The Outcome of Kidney Retransplantation

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The survival of 66 patients with retransplanted kidneys, from August 1963 to March 1973, was evaluated. The life expectancy after retransplantation is less than that after primary transplantation but the difference is mainly due to an increased early postoperative mortality. The prognosis after retransplantation is greatly improved if the second kidney is from a related donor. The prognosis is likewise improved if a longer period of time has elapsed between the two transplantations. Surprisingly, previous exposure to specific HL-A antigens does not worsen the prognosis for a subsequent transplanted kidney.

Most dialysis centers have an excessive number of uremic patients. Since patients who have rejected their transplanted kidneys add significantly to the pool of dialysis cases, it is an important question whether, and at what time, retransplantation should be carried out. A number of publications have implied that the results after retransplantation are equivalent to those following a first procedure.[1-3] This has not been our experience, as documented in this report of patient and kidney survival after retransplantation. An analysis is also presented of the contribution to the outcome of other factors, such as HL-A mismatch, time of retransplantation in relation to time of first transplantation, cause of primary graft failure, and original kidney disease.

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Clinical Population

At our transplantation unit, 66 patients receiving their first renal homografts between November 1962 and August 1972 have later undergone one to four retransplantations. Follow-up data are available from a few months to more than nine years after the retransplantations. The immunosuppressive treatment after retransplantation was frequently different from that used intially, since the therapy provided was dependent on the management currently under evaluation for new cases.[4] Also, if the patients had received ALG earlier, they usually did not receive it after retransplantation. About half of the patients underwent retransplantation without removal of the previous graft and without a period of dialysis prior to regrafting.[5]

Results

The total experience of retransplantation with our 66 patients is summarized in Fig 1. More than one half (35 of 66) have been followed up for more than five years from the time of their primary transplantation. The life survival, using the time of the first transplantation as the starting point, was superior at all subsequent levels of follow-up to that when the date of retransplantation was accepted as the starting basis for calculation. The main difference in survival was due to a heavier mortality in the first three months after retransplantation than during the comparable period after the primary grafting. This mortality was not a function of whether homograft nephrectomy and interval dialysis was elected versus prompt retransplantation, leaving a failing graft in situ without discontinuance of immunosuppression. By the end of three months, in cases of retransplantation, there was a gap of almost 20% and, subsequently, the differential remained about the same (Fig 1).

The survival after secondary transplantation was somewhat influenced by the kind of kidney that was used at the first transplantation (Fig 2). If the first kidney was from a related donor, the overall five-year survival after the first transplant was 15 of 27 patients (56%), but after the second transplantation, the survival after five years, calculated from the time of retransplantation, was only 21% (three of 14 patients). The poor results were at least partly attributed to a heavy reliance on cadaveric kidneys for retransplantation.

When the primary kidney came from an unrelated donor, the early

patient survival after retransplantation was less than that after primary transplantation, but the later survival figures were similar. It is noteworthy that three of the 21 recipients were given kidneys from related donors the second time; after more than five years following retransplantation, all three are well.

As implied, the source of the secondary kidney graft was profoundly influential in determining subsequent patient survival (Fig 3). When the organs could be obtained from related donors, the results, while not as good as for the primary consanguineous transplantations, represented a survival better than 50% for five years. In contrast, recipients of unrelated (usually cadaveric) kidneys for retransplantation had a much poorer long-term prognosis. In this latter category, none of 12 patients has survived four years.

The time between first and second transplantation influenced the kidney survival after the second transplantation (Fig 4). The kidney survival was better the longer the time between the two graft procedures.

The kidney survival with and without known specific HL-A presensitization is shown in Fig 5. There were 65 grafts that, on the basis of the antigens then identifiable, did not share HL-A antigens with a previously rejected transplant, and 18 grafts in which one (17 cases) or two (one case) antigens, clearly present in a nonprimary donor and foreign to the recipient, had been present in a donor of a previous transplant. The differences in results were not different in a statistically significant way, but if anything, it was possibly slightly advantageous to have had an HL-A presensitization. The HL-A antigens involved in the cases of presensitization were as follows: A2 in seven cases; A1 in three cases; A12 in two cases; and A3, A7, A10, A11, W17, W27, and Te60 in one case each (Terasaki nomenclature).

An attempt was also made to analyze whether either the cause of the first graft failure or the original disease of the patients influenced the results. These attempts proved unrewarding in the first instance because

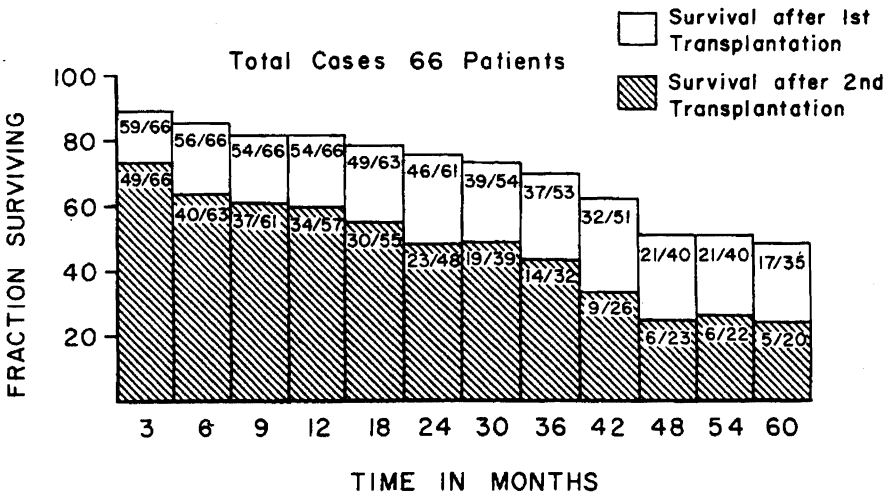
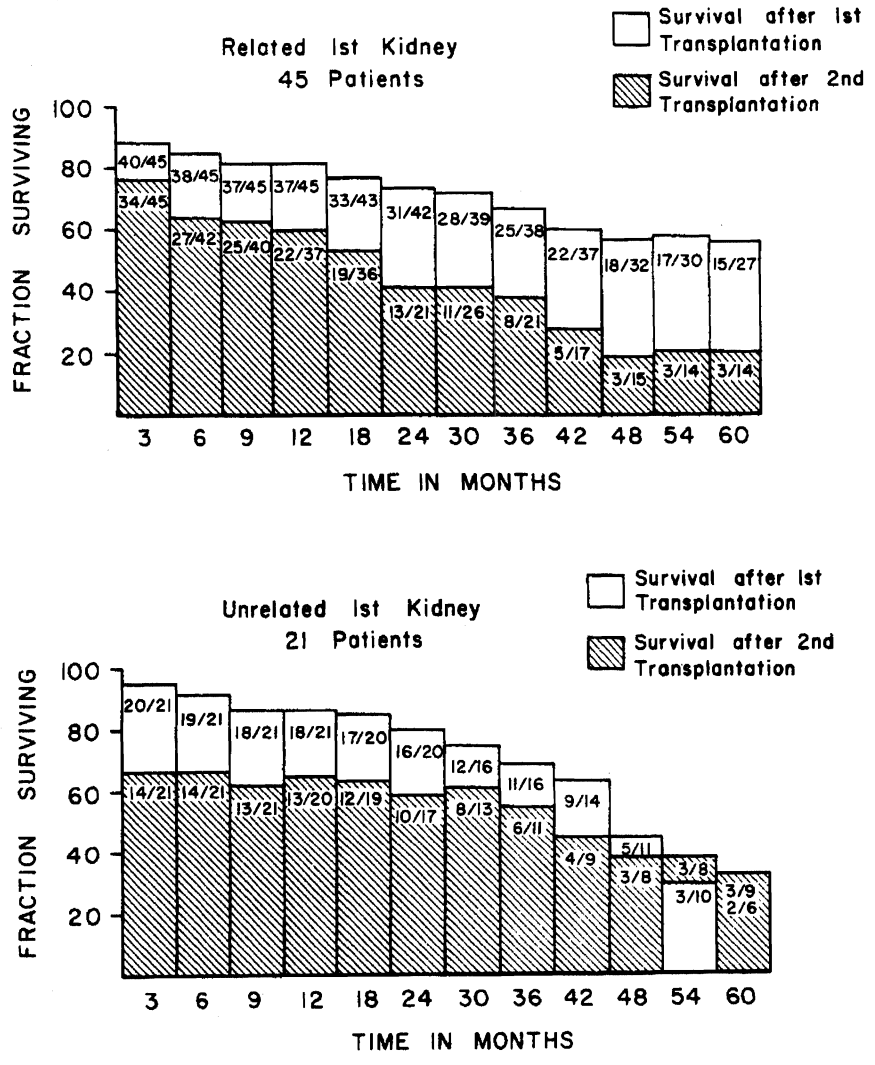
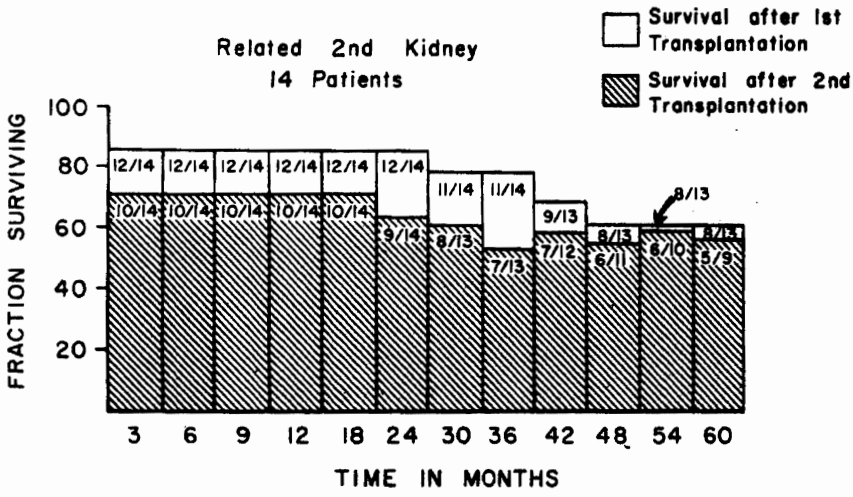


Fig 1.—Numerators and denominators indicate patients surviving and patients at risk, respectively, during each time period (follow-up to Aug 1, 1973).

Fig 2.—Top, Survival of 45 patients with retransplanted kidneys after first related grafts had failed. Bottom, Survival of 21 patients with retransplanted kidneys after first unrelated transplants were rejected. Numerators and denominators as in Fig 1 (follow-up to Oct 1, 1973).





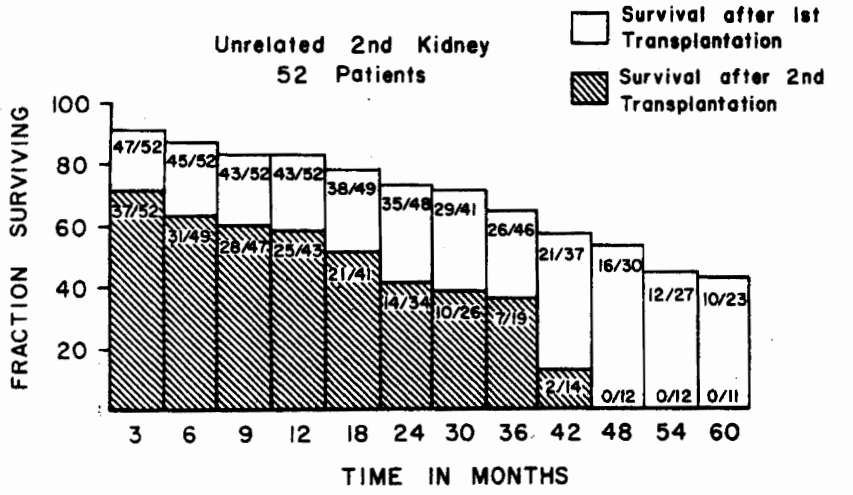


Fig 3.—Top, Survival of 14 patients with retransplanted kidneys from a relative after first transplant had failed. Bottom, Survival of 52 patients with retransplanted kidneys from unrelated donors after first transplants had failed. Numerators and denominators as in Fig 1 (follow-up to Oct 1, 1973).

of difficulties in clearly separating the patients into different nonmixed cause categories, and in the second instance because of a heavy dominance of chronic glomerulonephritis in the case material, exceeding 80%. This proportion did not differ greatly from that in our total transplant population.

Report of a Case

The course of a 39-year-old woman with HL-A phenotype A3, W28; W10, W22 illustrates some of the perplexing immunologic considerations of primary and secondary renal transplantation. The first cadaveric homograft, on April 13, 1971, was provided from a donor with HL-A phenotype A2; A7, A12. The kidney did not function well, failing to lower the blood urea nitrogen level below 70 mg/100 ml. On May 17, 1971, a second cadaveric homograft was provided, this time from a donor with HL-A phenotype A2, A3; A7, Te52. Cytotoxic antigraft antibodies were not demonstrable

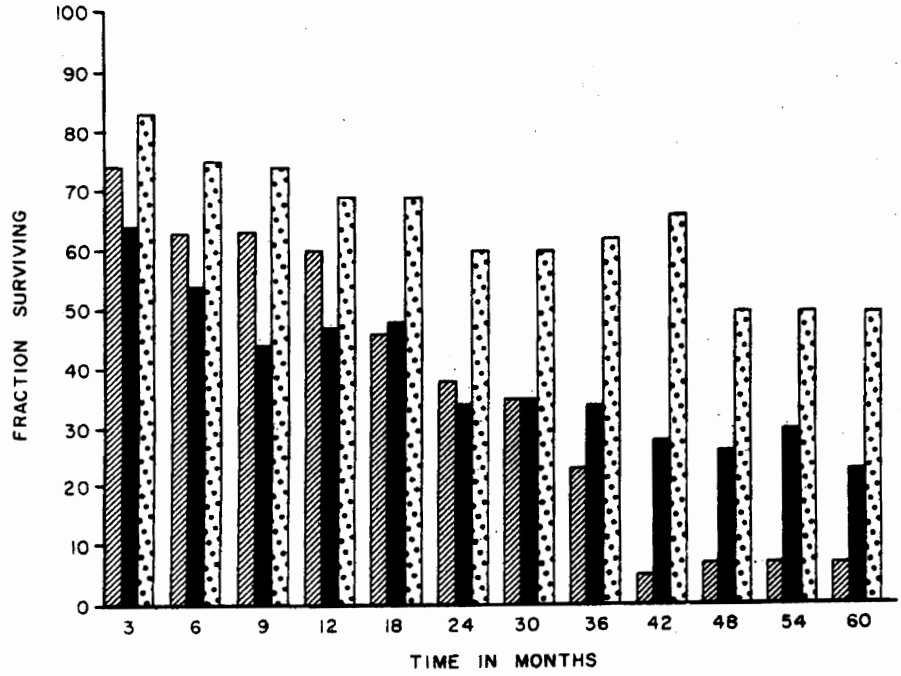


Fig 4.—Kidney survival of second transplant (follow-up to Oct 1, 1973).

(negative cross-match). In spite of the five weeks presensitization to HL-A antigens A2 and A7, the second kidney has functioned well until now. In July 1972, the first graft was removed, 15 months after its insertion, because of vague pain in the general area of the graft and poor kidney perfusion as determined by renal scan. On histopathologic examination, the kidney was found to be rejected.

Comment

It appears that the outcome of retransplantation in a group of patients having rejected their first grafts is worse than that after primary transplantation, but not to a great degree. The difference is mainly accounted for by an increased early postoperative mortality. It is an important and interesting practical consideration that such patients also have a substantially depreciated prognosis if they are returned to long-term hemodialysis."

The type of kidney used primarily has not been considered an overriding factor in the decision of whether or not to perform a retransplantation. It has been considered justified to use kidneys of relatives for retransplantation if such are available, as the subsequent result has been superior to that with secondary cadaveric kidneys. The prognosis after retransplantation has been better if a long period of time elapsed after first transplantation. Possibly a long uninterrupted period of immunosuppressive treatment makes the recipient better able to accept a second transplant. Alternatively, patients who have borne chronically functioning homografts without dramatic, acute rejection episodes may represent a favorable subpopulation that has been refined by natural selection.

Specific HL-A presensitization *in the absence of positive direct crossmatch* does not contraindicate a retransplantation procedure. This could be construed as further evidence of the now well accepted poor discrimination of HL-A matching in predicting the outcome after organ transplantation.[7] Or if HL-A antigens are directly related to histocompatibility, there is even a possibility that specific blocking antibodies were produced as a response to the sensitizing antigen, since the results, if anything, were slightly better if there had been prior exposure to an HL-A antigen found in a nonprimary donor.

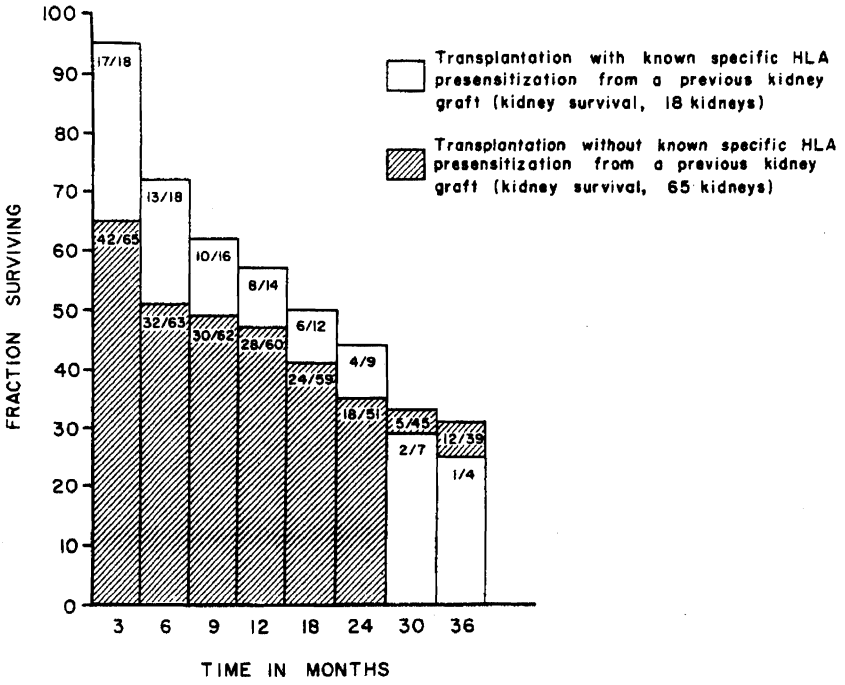


Fig 5.—Numerators and denominators indicate kidneys functioning and kidneys at risk during each time period (follow-up to Oct 1, 1973).

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