RESULTS OF KIDNEY TRANSPLANTATION IN RELATION TO HLA-A, B, DR MATCHING AND QUALITY OF DONOR ORGAN

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Summary

The influence of HLA compatibility as well as immediate postoperative function on survival rates was investigated in 203 cadaver kidney transplants. HLA compatibility, especially DR compatibility, improved transplant survival significantly. A direct correlation was found between primary transplant function and long-term results. HLA compatibility and quality of the donor organ had a cumulative effect on kidney transplant survival. Our results are a further indication that besides HLA compatibility, optimal quality of donor organs has crucial significance for the results of transplantation.

Introduction

The long-term prognosis of a kidney transplant is mainly determined by histocompatibility of donor and recipient. The primary function of the transplant depends on the quality of the donor organ. Various factors, such as kidney function in the donor before nephrectomy, warm ischaemia time, technique of nephrectomy and method of preservation influence the viability of the transplant. The problems and complications which occur in a patient with a primarily non-functioning transplant are generally known. Only the higher rate of infections in the patients as well as the difficulties with regard to immunosuppressive therapy should be mentioned. Diagnosis of an incipient transplant rejection is more difficult and is more likely to be overlooked in a patient with a non-functioning kidney than in a patient with immediate transplant function, since the decrease of urine output and the rise in serum creatinine constitute important symptoms of rejection. However, there are divergent findings on the correlation between primary transplant function and long-term prognosis. Some authors have reported that an acute postoperative transplant failure is not associated with an unfavourable prognosis [1, 2]. Other investigators have found that poor transplant survival rates correlated with acute renal failure after transplantation [3–7].
The objective of the present study was to compare the survival rates of locally removed and transplanted kidneys and survival rates of transplant kidneys made available to us from outside centres. The results were correlated with ischaemia times, immediate postoperative function and HLA compatibility.

Patients and methods

We analysed a total of 203 cadaver kidney transplantations carried out in Heidelberg from 1975 to 1980. Eighty-one donor kidneys derived from the Heidelberg Centre (HC), and 122 kidneys were made available to us from outside centres (OC). Standard immunosuppression consisted of azathioprine and prednisone. In rejection reactions, methylprednisolone was administered i.v. and the dose of oral prednisone was raised. Antilymphocyte globulin was used in a few cases. All donor kidneys were preserved by hypothermic perfusion and subsequent cold storage (mostly with Collins solution). Transplants in which kidneys were preserved by perfusion machines are not considered in this study. In all transplants, we registered the warm and cold ischaemia time of the transplant. Irrespective of its cause, acute postoperative renal failure was defined as present when oligo-anuria occurred after the transplantation, the serum creatinine rose and dialysis became necessary. In all cases, typing for HLA-A, B antigens was performed and additionally for HLA-DR in 127 combinations. The patients were subdivided according to HLA compatibility: HLA-A, B matched \( \geq \) B locus identity, HLA-A, B mismatched \( < \) B locus identity, HLA-A, B and DR matched \( \geq \) B locus identity and \( \geq 1 \) DR-identity, HLA-A, B and DR mismatched \( < \) B locus identity and \( < 1 \) DR-identity. A negative crossmatch was a prerequisite for transplantation. The actuarial transplant survival rates were calculated according to the method of Merrell and Shulman [8]. Statistical analysis of significance was performed with the log rank test.

Results

The one-year survival of all transplants was 62.4%. The difference between the HLA-A, B compatible \((n = 87)\) and the incompatible transplants \((n = 116)\) was 9.6% \((67.6\% \text{ vs } 58.3\%, p = 0.03)\). With additional compatibility, the results were further improved. One-year survival rate of HLA-A, B and DR compatible transplants \((n = 51)\) was 78.3% as compared to only 48.2% in the HLA-A, B and DR compatible group \((n = 76)\). These results confirm that the survival rates of cadaver kidney transplants can be appreciably improved by DR matching.

Figure 1 shows the survival rates of donor kidneys supplied to us from outside centres (OC) as well as of kidneys removed in our own centre (HC). The one-year survival rate of the HC kidneys \((67.3\%)\) was significantly better than that of OC kidneys \((56.4\%)\) \((p = 0.02)\).

The HLA incompatibility index for HLA-A, B as well as for HLA-B and HLA-DR separately, the ischaemia times as well as the immediate postoperative function of the OC and HC kidneys are shown in Table I. The HLA compatibility of the OC transplants was distinctly but not significantly better than that of the HC transplants. The warm and cold ischaemia times differed only slightly. However, a significant difference between OC and HC transplants was to be detected in the
Figure 1. Graft survival rates of donor kidneys obtained from outside centres (OC) and of kidneys removed in the Heidelberg Centre (HC)

TABLE I. HLA incompatibility index, ischaemic times (mean ± SD) and immediate post-operative function (%) of donor kidneys made available from outside centres (OC) or kidneys removed in the Heidelberg Centre (HC)

<table>
<thead>
<tr>
<th>Donor Nephrectomy Performed</th>
<th>N</th>
<th>HLA incompatibility index</th>
<th>Ischaemic times of transplants</th>
<th>% Post-transplant failure (24hr after TX**)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AB  B DR*</td>
<td>Warm (min)</td>
<td>Cold (hr)</td>
</tr>
<tr>
<td>OC</td>
<td>122</td>
<td>1.3 ± 0.7 0.6 ± 0.4 1.1 ± 0.2</td>
<td>4.6 ± 3.8 16.3 ± 5.2</td>
<td>21.3 p &lt; 0.01</td>
</tr>
<tr>
<td>HC</td>
<td>81</td>
<td>1.5 ± 0.7 0.8 ± 0.6 1.3 ± 0.4</td>
<td>4.8 ± 4.1 13.9 ± 5.6</td>
<td>11.1</td>
</tr>
</tbody>
</table>

* N = 127
** Tx = Transplantation

Immediate postoperative function. Whereas only 9 out of 81 (11.1%) of the HC kidneys had acute post-transplant failure, 26 out of 122 (21.3%) of the OC transplants did not resume immediate function (p < 0.01).

The long-term survival rates in relation to primary transplant function are shown in Figure 2. Whereas transplants with immediate function were still surviving after
Figure 2. Graft survival rates in relation to immediate postoperative function (IF)

Figure 3. Graft survival rates in relation to immediate postoperative function and on origin of the transplant (OC = donor kidneys obtained from outside centres; HC = donor kidneys removed in Heidelberg centre)
one year in 68.9%, in transplants with primary non-function, only 46.7% were still surviving after one year (p < 0.01).

In a further analysis, the results were compared in relation to primary non-function and origin of the donor kidneys (OC vs HC) (Figure 3). HC and OC grafts with immediate function (IF) and comparably good long-term results (71.2% vs 67.3% at one year, p = NS). In kidneys with primary non-function and therefore unfavourable prognosis, the results likewise did not differ significantly in two groups (HC grafts, no IF: 43.6% at one year; OC grafts, no IF: 53.9%; p = NS).

The effect of HLA compatibility on the survival rates of OC and HC kidneys is shown in Figure 4. The influence of HLA-A, B compatibility in OC kidneys

![Graph showing graft survival over time](image)

Figure 4. Effect of matching for HLA-A, B and DR antigens on survival rates of donor kidneys obtained from outside centres (OC) and of kidneys removed in the Heidelberg Centre (HC)

(HLA-A, B matched: 68.3%, HLA-A, B mismatched: 49.4%, p < 0.05) was greater than in HC kidneys (69.6% vs 59.3%, p = NS). Best results were attained when there was compatibility for HLA-A, B and DR (78.3% after one year), irrespective of whether the donor kidneys came from outside centres or whether these had been removed locally.
Discussion

Our results show that besides the HLA compatibility the immediate postoperative function is a crucial factor in the long-term prognosis of kidney transplants. This explains why the overall results of OC kidneys were more unfavourable than those of HC kidneys. In OC transplants, we found acute kidney failure after transplantations in a very much higher proportion than in HC transplants. Our results contrast with reports of Williams et al [1] as well as Kjellstrand et al [2], who found no correlation between postoperative function and long-term transplant prognosis. On the other hand, our data largely agree with those of Sheil et al [3], Whittaker et al [5], Baxby et al [6] as well as Scholz et al [7]. These authors observed unfavourable transplant survival rates after delayed resumption of renal function.

The factors which unfavourably affect the quality of the donor organ are likely to be the following: hypoxic damage to the kidneys before nephrectomy, long period of warm ischaemia, poor removal technique as well as inadequate or too long preservation. We believe that essentially two factors are decisive for the significantly lower proportion of primary non-functioning, locally removed transplant kidneys: (1) An intensive pretreatment of the kidney donor consisting of adequate hydration, maintenance of blood pressure, induction of diuresis by means of diuretics, prevention of renal vasoconstriction and of intravascular clotting and; (2) ‘in situ’ perfusion as well as ‘en bloc’ removal of donor kidneys (reviewed in [9, 10]). A loss of viability of the transplant kidneys can be largely prevented by these measures. Like other authors [11, 12], we also found that in HLA compatibility, especially in DR matching, the transplant survival rates are appreciably improved. However, our data also show that HLA compatibility and quality of the donor organ have a cumulative effect on the long-term function of the transplant. Thus, the best results can be attained with HLA-A, B and DR-compatible organs with good viability. Primary non-function combined with HLA incompatibility is prognostically unfavourable.

In conclusion, besides HLA compatibility the value of a good quality of the donor organ has to be emphasised.

References

7. Scholz D, Horpacy G, Mebel M. Europ Urol 1979; 5: 14
Open Discussion

BRYNGER (Chairman) Do you have any speculations about why you lost kidneys within the first 3 months and you established a difference between the non-functioning and functioning kidneys within 3 months. Do you have problems with rejection diagnosis?

LENHARD I think it is as well to know that the diagnosis of incipient rejection is much more difficult in patients with primary non-functioning kidneys than in patients with a good functioning kidney. That is a problem in all centres, I think, to get early diagnosis of incipient rejection, but this is not a good explanation for the data.