodialysis significantly lower than that of transplantation.

Once the set of eligible patients for an available donor kidney is identified by this method, it also could be used to determine which patient would benefit the most from the transplant, as measured by the difference in quality-adjusted life expectancy with transplant and dialysis. As in the UNOS Point System, extra points could be accumulated for patients who have waited excessively for a transplantation to thereby assure a more equitable chance of transplantation for patients with less favorable transplant characteristics.

The advent of modern desktop computers permits such a system to be implemented in clinical practice today. As patients are seen for their first evaluations for consideration of kidney transplantation, patients’ health and demographic characteristics would be entered into a computerized database. The patient-specific score predicting 1-year graft survival \( S \) would be calculated automatically. The patient’s preferences for the five health states would be surveyed using utility-assessment methods that are being applied increasingly in clinical practice (Hornberger, Chernew et al. 1992). In our experience, valid assessments by patients with end-stage renal disease can be made in less than 20 minutes using computer-aided survey tools (Lenert and Hornberger 1991; Hornberger, Chernew et al. 1992). Data from such assessments would be entered into a computerized database to estimate \( d \) and expected quality-adjusted life expectancy. The patient and transplant team then could be given examples of the acceptable and unacceptable donor kidneys and further discussion might ensue to learn if they agree with the recommendation. Because patients’ attitudes may change with time, repeat assessments may be indicated at regular intervals, e.g., every 6 months, or at the patient’s request.

It may be argued by some that patients should not be involved in decisions affecting allocation of medical resources as scarce as donor kidneys. We disagree for two reasons. First, individual patients would describe their preferences for different health states only, but would have no direct input into deciding the probability of health outcomes. Panels of health experts and patient representatives would use the best available evidence in deciding transition probabilities for particular patient types. It is possible to estimate transition probabilities from existing clinical databases, such as collected by the UCLA Transplant Registry and the U.S. Renal Data System. Surveys of hundreds of patients with end-stage renal disease indicate that they can make valid and reliable judgments about their health (Sackett and Torrance 1978; Hornberger, Chernew et al. 1992). For the minority of patients who may find such assessments problematic, it may be inappropriate to place them on the transplant list at all because the safe use of immunosuppressive drugs requires a knowledgeable patient. Second, there may be concerns that patients could systematically alter their responses on quality-of-life surveys—and thereby not report their true preferences—to reduce their waiting times. There is no advantage to this strategy because patients would make themselves vulnerable to receiving an unacceptable kidney or to waiting even longer for a transplant.

A national consensus on the statistical model used to calculate patient survival and 1-year graft survival may be difficult to achieve. Some experts argue that less emphasis should be placed on immunologic characteristics (Gaston, Ayres et al. 1993); others argue for the importance of these factors in allocation decisions (Starzl, Hakala et al. 1987). These differing opinions do not invalidate our framework. It could be debated as to whether the framework should be implemented as a national guideline, such as the UNOS Point System, or whether regional transplant groups would be able to customize probabilities in the model to reflect local opinions (Hyver and Petersen 1989).
Table 7 The Estimated Parameters, Means, and Standard Deviations of $f(x)$ for Each Patient

<table>
<thead>
<tr>
<th>Patients</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>$*\beta$</td>
<td>(38, 14)</td>
<td>(71, 13)</td>
<td>(38, 17)</td>
<td>(37, 12)</td>
</tr>
<tr>
<td>Mean$^a$</td>
<td>0.731</td>
<td>0.845</td>
<td>0.691</td>
<td>0.755</td>
</tr>
<tr>
<td>SD$^a$</td>
<td>0.061</td>
<td>0.039</td>
<td>0.062</td>
<td>0.061</td>
</tr>
</tbody>
</table>

$^a$ For each patient was fitted by a beta distribution with parameters $\beta_0$ and $\beta_1$. $\beta$, $\beta_0$, $\beta_1$, defined in Section 6.2.

$^b$ Represents the mean of the beta distribution, or the expected 1-year graft survival rate for all donor kidneys.

$^c$ Represents the standard deviation of the beta distribution.

5.1. Summary

We propose a new system for selection of donor-kidneys by transplant recipients that accounts for variations in patient preferences for health outcomes. We expect that adoption of such a system would result in an allocation system that is more responsive to patients' preferences.$^1$

$^1$ The authors wish to thank Doug Owens, Margaret Brandeu, and three referees of Management Science for their helpful comments.

6. Appendix

Section 6.1 explains the method for estimating the expected 1-year graft survival rate for a given patient transplanted with a specific type of donor kidney. Section 6.2 describes the method for estimating the distribution of future 1-year graft survival rates for the pool of donor kidneys. Section 6.3 describes the model for estimating a patient's minimum 1-year graft survival rate that would be acceptable for transplantation.

6.1. Estimating Expected 1-year Graft Survival Rates

The logistic-regression model published by Gjertson (1991b) included 11 patient characteristics: (1) age, (2) gender, (3) ethnic group, (4) original disease causing end-stage renal disease, (5) number of transfusions, (6) graft number, (7) highest PRA level, (8) year of transplant, (9) use of cyclosporine to prevent rejection, (10) center of transplantation, and (11) donor relationship (i.e., cadaver versus living-related). The model also included five donor-kidney characteristics: (1) age, (2) gender, (3) ethnic group, (4) HLA mismatches, and (5) cold-ischemia time. These 16 characteristics were used to estimate the probability of graft survival at 1 year. Each characteristic in Gjertson's model had many levels—e.g., gender has two levels: man or woman—and regression coefficients were estimated for the effect of each level on 1-year graft survival. It is possible then to classify any patient based on the combinations of the 11 patient characteristics and any donor kidney based on the 5 donor-kidney characteristics. There were 192,000 possible patient types and 3,024 possible donor-kidney types.

Let $x_i$ equal the expected 1-year graft survival rate for the $k$th-type patient transplanted with the $l$th-type donor kidney. For a patient of type $k$, it is possible to sum the regression coefficients for each patient characteristic into a weighting score, $w_i$. Also, for a donor kidney of type $l$, it is possible to sum the regression coefficients for each donor-kidney characteristic into a weighting score, $w_i$. The expected 1-year graft survival rate for the $k$th-type patient transplanted with the $l$th-type donor kidney is estimated as:

$$x_i = \frac{1}{1 + e^{-w_i}}$$

where $w_i = w_k + w_l$ is the weighting score for a specific pair of a patient and a donor kidney.

6.2. Predicting Future Donor Kidneys and Their Expected 1-year Graft Survival Rates

We denote by $x$ a random variable representing the 1-year graft survival rate of future donor kidneys and by $f(x)$ the probability density function of $x$ for the $k$th-type patient. We calculated the frequency of kidneys of each type that would be observed in the next month by randomly assigning characteristics to the donor kidneys according to their frequency in the population of 30,000 donor kidneys transplanted between 1985 and 1989 reported by Gjertson (1991b). For illustration, we assume independence among the characteristics of the donor kidneys based on the published data. In practice, it is possible to specify the precise distribution of donor-kidney types from data maintained by the UCLA Transplant Registry. We then calculated each of these kidneys' expected 1-year graft survival rate and fit these data to a beta distribution:

$$f(x) = \frac{x^{\alpha-1}(1-x)^{\beta-1}}{\Gamma(\alpha)\Gamma(\beta)}$$

for $0 < x < 1$. (3)

The two parameters of $\alpha$, $\beta$, and $\beta_0$, were calculated by solving two simultaneous equations that equal the mean and variance of expected 1-year graft survival rates in the pool of donor kidneys. The mean
equals $\beta_i/(\beta_a + \beta_i)$ and the variance equals $\beta_i\beta_a/(\beta_a + \beta_i)^2(\beta_a + \beta_i + 1)$. Table 7 shows the parameters, mean, and variance of $f_i$ for each patient.

6.3. Estimating Minimum Acceptable 1-year Graft Survival Rate

We estimated the quality-adjusted life expectancy for a patient of type $k$ from each of the five health states represented in the model. We denote quality-adjusted life expectancy upon entry into the ith state as QALE. Let QOL represent the patient's stated quality of life in the ith state and $P_i$ equal the monthly transition rate from state $i$ to state $j$. For formulation purposes, we assume that the patient enjoys QOL, the quality of the month and transition occurs at the end of the month.

From state 1, the patient may observe a donor kidney of type $l$ that satisfies the minimum 1-year graft survival rate—i.e., $x_{il} > d^*$—and then either (1) have a successful transplantation with quality-adjusted life expectancy of QALE, or (2) have failed transplantation with quality-adjusted life expectancy of QALE, or (2) ineligibility for transplantation (QALE), or the patient may die (QALE). Because QALE is equal to 0, we omitted this term from all equations. These possibilities are combined mathematically as:

$$\text{QALE}_1 = \alpha \int_0^l [1 - \text{QALE}_1] dx + \alpha \int_0^l f_i(x) dx [P_{i1}\text{QALE}_1 + P_{i2}\text{QALE}_2] + \text{QOL}_1.$$  (4)

From state 2, the patient may: (1) return to state 1 to become again eligible for a transplant ($S_1$), (2) stay in state 2 ($S_2$), or (3) die ($S_3$). We therefore express the quality-adjusted life expectancy in state 2 as:

$$\text{QALE}_2 = \alpha [P_{i1}\text{QALE}_1 + P_{i2}\text{QALE}_2] + \text{QOL}_2.$$  (5)

From which

$$\text{QALE}_2 = \frac{\text{QOL}_2 + \alpha P_{i2}\text{QALE}_1}{1 - \alpha P_{i2}}.$$  (6)

From state 3 during the first year, the patient may have a successful transplant. We assumed the overall quality of life in state 3 was equal to the patient's stated quality of life (QOL) without any side effects of transplantation minus an amount accounting for the potential loss in quality of life associated with side effects of immunologic drugs (e.g., infection, cancer). Specifically, $1 - x$ represents the loss of quality of life of these side effects and we assumed that these side effects are proportional to the probability of rejection, $1 - x$, because more frequent use of immunologic drugs are required to prevent rejection. The quality-adjusted life expectancy during the first year then is:

$$(1 + \alpha + \cdots + \alpha^3)[\text{QOL}_3 - (1 - x)^3]$$

$$= \left(1 - \frac{\alpha^4}{1 - \alpha} \right) \text{QOL}_3 - (1 - x)^3]$$  (7)

After the first year of successful transplantation, the patient may continue to have a successful transplant ($S_3$), have a failed transplant ($S_4$), or die ($S_5$). Let quality-adjusted life expectancy after the first year of a successful transplant equal $S$, then:

$$S = \text{QOL}_3 - (1 - x)^3 + \alpha P_{i3}\text{QALE}_4.$$  (8)

Solving,

$$S = \frac{1}{1 - \alpha P_{i3}} \text{QOL}_3 - (1 - x)^3 + \alpha P_{i3}\text{QALE}_4.$$  (9)

Combining Eqs. (8) and (10), quality-adjusted life expectancy upon entry into state 3 is:

$$\text{QALE}_4 = \left[1 - \frac{\alpha^3}{1 - \alpha} \right] \text{QOL}_3 - (1 - x)^3 + \alpha^2 \left[ \frac{\text{QOL}_4 - (1 - x)^3}{1 - \alpha P_{i3}} + \frac{\alpha P_{i4\text{QALE}_4}}{1 - \alpha P_{i3}} \right].$$  (11)

If a patient suffers a failed transplant, we assumed he or she will wait at least 6 months before becoming eligible for retransplantation—i.e., returning to state 1. We chose 6 months because this time reflects the duration on average that retransplant patients wait longer than first-transplant patients for a transplant (Sanfilippo, Vaughn et al. 1992). The quality-adjusted life expectancy of a failed transplant in the first 6 months then is:

$$\frac{1 - \alpha^3}{1 - \alpha} \text{QOL}_4.$$  (12)

After 6 months, some patients may no longer be eligible for retransplantation because of debilitated health or their own choice. We chose to model this possibility by assigning a probability, $\delta$, to the patient's chance of ever becoming eligible for retransplantation. We could have assigned alternative states to (1) failed transplant, waiting for repeat transplant, and (2) failed transplant, not waiting for repeat transplant. $\delta$ then represents the transition probability from the first to the second of these states in month 6. This formulation, which would provide a different notation, yields the same result as our method. Quality-adjusted life expectancy after the first 6 months of a failed transplant then equals:

$$\alpha^3 \left( \frac{\text{QALE}_4(1 + \delta)}{1 + \alpha P_{i4}\text{QALE}_4} \right).$$  (13)

From Eqs. (12) and (13), the quality-adjusted life expectancy from the first month of a failed transplant is:

$$\text{QALE}_4 = \left[1 - \frac{\alpha^3}{1 - \alpha} \right] \text{QOL}_4 + \alpha^3 \left(\text{QALE}_4(1 + \delta) \frac{\text{QOL}_4}{1 + \alpha P_{i4}\text{QALE}_4} \right).$$  (14)
The minimum acceptable 1-year graft survival rate, $d^*$, was calculated as that $d^*$ that maximizes QALE, by substituting equations and simplifying, we can rewrite Eq. (4) as:

$$QALE_i = a \int_0^a \left( x \left( \frac{a^{12}}{1 - aP_{33}} + \frac{1 - a^{15}}{1 - a} \right) QOL_5 + (x - 1)Imm \right) f_i(x)dx$$

$$+ a \int_0^a \left( 1 + \left( \frac{(a^{12}P_{24} + aP_{33} - 1)x}{1 - aP_{33}} \right) \left( \frac{1 - a^{12}}{1 - a} QOL_4 + a^{\delta} \left( QALE_i + (1 - \delta) \left( \frac{QOL_5}{1 - aP_{33}} \right) \right) \right) f_i(x)dx$$

$$+ a \int_0^a f_i(x)dx \left( \frac{(P_{11} - a)(P_{12}P_{33} - P_{13}P_{23})QALE_i + P_{13}QOL_2}{1 - aP_{33}} \right) + QOL_i.$$  \hspace{1cm} (15)

To find the $d^*$ that maximizes quality-adjusted life expectancy from state 1 for a patient of type $k$, we differentiated Eq. (15) with respect to $d$:

$$\frac{\partial QALE_i}{\partial d} = a^{\delta} \left( \frac{a^{12}}{1 - aP_{33}} + \frac{1 - a^{15}}{1 - a} \right) QOL_5 + (d - 1)Imm \right) f_i(d)$$

$$- a \left( 1 + \left( \frac{(a^{12}P_{24} + aP_{33} - 1)d}{1 - aP_{33}} \right) \left( \frac{1 - a^{12}}{1 - a} QOL_4 + a^{\delta} \left( QALE_i + (1 - \delta) \left( \frac{QOL_5}{1 - aP_{33}} \right) \right) \right) f_i(d)$$

$$+ a \int_0^a \left( 1 + \left( \frac{(a^{12}P_{24} + aP_{33} - 1)x}{1 - aP_{33}} \right) \left( \frac{1 - a^{12}}{1 - a} QOL_4 + a^{\delta} \left( QALE_i + (1 - \delta) \left( \frac{QOL_5}{1 - aP_{33}} \right) \right) \right) f_i(x)dx + a^{\delta} \left( \frac{P_{11} - aP_{12}P_{33} - P_{13}P_{23})QALE_i + P_{13}QOL_2}{1 - aP_{33}} \right)$$

$$+ a \int_0^a f_i(x)dx \left( \frac{(P_{11} - a)(P_{12}P_{33} - P_{13}P_{23})QALE_i + P_{13}QOL_2}{1 - aP_{33}} \right).$$ \hspace{1cm} (16)

We set $\frac{\partial QALE_i}{\partial d}$ in Eq. (16) equal to 0 to obtain the minimum 1-year graft-survival rate, $d^*$. Because $f_i(x) > 0$ for all values of $x$ between 0 and 1, $d^*$ satisfies the following equation:

$$\left[ -Imm \left( \frac{a^{12}}{1 - aP_{33}} + \frac{1 - a^{15}}{1 - a} \right) d^2 \right.$$  

$$+ \left( \frac{a^{12}}{1 - aP_{33}} + \frac{1 - a^{15}}{1 - a} \right) \left( 1 - a^{12} \right) QOL_5 + \left( \frac{a^{12}P_{24} + aP_{33} - 1}{1 - aP_{33}} \right) \left( 1 - a^{12} \right) QOL_4 + a^{\delta} \left( \left( QALE_i + (1 - \delta) \left( \frac{QOL_5}{1 - aP_{33}} \right) \right) \right) \right] d^*$$

$$+ \left[ - \frac{1 - a^{12}}{1 - a} QOL_4 - a^{\delta} \left( QALE_i + (1 - \delta) \left( \frac{QOL_5}{1 - aP_{33}} \right) \right) \right] \left( P_{11} - aP_{12}P_{33} - P_{13}P_{23})QALE_i + P_{13}QOL_2 \right) \left( \frac{1 - aP_{33}}{1 - aP_{33}} \right) \right] = 0. \hspace{1cm} (17)$$

To find a solution for $d^*$, it is necessary to solve Eqs. 15 and 17 simultaneously. We used numerical methods, using Mathematica* (Wolfram 1991) computer software, to find the $d^*$ that maximized quality-adjusted life expectancy in state 1. It also can be shown that the $d^*$ derived by solving these simultaneous equations is the point that maximizes QALE, (Ahn 1993).

**Notation**

<table>
<thead>
<tr>
<th>Notation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNOS</td>
<td>United Network for Organ Sharing</td>
</tr>
<tr>
<td>ESRD</td>
<td>End-Stage Renal Disease</td>
</tr>
<tr>
<td>$x$</td>
<td>1-year graft survival rate</td>
</tr>
<tr>
<td>$f(x)$</td>
<td>density function of 1-year graft survival for pool of donor kidneys</td>
</tr>
<tr>
<td>$S_i$</td>
<td>$i$th health state ($i = 1, \ldots, 5$)</td>
</tr>
<tr>
<td>QOL, Imm</td>
<td>quality of life in S, quality-of-life adjustment for side effects of immunosuppressive drugs</td>
</tr>
<tr>
<td>QALE</td>
<td>quality-adjusted life expectancy in S</td>
</tr>
<tr>
<td>$d$</td>
<td>monthly fixed discount rate (0-1)</td>
</tr>
<tr>
<td>$d^*$</td>
<td>minimum acceptable 1-year graft survival rate</td>
</tr>
<tr>
<td>$P_s$</td>
<td>monthly transition probability from S to -S</td>
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<tr>
<td>$W$</td>
<td>overall score for Gjertson's logistic regression model of 1-year graft survival</td>
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<tr>
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<td>patient-specific score</td>
</tr>
<tr>
<td>$W_i$</td>
<td>donor-kidney-specific score</td>
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<tr>
<td>$\delta$</td>
<td>probability of being eligible for retransplantation 6 months after failed transplant</td>
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References


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