CHAPTER 14

Kidney Transplantation in Pittsburgh: Experience and Innovations

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The first kidney transplant at the University of Pittsburgh was performed in 1963, but it was not until 1977 that kidney transplants were done on a regular basis. Since then the University of Pittsburgh has developed into a major transplant center. In 1986 alone 271 kidney transplants, 344 liver, 104 heart, and 15 heart/lung transplants were performed at the University Health Center of Pittsburgh.

The data presented here are maintained on a newly developed center-oriented computerized transplant data management system. A scoring system for equitable allocation of kidney transplant organs is an integral part and will be discussed further.

MATERIALS AND METHODS

From 1977 to the end of May 1987, 1,243 cadaveric kidney transplants, 17 kidney transplants from living related donors, and 16 multiorgan transplants including a kidney were performed at the University Health Center in Pittsburgh, Azathioprine and steroid immunosuppressive baseline treatment was routinely used until a randomized trial versus combined CsA and steroid treatment was performed in early 1981. This was followed by the formal introduction of CsA and steroids as the baseline immunosuppressive treatment. Azathioprine and steroids remained the first choice only for living related kidney transplants. Since November 1984 the murine monoclonal antibody OKT3 (ORTHOCLONE OKT3, ORTHO Pharmaceutical Corporation, Raritan, NJ) has been used for treatment of severe rejection episodes.

Statistical analysis was performed using the SPSSPC (SPSS/PC Software Inc., Chicago, IL) (1) and BMDP/PC (BMDP Software Inc., Los Angeles, CA) software packages. Statistical analysis of differences in actuarial survival among groups was done by the Breslow (generalized Wilcoxon) and the Mantel-Cox (generalized Savage) test. The Breslow test is weighted towards earlier events and the Mantel-Cox test towards later events (2).

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For analysis of transplant outcome in various groups, all grafts or patients lost were included for analysis. No patient was omitted, even if the graft was lost because of reasons presumably unrelated to transplantation. Follow-up of patient data continued until the end of July 1987. When not stated otherwise, actuarial survival is reported for the one-, 2-, and 5-year periods.

RESULTS

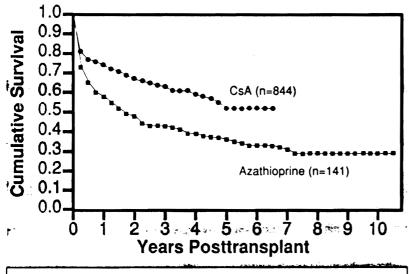
Demographics

The age of the kidney transplant patients ranged from 0.6 to 73.6 (mean 37.9 \pm 4.5 SD years). Of these patients, 1,104 received 1,276 cadaveric kidney transplants; 985 of these were primary cadaveric transplants, 258 cadaveric retransplants, 16 combined organ transplants including a kidney, and 17 living related kidney transplants (Table 1). Of the pediatric age group, 87 patients (<18.0 years, mean 12 \pm 4.6 SD years) received 112 grafts and 1,017 patients belonging to the adult patient group (\geq 18.0 years, mean 40.4 \pm 12.6 SD years) received 1,164 grafts. Of these, 12 were below 5 years and 181 equal or over 55 years. Seven hundred seventy-seven kidney grafts were transplanted into male versus 499 grafts into female recipients.

Multiorgan Transplants Including the Kidney

Ten combined liver/kidney, 3 of them in the pediatric age group, one heart/kidney, and 5 pancreas/kidney transplants were performed using organs from the same donor. Seven of the combined liver/kidney recipients are currently alive with 6 patients having functioning kidneys (3). Of the pancreas/kidney recipients 4 are still alive with functioning kidney grafts. The heart/kidney recipient died 3 months following the combined transplant procedure.

Analysis of panel-reactive antibody (PRA) and donor-reactive crossmatch data in combined liver/kidney transplants has shown in some patients a significant decrease in PRA and donor-reactive antibodies starting immediately after induction of blood flow through the liver donor. Three recipients had a strong donor-positive crossmatch. In 2 patients the donorspecific antibody titer was decreased after the liver transplant. The kidneys from the same donor transplanted shortly thereafter were not affected by humoral rejection. The third patient presented with persistently high levels of donor-specific antibodies. The kidney graft in this patient did not begin to function (3,4).



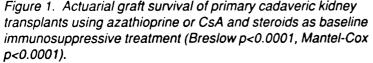


Table 1. Cadaveric kidney transplants performed at the University of Pittsburgh between 1977 and May 1987^a.

Transplant	Total	Primary	Retransplan
Year	Number	Transpla	nts
1977	17	16	1
1978	25	18	7
1979	42	37	5
1980	45	39	6
19 81	100	69	31
1982	118	97	21
1983	16 0	135	25
1984	204	164	40
1985	175	138	37
1986	26 3	200	63
19 87^b	94	72	22
Total	1243 ^a	985	258

^a Additional 17 living-related and 16 combined kidney transplants were performed.

^b From January to the end of May 1987.

Survival Analysis

Azathioprine versus CsA

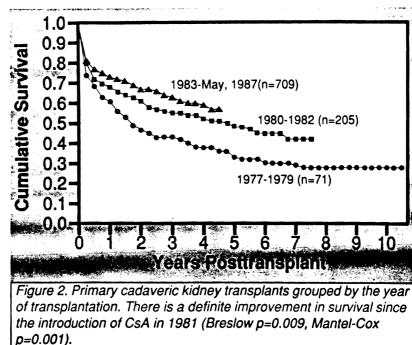
One hundred forty-one primary, cadaveric kidney transplants were performed using azathioprine and steroids as the baseline immunosuppressive therapy. One-, 2- and 5year actuarial graft survival was 58.9%, 48.2%, and 36.1%, respectively. Since the introduction of CsA and steroid treatment in 1981, 844 patients received primary cadaveric kidney transplants. Actuarial graft survival was 74.1%, 67.8%, and 52.7%, respectively (Breslow p<0.0001, Mantel-Cox p<0.0001) (Fig. 1).

One, 2-, and 5-year actuarial patient survival of primary cadaveric kidney transplants in the azathioprine era was 77.7%, 72.6%, and 63.6% while 91.3%, 89.2%, and 83.3% in the CsA era.

The primary cadaveric kidney transplants when divided into various years of transplantation showed again a definitive improvement during recent years since the introduction of CsA. One-, 2- and 5-year actuarial graft survival for 71 transplants performed during 1977 to 1979 was 61.9%, 47.9%, and 33.8%. From 1980 to 1982, 205 transplants showed 68.6%, 61.5%, and 48.2% graft survival. Since 1983, 708 kidneys were transplanted with a survival of 73.9%, 67.7%, and 59.5% (at 4 years) (Breslow p=0.009, Mantel-Cox p=0.001) (Fig. 2).

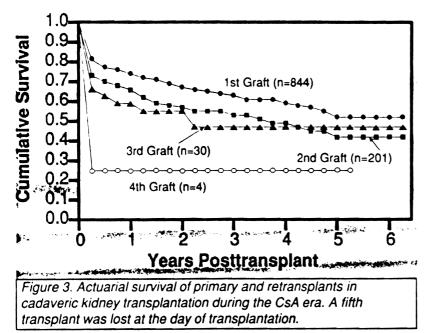
Retransplantation

Two hundred and one second, 30 third, 4 fourth, and one fifth cadaveric kidney transplants were performed during the CsA era. Many of the patients had previous transplants at other institutions. One-, 2- and 5-year actuarial graft survival for second transplants was 66.2%, 57.6%, and 42.7% and for third transplants 59.7%, 55.5%, and 47.5%. A single fourth kidney graft (25%) continued to function at these time intervals and a fifth transplant was lost at the day of transplantation (Fig. 3).



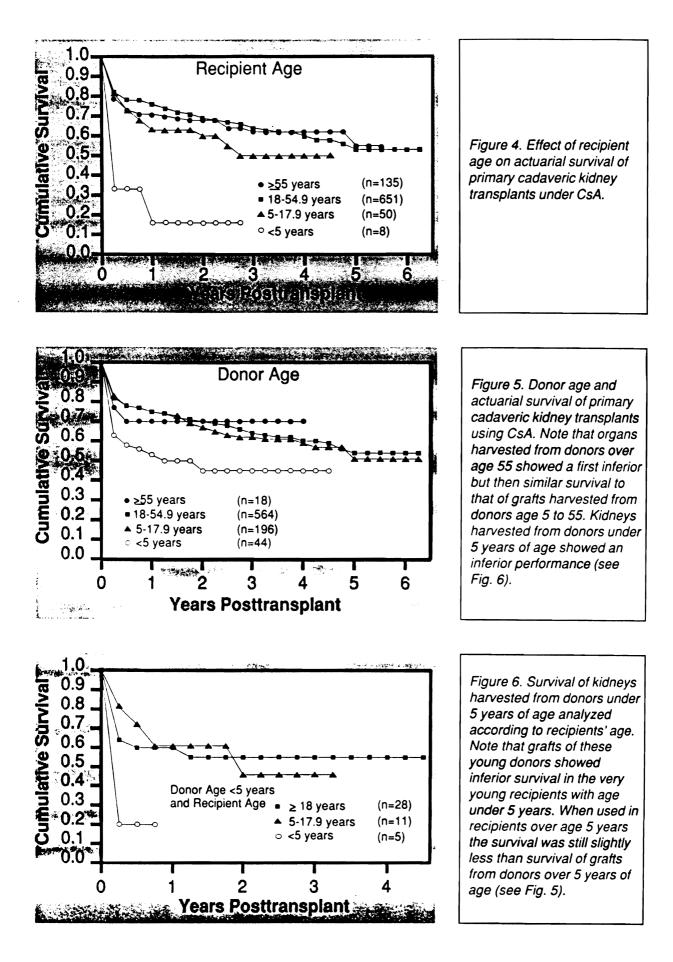
Living-Related Transplants

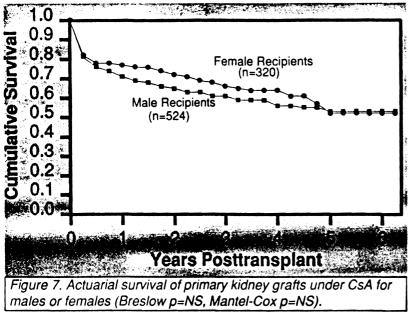
Living-related kidney transplants were performed at a very low rate of only 17 transplants (1.3%) since 1977, with only one living-related transplant since 1983. All used azathioprine as the basic immunosuppressive drug. Complete follow-up data were available for 16 of these. The survival of living-related kidney transplants was not improved (5-year actuarial survival of 53.3%) over cadaveric transplants with CsA.



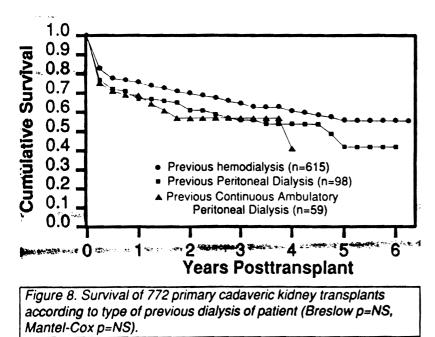
Recipient and Donor Age

In recipients age 55 or older, 135 primary cadaveric kidney transplants were performed during the CsA era. Actuarial one-, 2- and 5-year graft survival was 71.7%, 68.1%, and 55.1%. This did not differ from the survival of 651 grafts transplanted in the patient group 18 to 54.9 years of age. Younger recipients showed a lower survival with 63.6%, 60.0% and 50.7% (at 4 years) for 50 recipients age 5 to 17.9. For 8 grafts in recipients under 5 years of age, survival was 16.7% at one to 3 years (Fig. 4).





There was no disadvantage in the longer follow-up of 18 grafts harvested from donors 55 or older even when the earlier function was slightly diminished. Long survival was similar to transplants using grafts harvested from donors of age groups 5 to 17.9 and 18 to 54.9. Instead, survival was inferior for 44 donor kidneys harvested from donors 5 years or younger (Fig. 5). Further analysis revealed that grafts of these very young donors, when used in recipients over 5 years of age, showed inferior survival than grafts from older or adult donors. Grafts of these very young donors when used in recipients under 5 years showed a drastically inferior



survival (Breslow p=0.007, Mantel-Cox p=0.002) (Fig. 6).

Recipient Presensitization

In the CsA era 774 primary cadaveric transplants were performed in recipients with a most recent PRA of zero to 39.9%. One-, 2- and 5-year actuarial graft survival was 75.7%, 70.0%, and 53.5%. For 66 transplants in patients with a most recent PRA of 40.0% or higher, actuarial survival was 55.7%, 46.3%, and 46.3%, respectively (Breslow p<0.0001, Mantel-Cox p<0.001).

Historically highest PRA values of zero to 39.9% were found in 658 recipients. Survival was 75.4%, 70.5%, and 55.5%. For 171 recipients the highest PRA was 40.0% or higher, with 68.6%, 58.9%, and 42.8% survival (Breslow p=0.005, Mantel-Cox p=0.004).

ABO, Sex

Five hundred fifty-two transplants were performed in blood group O patients, 502 in blood group A patients, 162 in blood group B patients, and 59 in blood group AB patients. No differences in actuarial graft survival for various ABO groups of the recipient or of the donor

> were detected. In contrast to previous reports (5) female recipients or grafts harvested from female donors showed a trend toward a slightly better survival (p=NS) (Fig. 7) in our series.

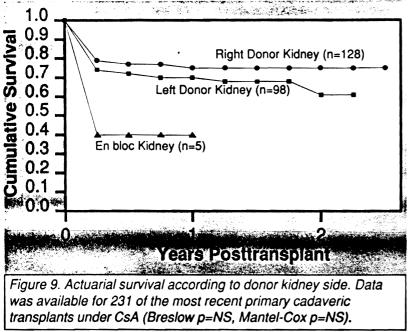
Dialysis

For 772 of the primary kidney transplants during the CsA era, information about the principal type of former dialysis was available. Kidney recipients with previous hemodialysis showed a trend toward a better survival than recipients with former peritoneal or continuous ambulatory peritoneal dialysis (Fig. 8). There was no significant difference 11

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in transplant groups according to length of previous dialysis, but a trend toward a better survival for patients with shorter dialysis history was noted.

Donor Kidney Side

For 231 of the most recent primary kidney transplants in the CsA era, the side of the harvested donor kidney was known. Actuarial one- and 2-year survival for 128 right donor kidneys was 75.6% and 75.6%; 98 left donor kidneys were transplanted with a survival of 70.8% and 61.8%. Five en bloc kidney transplants showed an inferior one-year survival of only 40.0% (Breslow p=0.036, Mantel-Cox p=0.039)(Fig. 9).

HLA

Throughout the analysis there was a trend towards enhanced survival for better HLA-A, B or DR matched kidney allografts. This effect was not statistically significant, presumably because of relatively low numbers in the analysis (Figs. 10-12).

DISCUSSION

Many of the patients transplanted at the University of Pittsburgh were referred from other institutions, either having previous transplants performed or because of clinico-pathologic circumstances presenting a higher risk for transplant outcome. Once feasibility for transplantation was established using predefined criteria, patients are activated on the candidate list. Lowest risk was not the primary guiding factor in patient selection.

The introduction of combined CsA and steroid treatment as the baseline immunosuppressive medication significantly enhanced the results of kidney transplantation in our series. But various other preexisting recipient or donor conditions may still have an important effect on kidney transplant survival and should not go unrecognized. Also in our series, a lower PRA antibody level was a main determinant for better success of the kidney transplant. HLA showed a trend towards enhanced survival for bet-

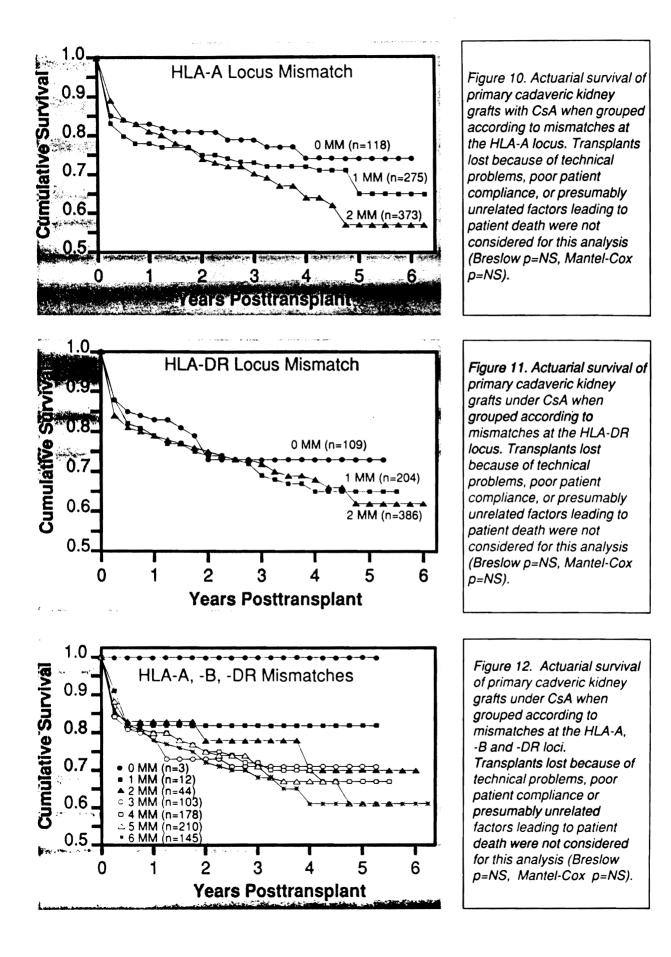
ter-matched grafts, but presumably

because of relatively small numbers, this trend was not statistically significant.

One main advantage of CsA was described to be the enhanced survival of older transplant recipients (6). Also in our series older recipients aged 55 or more showed a good survival similar to that of younger adult recipients.

Combined liver/kidney transplants have been shown to offer a favorable treatment modality for patients with endstage liver and renal disease. It is important to note that 2 of the kidney allografts performed against a positive donor-specific crossmatch seemed to be protected against a deleterious immune response by the liver allograft transplanted only hours before (3,4).

Living-related kidney transplants were almost totally abandoned at our institution with only one living-related transplant since 1983. Reasons for this approach are the increased availability of cadaveric donor organs, the improved results with cadaveric transplants under CsA, and the possible risks to the living donors (7). The latter seems of major importance since an increased incidence of hypertension might appear in these donors and long-term follow-up studies are still rare. This is of special significance since living-related donors are in perfect health. In addition psychological and other undiscovered factors influencing the decision of a parent, brother, sister, or other living donor might not be fully appreciated by the surgeon. Nevertheless, in countries with a more limited availability of cadaveric donor organs, another approach must depend on the surgeon and patient decisions.



In reviewing the type of dialysis, a trend towards better survival of a following kidney transplant in patients on hemodialysis versus peritoneal or continuous ambulatory peritoneal dialysis was noted. In addition a shorter dialysis history seemed to improve kidney graft survival. How far this was influenced by other circumstances leading to a particular dialysis method or by the dialysis method itself could not be determined from our series. It seems likely that patient conditions, such as hemodynamic instability, no access sites for hemodialysis, and higher presensitization with HLA antibodies and a subsequently longer waiting time, were influencing the outcome. If possible hemodialysis might suggest the better choice, but further studies are needed.

Interestingly, the donor kidney side showed a benefit in survival for right donor kidneys in comparison to left donor kidneys. En bloc transplants showed an inferior survival possibly because of additional size considerations, preexisting anatomic factors, and increased technical difficulties. Both these findings need to be evaluated in a larger transplant population in order to draw firm conclusions.

TIMY - Transplant Information Management System

A center-oriented computerized transplant information management system (TIMY) was developed for processing the kidney transplant data. The system focuses on the everyday informational needs of both the clinician and the researcher. Therefore the computer must be user friendly and readily accessible to all levels of the departmental staff according to their specific information needs. Similar systems are currently in use for the liver transplant program and to some extent for the heart transplant service.

Using the DATAEASE database program (DATAEASE INTERNATIONAL, Trumbull, CT), TIMY was designed and implemented using an IBM-AT with a 30 megabyte harddisk. Part of the data was transferred from a previously existing database. Many of the dataentry fields are choice fields which help to eliminate data-entry errors, with additional precoding of fields allowing for convenient statistical analysis. System modifications required to customize the database according to the needs of the individual transplant center are readily accomplished.

The system design covers the candidacy, transplant, and the follow-up phases. Data can be entered in the appropriate forms (Figs. 13-15) with easy movement between the various patient records. In addition, addresses and telephone numbers of referring physicians, patients, and their home dialysis centers are stored in specific files and used to print the weekly candidate list. Various established reports are available for clinical and research tasks. Included are the comprehensive candidate listings, regular summary reviews, and statistics (Figs. 16-17).

The database is available to the transplant coordinators via a laptop computer. Therefore pertinent patient data can be reviewed from any telephone connection, facilitating the coordinators' work during nights and weekends. The dynamic nature of the data requires constant updating and the coordinator can review any data changes since the last printing of the candidate list.

The system structure encompasses the data necessary for reporting to government agencies as well as to the UCLA and CTS Kidney Transplant Registries. The electronic data transfer via diskettes or modem to the UCLA Kidney Transplant Registry and to the CTS study at the University of Heidelberg, West-Germany, is currently being implemented.

Scoring System

In order to facilitate the allocation of the best suitable transplant candidate when a donor organ is offered, an integral computerized scoring system was developed as an objective allocation method (8). The results do not mandate, but facilitate the decision-making process of the surgeon. Currently in Pittsburgh the Transplant Organ Procurement Foundation is running this scoring system.

Various factors were thought to play an important role in the assessment of a suitable candidate. Of these, the 5 most significant are used in the scoring system: time of waiting, quality of HLA antigen match, presensitization state with PRA, medical urgency, and logistical factors. Since donor and recipient should be of the same blood group with only rare exceptions, renal candidates are grouped according to whether their blood type is O, A, B, or AB. Candidates who weigh less than 27 kg or are 10 years or younger are listed separately. Sera from all candidates of the appropriate blood type and size are matched against lymphocytes from the donor of the offered kidney. A negative crossmatch, connoting the absence of antidonor cytotoxic antibodies in the recipient serum, is a necessary condition for placement on the list of potential candidates.

The waiting score is determined as a rank order of waiting time, established from the date of referral for consideration of transplantation. A maximum of 10 points is awarded to the candidate waiting for the longest period, with fewer points given for shorter waits.

The quality of antigen match points is determined by the grade of histocompatibility at the HLA-A, B, and DR loci. Two points are given for each antigen matched, with a score of 12 being possible.

The present state of alloimmunization, as defined by the most recent PRA level, is used for calculating the PRA score. One point is given for each 10% PRA value up to a maximum of 10 points.

The medical urgency score is used in cases where dialysis is not a feasible option for the patient, so transplantation within a short period of time is essential. This is used, for example, in patients whose access sites for dialysis had been exhausted. A total of 10 points can be assigned to such a patient.

A maximum logistics score of 6 points can 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 candidate whose proximity to the hospital and history of recent dialysis could permit prompt transplantation.

As stated above, the result of the scoring system does not mandate, but facilitates the selection of an appropriate candidate for this particular donor organ. Certainly additional medical circumstances, such as CMV status of donor and recipient, size limitations, etc. have to be considered. When there is a deviation from the computerized scoring result, an explanation is documented. Scoring results and overriding explanations are routinely reported to community boards for review purposes. Since its introduction in 1986 this computerized scoring system has proven to be a very valuable tool in the transplant candidate selection process.

A similar scoring system is routinely used for candidate selection in our liver transplant program (9). A system for heart transplantation is currently under evaluation.

	LAST NAME	FIRST NAME	
ATE OF BIRTH			
EX	RACE	LEWIS ANTIGEN A	
LOOD GROUP ABO	RH	_ LEWIS ANTIGEN A	_ B
		_DRw, TISSUE TYPIN	
IAGNOSIS		_	
ATE DIAGNOSIS WA	S FIRST MADE		
OMMENT			
***********************			**********
PATIENT LOST TO P	FOLLOW-UP, ENTER DA	TE OF LAST FOLLOW-UP _	
PATIENT DIED, ENT	ER DATE OF DEATH	_	
RIMARY CAUSE OF			
SECONDARY CAUSE	S OF DEATH		
2.			
5.			
5 OMMENT			
OMMENT			

	FIRST_		
CURRENT RECORD CANDIDACY	FOR GRAFT #_ ABO	ALIEN	
PHYSICIAN CODE DIALYSIS C		SEND LETTER	
	PREFERENCE		
NSURANCE			
AGE AGE GROUP HEIGHTftin ORcm	TOTAL PREGNANCIE WEIGHTIbs O	S LIVE BIRTHS Rkg	-
PRA HIGHEST DATE	PRA RECENT_		
HAAb HBsAg HBs CMV HIV ELISA TESTING	Ab HBcAb WESTEF	IN BLOT	
WASHED CELLS FROZEN/FILTERE IF LIVING DONOR, ENTER # OF DONC DATE OF LAST PRE-KTX TRANSFUSIO			
DATE OF LAST PRE-KTA TRANSPUSI			
START OF DIALYSIS NEPHRECTOMY SPLENECTOMY	TYPE DATE DATE	REASON	
START OF DIALYSIS NEPHRECTOMY SPLENECTOMY	TYPE DATE DATE	REASON	
START OF DIALYSIS NEPHRECTOMY SPLENECTOMY ADDITIONAL DIAGNOSIS HEPATIC PULMONARY CARDIOVASCULAR JUVENILE DIABETES MELLITUS	TYPE DATE DATE DATE S	REASON	

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TRANSPLANT INFORM	ATION MANAGEMENT SYSTEM - KIDNEY REGISTRY - TRANSPLANT DATA
ID#L	AST NAME FIRST
	FT (GX#) TRANSPLANTED ORGANS
	SERVICE DONOR# TRANSPLANT ID#
AGE AT KTX	
	BASELINE CyA STARTED DAY
DONOR LOCALITY	OTHER
HARVEST MODE	COLD STORAGE
	PERFUSATE
ISCHEMIA TIME WARM	DONORmin COLDhrmin WARM RECIPIENTmin
RECIPIENT SURGEON	1st ASSISTANT DONOR SURGEON
WASHED CELLS	OD-TRANSFUSIONS WHOLE BLOOD PACKED RED CELLS _ FROZEN/FILTERED PLASMA PLATELETS
DONOR INFORMATION LAST NAME	FIRSTSEX
	AGE RACE RH LEWIS ANTIGEN A B
	CANCER
HBsAg CMV OTHER INFECTION	VDRLHIV ELISAWESTERN BLOT IF YES, SPECIFY
RECENT BUN	RECENT CREATININE
TISSUE TYPING #	HLA TYPE_ABBwDRDQDRw
	CROSSMATCHTEST TYPE
	AUTOLOGUS CONTROL TEST TYPE
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RESULTS OF SCORING	
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	F OVERRIDEN PATIENTS. EXPLANATION HAS TO BE GIVEN IN CONMENTS
	FOR ALL TIMES WITH SCORING PRINTOUT ATTACHED TO IT!
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KIDNEY TRANSPLANTATION-PITTSBURGH

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• BLOOD GROUP O •		PAGE 1
Doe, John ID#: 999-99-9999		DATE REFERRED: 12/01/86
ABO: O AGE: 53.6 SEX: MALE		DOB: 01/01/34 HT: 173 WT: 77.9
CANDIDACY FOR GX#: 1 STATU	IS: ACTIVE	URGENCY:
DIAG: Diabetic Nephropathy		DIALYSIS: Hemodialysis
PRA HIGH: 2.0 DATE: 01/01/87		PRA RECENT: 0.0 DATE: 04/07/87
TISSUE TYPING #: 77777 HLA T	YPE:	A 2, 3 B 7,62 DR 3,5
HAAB: Neg HBsAg: Neg HBsAb	: Neg	HBcAb: Neg CMV: Neg
INSURANCES: Blue Cross/Blue St		NEPHRECTOMY: None
COMMENTS: Patient had myocard	ial infarct in 1	0/85
ADDRESS: 1122 Beechwood Ave	, Pittsburgh, I	PA. 15219
PHONE HOME: (412) 999-9999		PAGER: (412) 999-9999
PHONE WORK: (412) 999-9999		TYPE: VOICE
RELATIVES: (412) 999-9999 - Sus	san - aunt	
RELATIVES: (412) 999-9999 - Jac		
DIALYSIS CENTER: ABC PHONE:	(412) 999-99	999 REFERRING MD: TES
Doe, John ID#: 999-99-9999		DATE REFERRED: 05/15/86
ABO: O AGE: 39.1 SEX: MALE		DOB: 07/08/48 HT: 193 WT: 83.4
CANDIDACY FOR GX#: 2 STATL	IS: ACTIVE	
DIAG: Polycystic Kidney Disease		DIALYSIS: Hemodialysis
PRA HIGH: 54.0 DATE: 03/19/86		PRA RECENT: 41.0 DATE: 06/29/87
TISSUE TYPING #: 99999 HLA T		A 1,28 B 7,60 DR 4,
HAAB: Neg HBsAg: Neg HBsAb	: Neg	
INSURANCES: Medicare		NEPHRECTOMY: Yes
COMMENTS: First kidney transplar	•	
ADDRESS: 1133 Fifth Ave, Pittsbu	-	
PHONE HOME: (412) 999-9999		PAGER: (412) 999-9999
PHONE WORK: (412) 999-9999		TYPE: VOICE
RELATIVES: (412) 999-9999 - Ter		
RELATIVES: (412) 999-9999 - Gre	-	
DIALYSIS CENTER: ABD PHONE:	(412) 999-99	
ETC. ETC. ETC.		
BLOOD GROUP A		
BLDOD GROUP B		
BLOOD GROUP AB		
ETC. ETC. ETC.		
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CANDIDATE LIST STAT	STICS	
FOR ALL BLOOD GRC	UPS	
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KIDNEY TRANSPLANTATION-PITTSBURGH

SUMMARY

1. The introduction of combined CsA and steroid treatment as the baseline immunosuppressive medication significantly enhanced the results of kidney transplantation in our series. But various other preexisting recipient or donor conditions may still have an important effect on kidney transplant survival and should not go unrecognized.

 Living-related kidney transplants were almost totally abandoned at our institution. Reasons for this approach are the increased availability of cadaveric donor organs, the improved results with cadaveric transplants under CsA and the possible risks to the living donors.

- 3. Combined liver/kidney transplants have been shown to offer a favorable treatment modality for patients with endstage liver and renal failure.
- A newly developed center-oriented Transplant Information Management System (TIMY) significantly facilitates the clinical and research tasks in our department.
- An integrated, computerized scoring system for equitable allocation of donor organs has proven to be highly effective during routine clinical use.

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