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M. J. Pacholczyk
B. Łągiewska
M. Szostek
A. Chmura
M. Morzycka-Michalik
D. Rowińska-Stryjecka
J. Wałaszewski
W. Rowiński

Transplantation of kidneys harvested from non-heart-beating donors: early and long-term results

M. J. Pacholczyk (✉) · B. Łągiewska · M. Szostek · A. Chmura · J. Wałaszewski · W. Rowiński
Department of General and Transplantation Surgery, Warsaw Medical School, Nowogrodzka 59, 02-006 Warsaw, Poland
Fax 48 (02) 6280088

M. Morzycka-Michalik · D. Rowińska-Skryjecka
Institute of Transplantology, Warsaw Medical School, Nowogrodzka 59, 02-006 Warsaw, Poland

Abstract The purpose of this retrospective study was to evaluate results of non-heart-beating donor (NHBD) kidney transplantation. Between Jan 1986 and Dec 1994, 80 out of 582 cadaveric kidneys were harvested from NHBD (31.9 min ± 24 after cardiac arrest). The results in the NHBD group (76 recipients) were compared with those obtained after transplantation of kidneys harvested from heart-beating donors (HBD) with respect to early graft function, and the graft and recipient's survival. Both groups were matched for sex, age, PRA level, number of HLA mismatches, and cold ischemia time. Triple immunosuppression therapy was used in both groups. Acute tubular necrosis (ATN) was observed significantly more frequently in the NHBD group (50 of 76 recipients vs 33 of 100 in the HBD group). The striking finding of this study was that the occurrence of primary non-function was the same in both groups and that the main cause of it was acute rejection. The 1-year patient and graft survival rates were 98.7 % and 81.6 % for the NHBD group and 99 % and 90 % for the HBD group, respectively. There was also no statistical difference in the serum creatinine concentration in both groups. We concluded that despite an increased incidence of ATN in the NHBD kidney recipients, the long-term results are good and comparable with those in the HBD group.

Key words Non-heart-beating donors · Kidney transplantation

Introduction

For many years and for a variety of reasons kidneys have quite often been procured in our center from non-heart-beating donors (NHBD). The purpose of this retrospective study was to evaluate early and long-term results of kidney transplantation in recipients of kidneys retrieved from NHBD.

Materials and methods

Between January 1986 and December 1994, 582 cadaveric kidney transplants were performed in our department. During this period 84 kidneys were procured from NHBD and transplanted. Seventy-six recipients were incorporated into our study (NHBD group). In 8 cases, an HLR machine was used in the donor after cardiac arrest so those previously reported cases were excluded [3]. For comparison, we selected a group of 100 recipients (heart-beating donor HBD] group) matched with the NHBD group according to sex (female/male ratio), age, HLA mismatches (HLA-MM), and maximum panel-reactive antibody (PRA) level.

Donors

NHBD group

This group consisted of 38 donors (female/male: 13/25) aged 35.5 ± 16.4 years. All donors in this group were treated in various hospitals in the Warsaw area. The causes of death were as follows: 27 donors died from head injury, 8 from spontaneous cerebrovascular bleeding, 2 from anoxia (drowning and hanging), and 1 from drug poisoning; in all donors in this group brain-stem death was diagnosed. They were hemodynamically unstable (group C by UNOS) and required high doses of dopamine, exceeding 20 μg/kg

Table 1 Recipients' demographics. Relevant recipient data are shown as mean ± standard deviation (*NHBI*) non-heart-beating donor, *HB* heart-beating donor)

	NHBD	HBD
Number of recipients	76	100
Sex f/m	33/43	45/55
Age (years)	40.12 ± 10.94	39.06 ± 11.04
HLA mismatches A, B	2.15 ± 0.9	2.06 ± 0.8
DR	1.08 ± 0.55	1.1 ± 0.42
PRA maximum (%)	16.3 ± 20.9	20.6 ± 30.4
Anastomosis time (min)	34.8 ± 11.8	30.5 ± 8.07

per min. In all these cases cardiac arrest occurred before the transplant team arrived. Cardiac massage, mechanical ventilation, and heparin infusion were continued in all NHBD before in situ perfusion was started.

Euro-Collins (EC) or Ringer solution was used for in situ perfusion. The kidneys were removed en bloc with the abdominal aorta and vena cava and flushed again on the back table with EC in 58 cases or University of Wisconsin organ preservation (UW) solution in 18 cases. The warm ischemia time between cardiac arrest and in situ perfusion was from 10 to 120 min (mean 31 ± 24 min). The cold storage time ranged from 9 to 42 h (mean 25.6 ± 8.9 h).

HBD group

Incorporated in this group were 50 donors (female/male: 12/38) aged 31.3 ± 11.7 years; 30 had died from head injuries, 19 from a cerebrovascular accident, and 1 from an intracranial isolated tumor. All donors in this group were classified into group A and B (by UNOS) and the mean dose of dopamine was 10.8 ± 10 μg/kg per min. A standard procurement technique was used, including in situ perfusion (EC or Ringer), en bloc nephrectomy, and back table flushing with EC (68) or UW (32). The cold ischemia time ranged from 7 to 48 h (average 27.5 ± 7 h).

Recipients

Table 1 shows a summary and comparison of all relevant recipient data in the two groups. None of these data showed a statistically significant difference between the two examined groups of recipients. In both recipient groups, standard triple immunosuppressive protocol was used. Preoperatively all recipients received azathioprine, 3 mg/kg p.o. and methylprednisolone 500 mg i.v. on induction. Postoperatively azathioprine was given once a day (3 mg/kg) and the dose was modified according to the WBCC. Methylprednisolone was given 6 and 12 h after kidney reperfusion to a total dose of 1 g on the day of transplantation, followed by 0.5 g on day 2, 0.250 g on day 3, and an oral dose of prednisolone, 0.5 mg/kg, was gradually reduced during the first month. The first dose of cyclosporine A was administered 18 h after reperfusion at a daily dose of 6 mg/kg body weight.

Statistical analysis

Data are reported as the mean ± SD. Data were compared using the unpaired Student's *t*-test and chi-squared analysis.

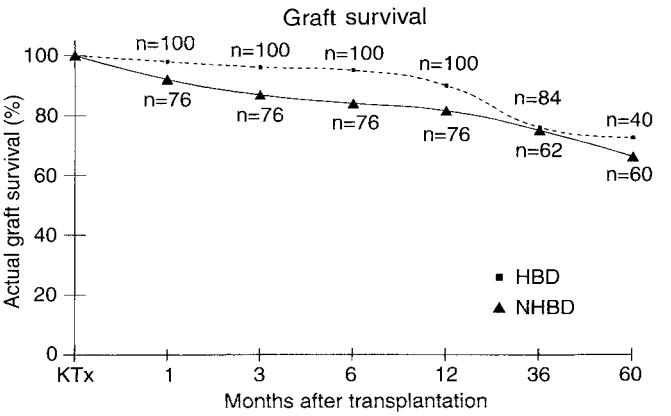

Fig. 1 Renal graft survival rates according to donors source: kidneys from heart-beating donors *(HBD)* vs non-heart-beating donors *(NHBD)* (*n* represents the total number of patients in the groups at each follow-up point, for whom survival rate was calculated)

Results

In the early postoperative period, 50 of 76 recipients (65.8 %) in the NHBD group and 33 of 100 recipients of the HBD group needed dialysis support. The mean time of hemodialysis (in days) was 16.8 ± 9.2 in the NHBD and 15.5 ± 8.4 in the HBD groups. The number of hemodialyses in the group of recipients who developed acute tubular necrosis (ATN) was 7.35 ± 3.2 and 7.05 ± 5.4 in the NHBD and HBD groups, respectively. Immediate graft function was observed in 23 recipients in the NHBD group (30.2 %) and in 64 recipients in the HBD group (64 %). There were three cases of primary non-function in the NHBD group (3.9 %) and three cases in the HBD group. The major cause of primary non-function in both groups (NHBD-2, HBD-2) was acute rejection following ATN (established by biopsy). In one case (NHBD), microscopy showed advanced graft necrosis. Renal artery thrombosis was found to be the direct cause of graft failure in one case in the HBD group.

In the early postoperative period (3 months), episodes of acute rejection confirmed by needle biopsy were observed in 50 of the 76 (65.8 %) recipients in the NHBD group and in 46 of the 100 recipients in the HBD group. The mean dose of steroids used for the treatment of acute rejection during the first 3 months was 5.4 ± 3.5 g in the NHBD group vs 4.0 ± 2.2 g in the HBD group.

The 1-year patient survival rate was 98.7 % for the NHBD group and 99 % for the HBD group. The 1-year graft survival rate was 81.6 % for the NHBD group and 90 % for the HBD group. The actual graft and patient survival rates at 3 and 5 years are shown in Figs. 1, 2. The courses of serum creatinine levels in the early and late postoperative periods for both groups are shown in Fig. 3.

During 5 years of observation, four patients died with a functioning graft in the NHBD group; one died at

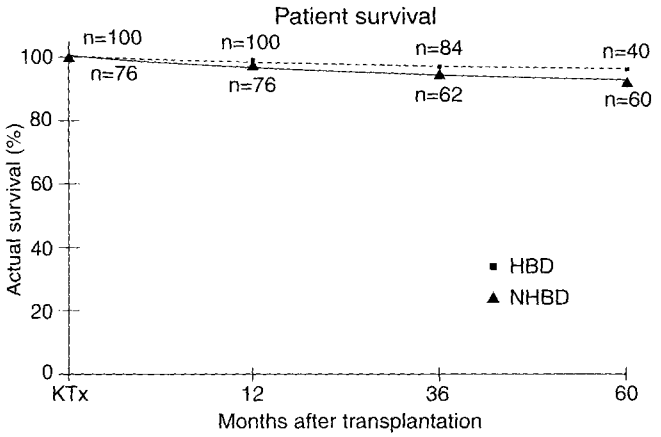

Fig. 2 Actual patient survival rates in *HBD* group vs *NHBD* (*n* represents the total number of patients in the groups at each follow-up point, for whom survival rate was calculated)

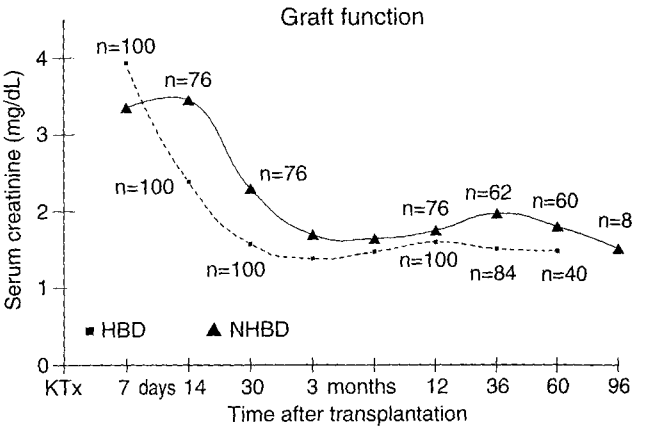

Fig. 3 Serum creatinine levels in the early (only for recipients who were not on dialysis at that time) and late postoperative periods (7, 14, and 30 days, 3, 6, 12, 36, 60 and 96 months after transplantation) in *NHBD* vs *HBD* groups

2 months from cytomegalovirus infection, and the other three died at 3 years from myocardial infarction (2) and pneumonia (1). In the HBD group, four recipients died; one died at 4 months from acute fulminant hepatitis (HCV), two patients died with functioning grafts at 2 years, one from a ruptured abdominal aortic aneurysm and one from myocardial infarction, and one died at home 3 years after transplantation from pneumonia.

Discussion

The purpose of this retrospective study was to compare the results of kidney transplantation in two groups of recipients: those who received kidneys from NHBD and those who received kidneys from HBD. Apart from the fact that delayed graft function was observed more frequently in the NHBD group ($P < 0.0003$), long-term follow-up showed that after 1, 3, and 5 years graft and patient survival were comparable with those in the HBD group [2, 4].

The important finding of our analysis was that the primary non-function rate in the NHBD group was no higher than that in the HBD group. The main cause of permanent graft failure in both groups was a combination of two factors, ischemia and acute rejection. In the first 3 months after transplantation, the episodes of acute rejection were observed more frequently in the NHBD group ($P < 0.03$). The cumulative dose (mean) of steroids used in NHBD recipients during this period was higher ($P < 0.03$) than in HBD recipients. Despite the increased occurrence of acute rejection in the NHBD group, long-term results were very good.

Therefore, we conclude that organ procurement from non-heart-beating donors should be performed and could be one of the ways of reducing the waiting list for renal transplantation [1, 4]. In all patients who have been diagnosed brain-stem dead, mechanical ventilation and cardiac massage should be continued in each case of sudden cardiac arrest, until surgical teams arrive.

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