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Original Contributions

A Multifactorial System for Equitable Selection of Cadaver Kidney Recipients

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During 1986, a total of 270 cadaver renal transplantations were performed at the University of Pittsburgh. Kidneys were allocated by a point system that awarded points to recipients for waiting time, antigen matching, antibody analyses, medical urgency, and logistic practicality. Kidneys were given to patients with the highest point totals in 98% of cases. To our knowledge, this is the first such multifactorial system for cadaver kidney allocation. Possibly it may be modified for extrarenal organs.

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TRANSPLANTATION of the cadaver kidney, liver, and heart has become increasingly successful and frequent since the introduction of cyclosporine. With these improved expectations have come concerns about how cadaver organs are allotted and to whom.

For editorial comment see p 3118.

In Pittsburgh, we have developed an objective system for the allocation of kidneys that has been in use for more than a year. We describe herein the essential components of the computerized system, how the system has functioned during the trial period, and the way in which it can be modified to serve pools of waiting liver and heart recipients.

CREDIT FACTORS FOR RENAL CANDIDACY

Preliminary Stratification

With rare exceptions, the donor and recipient should be of the same ABO blood type. Thus, the renal candidates were grouped according to whether their blood type was O, A, B, or AB. In each group, particular note was made of recipients who were 10 years old or younger, who weighed less than 27 kg, or both. These small recipients were listed separately. Sera from all candidates of appropriate blood type and size were matched against lymphocytes from the donor of the kidney to be allocated. A negative cross match, connoting the absence of antidonor cytotoxic antibodies in the recipient serum, was a necessary condition for placement on the list of potential recipients.

Time of Waiting

In each of the four groups and in the children's subgroups, candidates were listed in a computer in order of their entry to candidacy. The time of entry was defined as the referral date for consideration of transplantation. A rank order of waiting time was thereby established automatically. A maximum of ten points was awarded to the candidate waiting for the longest period, with fewer points for those with shorter tenure. For example, if there were 75 persons of O blood type waiting for kidneys, the person waiting the longest would receive $(75/75) \times 10 = 10$ points. A person whose rank order was 60 would have $(60/75) \times 10 = 8$ points. The 15th person on the candidate list would receive $(15/75) \times 10 = 2$ points. The most recent entry would be given $(1/75) \times 10 = 0.13$ points. An example of computations with a shorter list of candidates having B blood type is shown in Table 1.

Quality of Antigen Match

There are two antigens each at the A, B, and DR histocompatibility loci. Two points were given for each antigen matched, for a possible total of 12. Examples in a hypothetical situation are shown in Table 1.

Presensitization State With Antibodies

Preformed recipient cytotoxic antibodies were measured in all of the po-

Table 1.—Hypothetical Case: Five Potential Recipients for Two Cadaver Kidneys of B Blood Type*

		No. of Points					
Waiting Time, mo	Patient	Rank Order Waiting Time	Antigens Matched	Panel Reactive Antibody Number	Medical Urgency	Logistical Factors	Total
5	A	(5/5)×10=10	2×2=4	10%=1	0	0	**15**
4½	B	(4/5)×10=8	2×2=4	20%=2	0	0	**14**
4	C	(3/5)×10=6	0=0	0%=0	5†	0	**11**
2	D	(2/5)×10=4	3×2=6	30%=3	0	0	**13**
1	E	(1/5)×10=2	6×2=12	90%=9	0	0	**23**

*Kidneys were removed 14 hours before they were offered for transplantation.
†Frequent clotting of atrioventricular fistula.

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Table 2.—Cadaver Kidney Transplantations in Pittsburgh in 1986

	No. of Transplantations
Total	270*
Primary	210
Retransplantation	60
Site of procurement	
Local	112
Distant	158
Nationality of recipients	
American	256
Foreign	14
ABO types	
A	123
O	107
B	30
AB	10
Antigens matched (of 6)	1.4 ± 1.2†

*Includes six liver-kidney and one heart-kidney combination.
†Mean ± SD.

Table 4.—Urgency Classification for Liver and Heart Candidates

Status	Description	Units
1	Working	2
2	Home bound, cannot work	4
3	Home bound, with care	6
4	Hospital bound, not in intensive care unit	8
5	Intensive care unit	10
6	Ventilatory or cardiocirculatory support (including artificial heart)	12

tential recipients. The extent of these antibodies was expressed with a panel reactive antibody (PRA) number. The PRA number projects the percentage of the human population against which the recipient possesses antibodies, as estimated by actually testing against a panel of lymphocytes obtained from 60 human volunteers. One point was given for each 10% PRA number measured in the most recent serum sample. Thus, someone with a PRA number of 0% would receive zero points. Someone with a PRA number of 100%, reflecting sensitization and antibody formation against essentially all of the human population, would receive ten points. Examples are shown in Table 1.

Medical Urgency

A maximum of ten points could be given for medical urgency. The most common urgent situation was in patients whose access sites for dialysis had been exhausted. Otherwise, dialysis was a reasonable option to transplantation, and if dialysis was feasible, medical urgency usually was not granted (Table 1). Medical urgency credits were given only three times in 1986.

Table 3.—Justification for Overriding the Point System

Bypassed Patient/Age, y/Sex	Month of 1986	Reason for Deviation	Subsequent Time to Transplantation
1/63/M	June	Disparity of age between donor and recipient	16 d
2/22/F	June	Questionable abdominal hernia, not verified	Same day
3/60/M	June	Recipient too old, with previous transplant and high panel reactive antibody number	1 wk
4/54/F	July	Suboptimal donor organ, with need to use hypogastric artery of young recipient	7 wk
5/55/M	July	Suboptimal donor organ, with need to use hypogastric artery of young recipient	8 wk

Logistical Score

A maximum of six points could be awarded for logistical factors, based on the ease and rapidity with which the transplantation could be performed. For example, if a kidney was offered near the end of its permissible storage time, logistical points might be given to a recipient whose proximity to the hospital and history of recent dialysis could permit prompt transplantation. Logistical points for time were not awarded unless the kidney was offered to us more than 24 hours after its removal from the donor.

Provision for Network Agreements

Some of the organ-sharing networks, including Southeastern Organ Procurement Foundation and United Network for Organ Sharing, have special arrangements for sharing of antigen-matched kidneys. Our own commitment has been to ship all locally procured kidneys if any group in the country has a candidate with a six-antigen match. If in turn such a perfectly matched kidney were offered to us for a specific patient, or even if the matching were less perfect than this, the sharing agreement was honored and the kidney was given to the specific recipient even though this required overriding of the local selection process by the point system. During 1986, this happened ten times. During the 12-month period, there were only two six-antigen matches.

Hypothetical Example

In the case summarized in Table 1, two kidneys from a B blood type donor became available 14 hours after donor nephrectomy at another center. Five potential recipients had negative cytotoxic cross matches. The candidate waiting for the shortest time became the first choice because of credit points gained from a perfect antigen match and because of points gained from a high PRA number. The second choice was a patient whose antigen match was mediocre but who had the longest waiting time. One of the patients was given points for medical urgency. All of the others were stable while undergoing dialysis. Logistical points were not awarded since there was a reasonable margin of safe cold ischemia time.

RESULTS

During the calendar year 1986, a total of 270 cadaver kidneys were transplanted, 210 to primary recipients and 60 to patients undergoing retransplantation. Seven of the recipients also were given livers or hearts, in six instances simultaneously.

The majority (59%) of the kidneys were accepted from other procurement agencies than our own, often after efforts to place the kidneys elsewhere had engendered a long period of cold ischemia. The distribution of blood groups was similar to that in the general population (Table 2). Fourteen (5.2%) of the kidneys went to nonresident aliens. Twenty-one of the 270 recipients were 16 years old or younger and therefore classed as children; 12 were 10 years old or younger and/or weighed less than 27 kg.

Excluding the seven kidneys given to liver or heart recipients, and the ten kidneys sent from outside for specific antigen-matched recipients, there were 253 grafts. Of these, 247 went to the recipients with the highest point score on the computer printout. The decision to override the system with the six exceptions was made by the operating surgeon. The reasons are summarized in Table 3. All five of the patients passed over received a kidney within a few days or weeks (Table 3).

COMMENT

To our knowledge, this kind of computerized system for cadaveric kidney allocation has not been used previously. A compromise was developed whereby tissue matching played a significant but far from overriding role. Although medical urgency and time constraints of organ ischemia were considered, the recipient's waiting time had the most pervasive influence since it provided points in every case.

A perfect tissue match would have

provided enough points to outweigh a long waiting time, but such matching usually was not possible even when a local or national search was conducted. Only two of the 270 kidney recipients had six-antigen matches with their donors. The average antigen match out of a possible six was 1.4 ± 1.2 (SD) (Table 2).

While the point system was being programmed for a computer, there was concern that the system might allow highly sensitized patients for whom cross match–negative donors had been found to be passed over, with loss of a golden opportunity. This concern was unfounded. Patients with a high PRA number received generous points to a maximum of ten, almost ensuring selection if points also accrued for antigens matched. Widely reacting cytotoxic antibodies often have specificity against the class 1 antigens of the A and B histocompatibility loci; because of this, the demonstration of a negative cytotoxic cross match for a highly sensitized patient should predict a good antigen match.[1] Thus, the antibody and antigen credits tend to be reinforcing. Finally, most highly sensitized patients have already had long waiting times, providing tenure points as well.

Avoidance of antigen matching as the sole or main criterion of recipient selection is justified on several counts. Insistence on perfect or even good matching would cause major wastage of kidneys. It has even been questioned whether the extra time consumed in a national search for good matching and in transporting the kidneys cancels any potential immunologic advantage.[2,3] Finally, a system based solely on antigen matching would create a genetically determined bias in which some patients would never be able to find well-matched kidneys whereas others would fare well. Numerous studies have shown how some patients with common antigen combinations can expect to receive a kidney promptly, whereas in less favored potential recipients with unusual antigen patterns, the chances can be almost nonexistent.

Introduction of an objective method for selection of a renal recipient selection has had a positive effect on our program. Ad hoc case selection at odd hours, guided by the often faulty memory of a transplant coordinator or by incomplete tabular information, has been eliminated. During the course of the trial year, waiting lists of nonsensitized A and AB recipients have been completely eliminated, and the duration of waiting of similarly "clean" O and B recipients has been greatly shortened. At the same time, kidneys have been found for large numbers of sensitized patients. A decision to proceed with transplantation still rests with the responsible surgeon, the only provision being that an explanation must be sent to the director of the organ procurement foundation and to a community oversight committee when there is a deviation from the standardized process.

Although all explanations for an override were accepted by the reviewing committees (Table 3), the necessity for justification may have subtly influenced the behavior of the transplant surgeons. During the first six months of the year, exceptions to the point system were made, but in the last half of the year, there were no such overrides.

Once patients are accepted on a waiting list, they are not discriminated against on the basis of race, color, creed, or national origin. In many centers, including Pittsburgh until 1984, and in some sharing networks, a policy has been followed of using only leftover, anatomically flawed, or otherwise suboptimal cadaver kidneys for foreign recipients. At the University of Pittsburgh, an ethics committee has examined this double-standard allocation of organs and has found it to be untenable. As an alternative, we imposed a quota in 1985 and now allow no more than 5% of kidneys for which there is competition by American citizens to be given to nonresident aliens. In the six consecutive years 1981 through 1986, the percentage of kidneys transplanted to foreign nationals, including those for whom no American recipient could be found, has been 12.5%, 5%, 7.5%, 15%, 7.2%, and 5%, respectively. Maintenance of these percentages at a reasonable level has required active discouragement of foreigners from migrating to Pittsburgh to undergo long-term dialysis with the ultimate objective of transplantation. Solicitation of non-Americans to candidacy always has been prohibited.

Whether similar selection techniques can be applied for liver and heart transplantation remains to be determined. The preliminary candidate stratification for these organs, including donor vs recipient size, is far more restrictive than for the kidney. Only a fraction of recipients on a liver or heart waiting list can be considered appropriate finalists; for these, all credit factors other than medical urgency become trivial since alternative forms of treatment are not available.

Consequently, our policy with heart and liver transplantation has been to treat the sickest patients first. Considerable effort has been made to define what constitutes urgency (Table 4). If waiting time was relevant in awarding points, the association might almost be inverse since the candidates with the greatest tenure on our liver and heart lists tend to have the most indolent disease courses, for which transplantation is least urgently needed.

With livers and thoracic organs, frequently there is not time for antigen matching or cross matching, and these studies are considered irrelevant except for sensitized candidates for heart transplantation. Finally, the safe preservation limit for hearts and livers is six hours or slightly more, a time so short that the logistical requirements of bringing together the donor organ and recipient become the only serious consideration other than medical urgency. The almost total preoccupation with medical urgency and logistic practicality is not apt to change until preservation of donor organs is improved or, even more importantly, until prosthetic hearts and livers can be developed for interim support.

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