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A reliable and safe way of shortening cadaver kidney ischemia time: prenephrectomy tissue typing using donor lymph node cells

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Abstract. The purpose of this study was to investigate the impact of prenephrectomy donor tissue typing on tissue typing quality and transplantation outcome in human kidney transplantation. We report on 680 consecutive kidney transplantations performed at the Vienna Transplantation Center from 1986 to June 1991. In 343 of them, HLA typing was performed using donor lymph node cells obtained in a small surgical procedure several hours before organ retrieval. The mean cold ischemia time (CIT) could be reduced to 17.7 h in these patients compared with 21.9 h in the control group ($n = 337$, conventional tissue typing using spleen lymphocytes obtained during the organ removal, $P = 0.0001$). There was a trend towards better initial and long-term function in the lymph node group; however, this did not reach statistical significance. The clarity of tissue typing results was significantly better when lymph nodes were used as the lymphocyte source. We conclude that prenephrectomy tissue typing is a feasable and inexpensive method of shortening CIT in renal transplantation and favors HLA typing, both likely to benefit transplantation outcome particularly within organ exchange programs.

Key words: Renal transplantation – Organ donor – HLA typing – Prenephrectomy tissue typing – Cold ischemia time

Despite the introduction of new storage solutions, cold ischemia time (CIT) remains of crucial importance to the functioning of a cadaveric renal graft, at least for the organ function in the immediate postoperative period. Some studies have been published showing an effect of CIT on long-term function, too. Furthermore, there is evidence that graft function depends mainly on the number of HLA antigens shared between the recipient and the respective donor. Organ exchange organizations such as Eurotransplant intend to minimize HLA-mismatches by selecting the optimal recipient for an organ available, based on the stored data of the thousands of patients on the multinational waiting list. The benefit of organ sharing in achieving the greatest possible HLA-matching between donor and recipient may be impaired by the additional time necessary for transportation of the organ from the donor center to the recipient center [2].

The aim of our study was to investigate the effects of prenephrectomy donor tissue typing on CIT and its impact on the quality of HLA type determination. Furthermore, we investigated the effects of CIT shortening on primary and long-term graft function.

Materials and methods

Since 1982, in Austria organ donation has been based on a law of the so-called presumed consent. This means that, if no declaration of dissent is found with a potential organ donor, he or she is considered as agreeing with organ donation [6]. The regulation is comparable with those of Belgium or France [10] and follows the guidelines of the European Council [3].

We report on 683 consecutive cadaveric kidney transplantations performed at our center using kidneys procured within our own catchment area from January 1986 to June 1991. Details about procurement strategies and logistics are described elsewhere [4, 5]. The remainder of the 1048 kidneys available (368, 35.1 %) were shipped to other centers of the Eurotransplant community. In 3 of the 683 consecutive cases (0.4 %), neither lymph nodes nor spleen could be obtained from the donor for various reasons. Tissue typing was performed using donor blood in these cases. The following analyses are confined to the 680 transplantations with HLA typing based on donor spleen or lymph nodes.

The 680 transplantations were divided into 2 groups: In group A ($n = 343$, 50.4 %) inguinal donor lymph nodes were obtained in a small surgical procedure after the first brain death determination hours before organ removal. After a short incision of the skin, the inguinal lymph nodes near the femoral vein were prepared, dissected, and stored in cold saline. The procedure was performed under sterile conditions by a transplant coordinator at the donor ICU, without the need for an operation theatre or nurse. In the first cases, the operation was done on both donor sides, but it quickly turned out that enough material could be obtained with one or two lymph nodes

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Table 1. Donor parameters

	Group A ($n = 343$)	Group B ($n = 337$)	P value
Age (years)	35.2 ± 14.7	37.5 ± 15.4	0.04
Sex (% male)	68.4	66.5	0.3
Blood group (O-A-B-AB)	129-149-51-14	126-150-45-16	0.7
Cause of death (% trauma)	60.2	55.3	0.7
Traffic accident (%)	36.2	29.8	0.06
Stay in ICU (days)	2.79 ± 0.16	2.69 ± 0.17	0.8
Circulation (% stable)	58.2	65.2	0.1
Reversible cardiac arrest (%)	8.72	9.29	0.6

ICU, intensive care unit

Table 2. Recipient characteristics

	Group A ($n = 343$)	Group B ($n = 337$)	P value
Age (years)	45.9 ± 13.6	46.3 ± 13.3	0.7
Sex (% male)	63.9	56.4	0.05
Days on dialysis	826.1 ± 58.0	935.2 ± 56.1	0.7
Duration of kidney disease (years)	8.85 ± 0.8	8.34 ± 0.6	0.8
Mismatches HLA-A + B	1.87 ± 0.06	1.92 ± 0.06	0.8
Mismatches HLA-DR	0.41 ± 0.04	0.48 ± 0.03	0.1
Retransplants (%)	16.9	14.9	0.8
Patients with PRAs (%)	29.2	33.6	0.5
Patients with PRAs > 40% (%)	11.1	12.5	0.7
Anatomical variations (%)	31.6	29.6	0.4
Anastomosis procedure (min)	38.5 ± 13.2	37.9 ± 12.7	0.9
Perioperative (30 days) mortality (%)	2.2	2.9	0.6
Immunosuppression (%	33.1	34.0	0.9
including ATG)	81.2	80.5	0.9
Immediate graft function (%)	17.7 ± 6.8	21.9 ± 5.6	0.0001
Cold ischemia time (h)			
One year graft survival, all patients (%)	87.7	84.6	0.09
One year graft survival, without PRNF (%)	92.4	87.2	0.05
Four year graft survival, all patients (%)	80.1	73.2	0.06

PRA, panel reactive antibodies; PRNF, primary nonfunction; ATG, antithymocyte globulin

from one side. Usually the complete procedure was finished within 30 min. Appropriate HLA tissue typing started immediately afterwards. This procedure was approved by the ethics committee of our institution. In group B ($n = 337$, 49.6%) tissue typing was performed using cells from the donor spleen removed at the time of organ retrieval.

The quality of the tissue typing results was assessed according to a score by doctors and technicians without knowledge about the way the lymphatic material had been retrieved from the donor. After determination of the donor's HLA type and crossmatching, recipients were selected in the same way in both groups, namely be HLA-matching, preimmunization, and waiting time as ranked selection criteria. Results of tissue typing were checked in the Eurotransplant laboratory. For organ perfusion and storage we used Euro-Collins and UW solution [7]. Transplantations were performed in a standardized surgical procedure, the immunosuppressive regimen consisted of cyclosporine and prednisone or was given as sequential immunosuppression with antithynocyte globulin (ATG) for the first 10 days and cyclosporine thereafter, as described elsewhere [1]. For stastitical analysis we used Student's t-test and χ^2 test whenever appropriate. Survival curves were calculated according to the Kaplan Meier method [8]. Differences between groups with respect to survival were tested using Mantel's test [9].

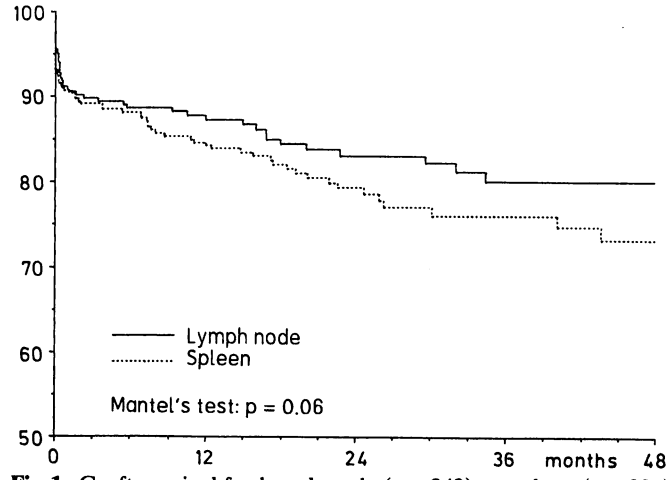

Fig. 1. Graft survival for lymph node ($n = 343$) vs. spleen ($n = 337$) tissue typing, no cases excluded

Results

The two groups were comparable with respect to all donor parameters (Table 1). Donor age, however, was slightly higher in group B (35.2 vs 37.5 years, $P = 0.04$). Cold ischemia time was significantly shorter in group A (17.7 ± 6.8 h) than in group B (21.9 ± 5.6 h) (mean ± standard deviation, $P < 0.0001$).

Recipient data and outcome of transplantations are summarized in Table 2. The primary nonfunction rate in group A was 4.2% compared with 7.1% in group B ($P = 0.06$). The actuarial 1-year graft survival was 87.7% in group A as compared with 84.6% in group B (no cases excluded, $P = 0.09$). If graft with PRNF were excluded, the figures are 92.4% and 87.2%, respectively ($P = 0.05$). After 4 years, 80.1% of grafts were functioning in group A and 73.2% in group B (no cases excluded, $P = 0.06$). The graft function curves for both groups are given in Fig. 1.

The quality of tissue typing remained unchanged, with virtually no discrepancies between the methods. However, in group A only 5.1% of reactions were difficult to interpret as compared with 16.7% ambiguous serological reactions in group B ($P < 0.0001$).

Discussion

We have shown the consequences of prenephrectomy tissue typing using donor inguinal lymph nodes. There is a significant impact on the CIT and clarity of tissue typing results. There is a trend towards fewer grafts with PRNF, most likely due to the shortened CIT. The 1-year and 4-year actuarial survival, too, show a trend in favor of lymph node typing. To statistically detect the effects of a 4-h difference in CIT, however, obviously requires very large data samples, with respect to the 1-year graft survival. The additional costs of the prenephrectomy lymph node sampling are minimal.

From these results, we conclude that tissue typing from donor lymph node cells obtained before nephrectomy

provides two major advantages, shortening of the CIT and facilitation of clearer typing results, without reducing the quality of HLA determination; both factors are likely to benefit organ sharing and the outcome of transplantations.

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