CHAPTER 30

The University of Pittsburgh: A Three and Three-Quarter-Year Experience with Cadaveric Renal Transplantation Under the Point System

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The goal of equitable access to cadaveric organs was the guiding principle behind the development and implementation of the point system. This computerized allocation program originated in Pittsburgh (1), and was later adopted by the United Network for Organ Sharing (UNOS); more recently it has been modified (2). We have previously described our experience with the point system and emphasized the importance of immunosuppression as a factor in determining graft survival (3,4). This report summarizes our 3.75-year experience with the point system for cadaveric kidney transplantation. As such, it serves as a benchmark of what can be obtained with CsA-based immunosuppressive protocols. Beginning in October 1989, FK 506 was used for immunosuppression after renal transplantation (5). and the results of that change will be evaluated in the coming year.

METHODS

Between January 1, 1986 and October 19, 1989, 806 cadaveric renal transplantations were performed in 741 patients at the University of Pittsburgh (Presbyterian-University Hospital and Children's Hospital). An additional 20 kidneys were excluded from analysis because of concomitant transplantation with another organ (liver, heart, or pancreas); similarly excluded were 34 kidneys from living-related donors. Seven hundred and fifty kidneys went to 692 adults, whose mean age was 42.4±12.8 years, and 56 went to 49 children. Four hundred and fifty-three (61%) of the recipients were male and 288 (39%) female. Six hundred and thirty-six (86%) of the recipients were White, and 105 (14%) were Black. One hundred and fifty-two (21%) were diabetic, and 112 (15%) had a panel-reactive antibody (PRA) level greater than 40%. Seventy-eight (11%) of the recipients were older than 60 years of age.

Immunosuppression in 1986 and 1987 was based on CsA and prednisone; approximately one-third of the patients transplanted in 1987, and essentially all of the patients transplanted in 1988 and 1989, were also given azathioprine. OKT3 was used occasionally from the outset in selected sensitized patients or for steroid-resistant rejection episodes (6).

Pretransplant crossmatching was performed by the standard lymphocytotoxic test with 2 washes, and the patients with positive crossmatches (20% killing of donor lymphocytes) using current sera were usually but not always precluded from transplantation. Pretreatment of recipient sera with dithiothreitol (7) was not routinely performed.

RESULTS

Patient Survival

One- and 2-year actuarial patient survival was 93% and 91% (Fig. 1). Fifty-nine (8%) patients have died between 1 day and 3.5 years after transplantation. The causes of death are noted in Table 1. Infections remain the most important cause of death, followed by cardiovascular events. There may have been a slight trend toward decreased mortality in the last 1 or 2 years.

Clinical Transplants 1989, P. Terasaki, Ed. UCLA Tissue Typing Laboratory, Los Angeles, California

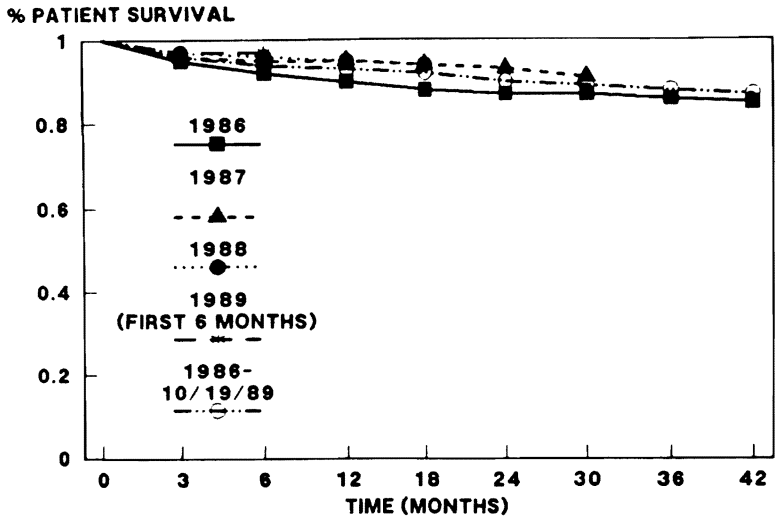

Figure 1. Patient survival after cadaveric renal transplantation.

Table 1. Causes of death after renal transplantation.

Cause of Death	Graft Functioning	Graft Removed or Non-functioning	Total
Infection	4	15	19
Cardiovascular	7	8	15
Gastrointestinal	1	7	8
Respiratory	0	2	2
Malignancy	1	1	2
Technical	1	2	3
Miscellaneous (DIC, multiple organ failure, hyperkalemia, bleed after biopsy, subdural hematoma, suicide, motor vehicle accident)	3	5	8
Unknown	0	2	2
Total	17 (29%)	42 (71%)	59

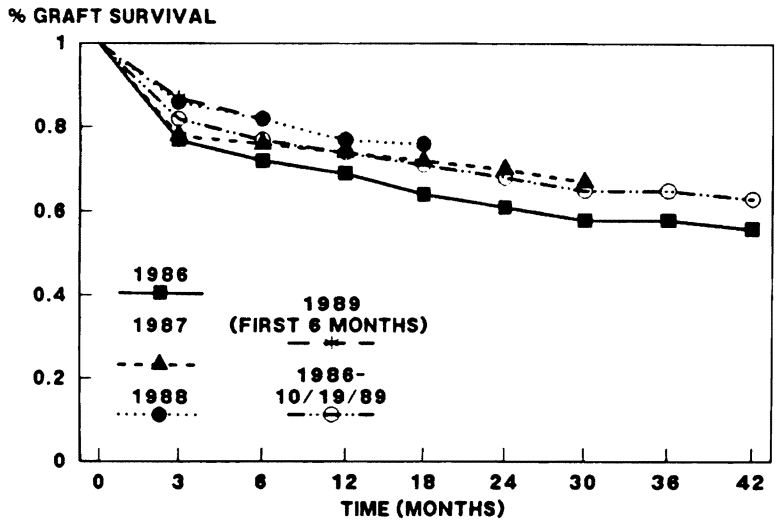

Figure 2. Graft survival after cadaveric renal transplantation.

Graft Survival

One- and 2-year actuarial graft survival was 74% and 68% (Fig. 2). Analysis of results by sex (Fig. 3) or race (Fig. 4) showed no effect of either variable. The irrelevance of recipient race to outcome has been noted previously (8). Adults and children had similar results (Fig. 5), as did patients receiving primary kidney transplants or retransplantations (Fig. 6). Analysis of graft survival on the basis of HLA antigen matches and mismatches was also performed. No discernible statistical effect was noted (Figs. 7 and 8).

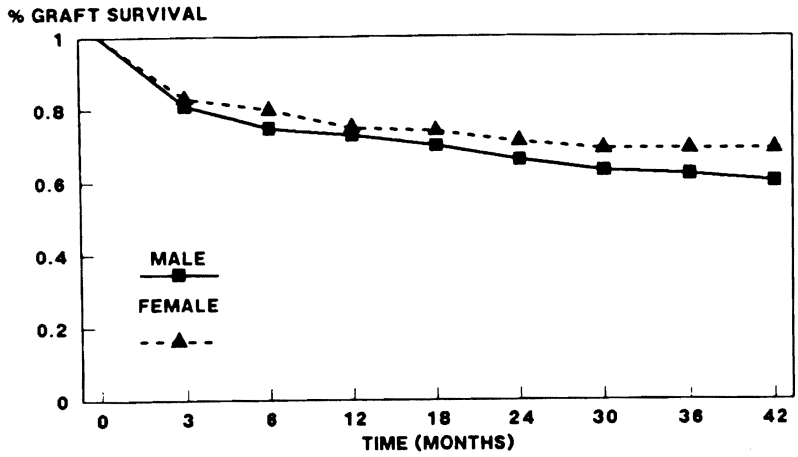

Figure 3. Effect of recipient sex.

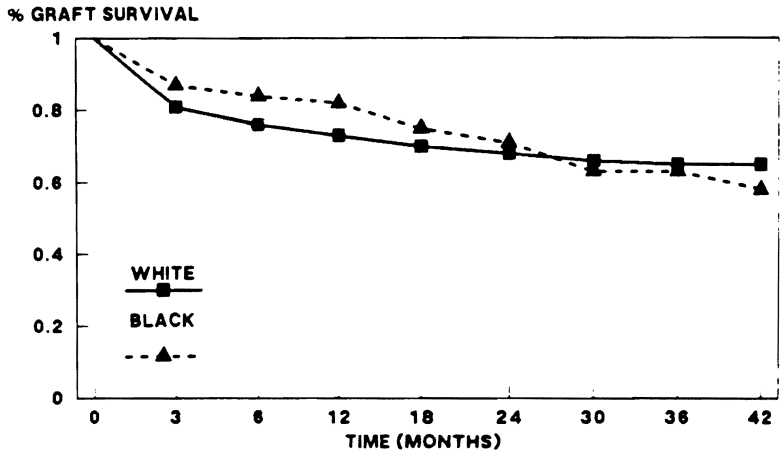

Figure 4. Effect of recipient race.

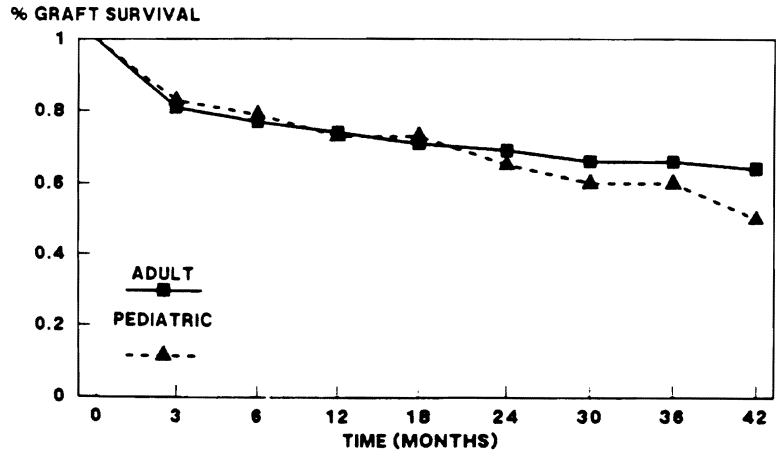

Figure 5. Adult versus pediatric recipients.

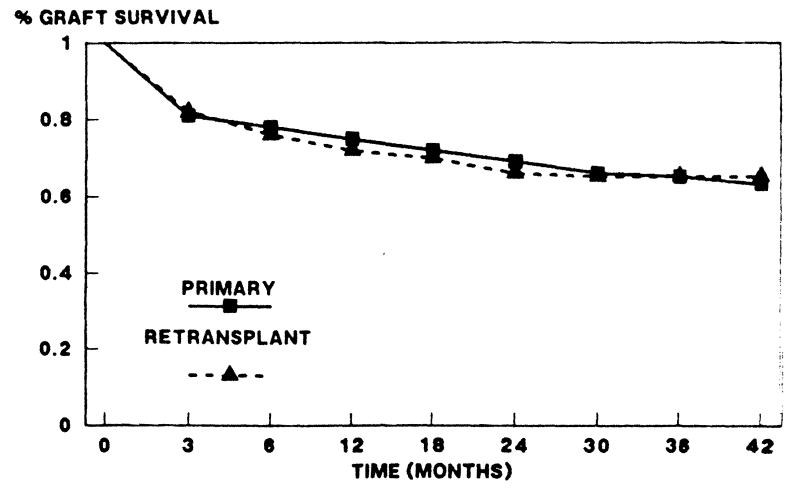

Figure 6. Primary versus retransplantation.

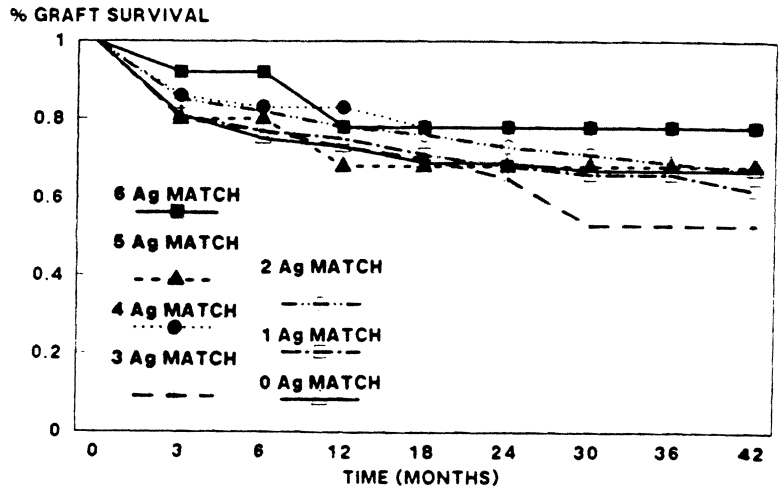

Figure 7. Effect of HLA matching.

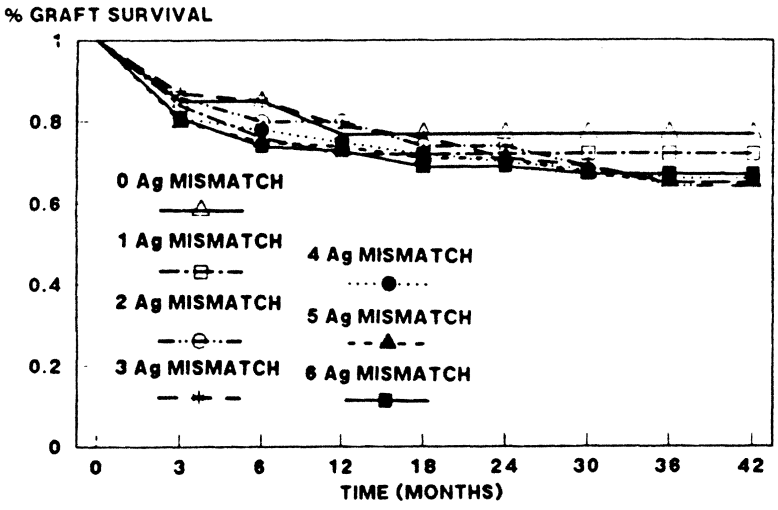

Figure 8. Effect of HLA mismatching.

Patients older than 60 years of age had similar graft survival (Fig. 9) but worse patient survival (Fig. 10) than patients younger than 60 years of age. Patients with high levels of anti-HLA antibodies (PRA > 40%) had slightly worse results than low PRA patients (Fig. 11).

Effect of Immunosuppression Protocol

The largest effect noted was the influence of immunosuppressive protocols on graft survival. Three-drug immunosuppression with CsA, azathioprine, and prednisone had consistently superior results when compared to immunosuppression with CsA and prednisone alone, with 80% 1-year graft survival (Figs. 12 and 13). This 10-15% improvement in graft survival has been a consistent finding in our patient population, a group well represented by older, sensitized, diabetic, and/or overweight patients.

DISCUSSION

The original intent of the point system was to design an allocation protocol that did *not* consider age, sex, race, or significant medical problems. As such, it ran counter to the philosophical goal of transplanting the "best" potential recipients (9). Our results represent the longest experience with the original point system, which has since been modified to give less emphasis to waiting time and more to HLA matching. It will be interesting to see whether the revised point system will in fact lead to greater matching in kidney transplantation and whether there will be any effect on graft survival; our own experience suggests that there will

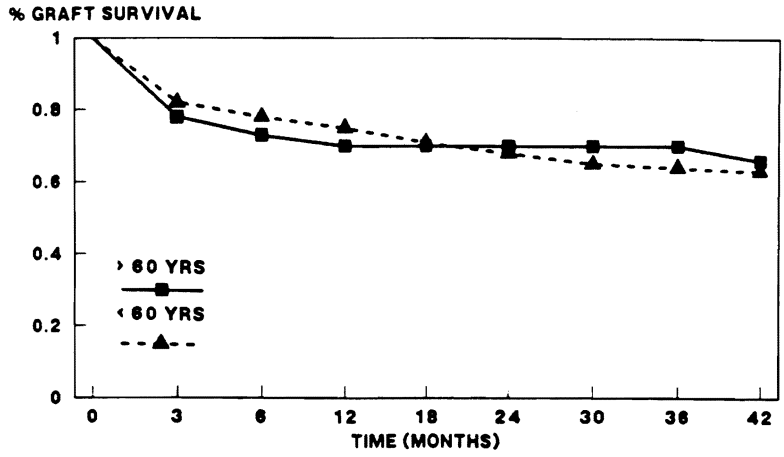

Figure 9. Effect of age on graft survival.

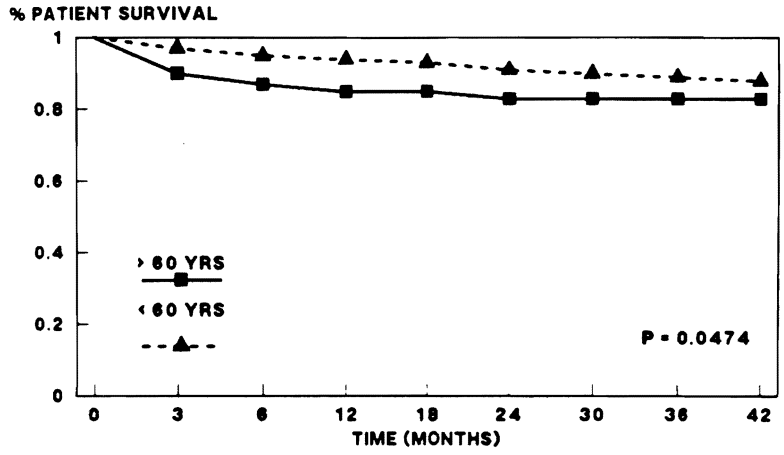

Figure 10. Effect of age on patient survival.

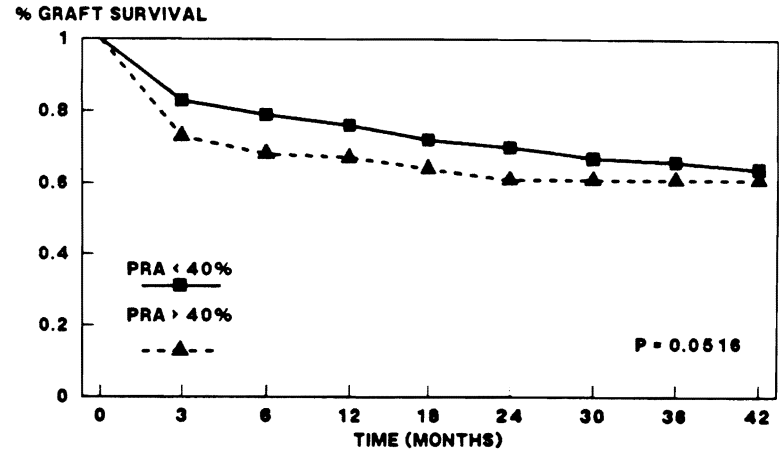

Figure 11. Effect of panel-reactive antibody (PRA).

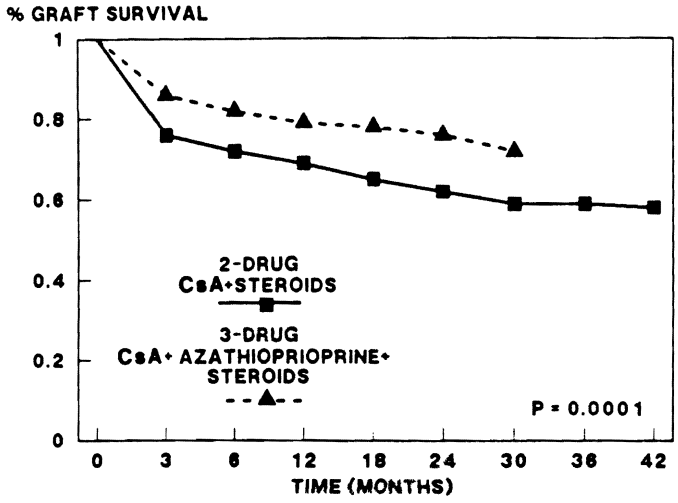

Figure 12. Effect of immunosuppressive protocol.

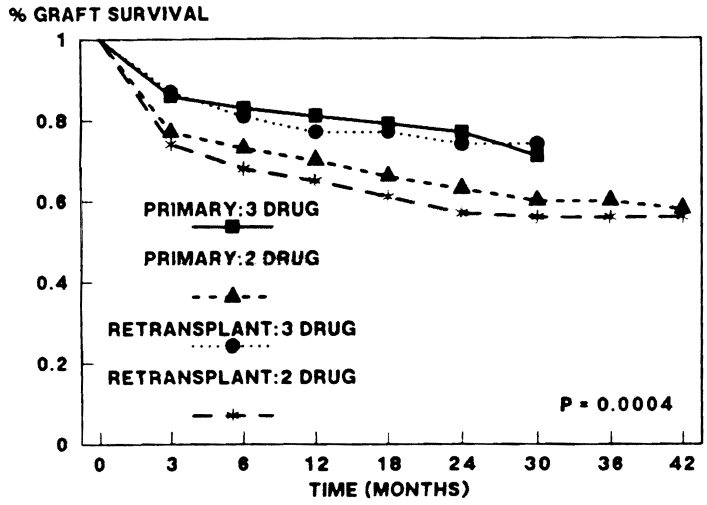

Figure 13. Effect of immunosuppressive protocol in primary and retransplantation.

not be any positive effect. Instead, the emphasis on matching can have unintended deleterious effects that will not necessarily be reported.

As an example, a patient of ours was transplanted in 1989 with a 3-antigen match kidney that had been recovered locally, had been shipped out for a 6-antigen match recipient, and then was returned because of a positive crossmatch with the intended recipient. We were not informed that the kidney had been placed on a perfusion pump while it was away and that a tie had been placed around the renal artery to secure the perfusion catheter. When the kidney was returned to Pittsburgh and transplanted here, the artery promptly thrombosed because of intimal injury from the tie. The patient died after allograft nephrectomy. The case is reported as a failure of an imperfectly matched kidney but was not recorded in the 6-antigen match statistics, even though the attempt at organ sharing ultimately led to the graft failure. Other examples, equally florid or more subtle, could be cited.

This report serves 2 purposes. First, it demonstrates what can be expected with CsA/azathioprine-based protocols using an equitable allocation policy which insures the systematic inclusion of high-risk recipients. Second, it can serve as an historical control in 2 ways; 1 to compare with different allocation protocols, and the other to compare with different immunosuppressive regimens. Although evaluation of the new immunosuppressive agent, FK 506, is planned with prospective randomized trials, this data base will be useful as an additional baseline for comparison.

SUMMARY

Eight hundred and sixty kidney transplants were performed at the University of Pittsburgh over a 3.75-year period between January 1, 1986 and October 19, 1989. Recipient selection was by means of a computerized point system designed to allocate organs equitably. Ninety-three percent 1-year patient survival and 74% 1-year graft survival were obtained in the overall group; 80% 1-year graft survival was obtained in patients receiving immunosuppression with CsA, azathioprine, and prednisone. These data serve as a measure of what can be achieved with an equitably based allocation system and can serve as a basis of comparison with other allocation protocols or new immunosuppressive regimens.

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ACKNOWLEDGMENTS

We wish to thank the following people:

Regina Fenton, R.N., Deborah Good, R.N. Joan Murray, R.N., Loraine Kaminski, R.N., Holly Woods, R.N., and Lisa Streb, R.N., for their invaluable contributions to the care of the patients and the data collection; Donna Ross for her untiring work in the preparation of the manuscript; Sandi Mitchell, MSIS, Jeannne Kowalski, and Kristine Smerdel for their help with the data analysis; Robert W. Karausky, Terry N. Trees Ph.D., and Richard James for their help in fashioning the slides, figures and tables.

Supported by Research Grants from the Veterans Administration and Project Grant No. DK 29961 from the National Institutes of Health, Bethesda, Maryland.

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