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HLA Matching Assessed From Early Graft Function

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NOW THAT THE RESULTS of kidney transplantation are improving to relatively high rates, we need more sensitive measures of transplant outcome than graft and patient survival. A subjective assessment by the transplant surgeon, evaluated as grade A, B, C, D, or F at 3 months, 6 months, 1 year, and annually thereafter has long been available to the UCLA Transplant Registry but has been largely unused, primarily on the basis of credibility. We are particularly interested now in exploiting the extensive information that is routinely recorded in the course of postoperative management of patients. It is not clear at present what forms of analysis will be informative. We report here the use of a summary score based on serum creatinine recorded during the early postoperative period—the first 60 days.

METHODS

Data on the posttransplant course of 438 transplants performed in 1982 and later at the University of Southern California, University of California at San Francisco, University of Texas at Houston, and the University of Pittsburgh were entered into computer storage. All patients were treated with cyclosporine A (CsA). Several different protocols were followed. Serum creatinine levels were expressed on a modified reciprocal scale ($y = 100/x$ if $x > 1$, $y = 20(6 - x^5)/5$ if $x < 1$), and the daily average serum creatinine score (SCS_{60}) was computed, interpolating at days not tested, for each patient. Graft failure was equated with indefinitely large creatinine values. Records were merged with other registry information regarding HLA matching, donor/recipient sex, and other items. The data were analyzed by cross-tabulations, Student's t tests, and regression analyses. Public HLA-A,B antigens were taken as defined by Konoeda and colleagues.[1]

RESULTS

The overall average SCS_{60} was 50 ± 25 (SD), corresponding to serum creatinine of 2.0 mg/100 mL. The averages by donor category were 43 (cadaver donor regrafts, n = 53), 46 (cadaver donor first grafts, n = 307), 66 (no common haplotype living-related donor, n = 9), and 71 (1 common haplotype living-related donor, n = 69). Results were consistent among the four centers. The difference between the one common haplotype living-related donor and first cadaver donor was strongly significant ($t = 7.2$, $P < .0001$). If one were to compare the two groups on a basis of 1-year survival (assuming 90% and 75% survival, respectively), approximately seven times the number of transplants (2,800) would be required to achieve the same level of statistical significance.

A preliminary finding of potential interest was a correlation among female recipients between the number of mismatches of both public and private A,B antigens with the creatinine score ($P = .02$). The number of mismatched antigens varied from 0 to 37. The regression equation was 63.0 − 0.57x. The regressions on numbers of A,B- and B,DR-mismatched private antigens were not statistically significant. In first cadaver transplants, female recipients tended to have better average graft function (50 v 42, $P = .003$) than did males, whereas transplants from male donors had better function (49 v 43, $P = .02$); the two effects were additive.

Function assessed by the transplant surgeon's rating at 3 months after operation was correlated with mismatches for B,DR (P =

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.0002, n = 2625 and $P = .02$, n = 3795 for transplants with and without CsA, respectively). For CsA transplants, the results were 89% ± 3% grade A or B for no B,DR mismatches and 74% ± 2% for 4 B,DR mismatches; corresponding values were 73% ± 3% and 63% ± 2% for non-CsA. These findings were based on transplants from many centers.

DISCUSSION

Although serum creatinine is not an ideal measure of kidney function,[2] it is both commonly used and accessible. The strongest indication for sensitivity of increased outcome assessment was based on the comparison of parent and cadaver donor transplants (which could be reliably detected with ~60 transplants—10 parent, 50 cadaver). It may be that the SCS_{60} is largely detecting an uninteresting difference in early function, although there is no doubt that transplants with good function through the early postoperative period have longer average survival rates than those with poor function.

We chose to use reciprocal creatinine concentration since it correlates with clearance,[3] has better statistical properties, and has the natural extension of zero corresponding to a failed graft.

There are many other possible ways of using serum creatinine. Among those that should be interesting are scores averaged over windows other than the first 60 days and life-table analysis using accumulated SCS as the measure of survival.

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