

## KIDNEY TRANSPLANTATION FROM DONORS WITHOUT A HEARTBEAT

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### ABSTRACT

**Background** The dramatic shortage of kidney donors has triggered interest in other sources of organs, such as donors without a heartbeat. Accumulating evidence suggests that the short-term survival of cadaveric kidneys from such donors is similar to that of cadaveric kidneys from donors with a heartbeat. However, no data from large, matched studies with long-term follow-up are available. We conducted a matched, single-center study of kidney transplants obtained from donors without a heartbeat and those from donors with a heartbeat, with a 15-year follow-up period.

**Methods** Between 1985 and 2000, 122 kidney transplantations involving donors without a heartbeat were performed at the University of Zurich, in Switzerland. Outcomes of these procedures were compared with those of 122 transplantations of kidneys from donors with a heartbeat. The recipients were matched according to age, sex, number of transplantations, and calendar period of transplantation.

**Results** The characteristics of the recipients did not differ significantly between the two groups. We observed a significantly higher incidence of delayed graft function among the patients who received kidneys from donors without a heartbeat (48.4 percent) than among the patients who received kidneys from donors with a heartbeat (23.8 percent) ( $P < 0.001$ ). However, the long-term rate of graft survival was similar in the two groups ( $P = 0.98$ ): at 10 years, the rate of graft survival was 78.7 percent for kidneys from donors without a heartbeat and 76.7 percent for kidneys from donors with a heartbeat.

**Conclusions** Although the incidence of delayed graft function is significantly higher with kidneys from donors without a heartbeat than with kidneys from donors with a heartbeat, there is no difference in long-term outcome between the two types of graft. (N Engl J Med 2002;347:248-55.)

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**T**HE number of patients awaiting organs for transplantation has grown dramatically during the past two decades, triggering interest in expanding the pool of organs beyond those obtained from brain-dead donors with a heartbeat. Alternative sources of organs include elderly, brain-dead donors whose hearts continue to beat, living donors, and donors without a heartbeat. A successful program of transplantation from donors without a heartbeat could increase the number of kidneys available for transplantation by 30 percent.<sup>1</sup>

Death in donors without a heartbeat is defined as

an irreversible cessation of circulatory and respiratory function,<sup>2</sup> whereas brain death in donors with a heartbeat is determined according to neurologic criteria. Therefore, by definition, a donor without a heartbeat has had a prolonged phase of hypotension (one that lasts several minutes) followed by cardiac arrest before organ harvesting. Insufficient perfusion or complete lack of perfusion of such organs has long been thought to cause irreversible damage, resulting in poor short-term and long-term outcomes after grafting.<sup>3</sup> With the exception of recent limited experience in liver transplantation,<sup>4</sup> the use of organs from donors without a heartbeat has been restricted to the kidneys, since dialysis is available for support in case the graft does not function after transplantation.

Data regarding the use of organs from donors without a heartbeat have remained scarce; data from several centers are often pooled to achieve relevant numbers (Table 1). None of the studies conducted so far have provided long-term follow-up data, and only a few have reported results more than five years after transplantation. In addition, some studies have not included comparison groups (e.g., matched groups of patients receiving grafts from donors with a heartbeat). Thus, the controversy surrounding the outcomes of kidney transplants from donors without a heartbeat has remained unsettled. In 1985, the University Hospital Zurich (Zurich, Switzerland) initiated a kidney-transplantation program involving the use of grafts from donors without a heartbeat. This program continues to operate and uses a well-established protocol. In the current study, we compared the results of the entire series of 122 patients in the Zurich program with the results from a group of 122 matched patients who received grafts from donors with a heartbeat.

### METHODS

Of 1133 kidneys transplanted at our institution between January 1985 and March 2000, 122 (10.8 percent) were obtained from donors without a heartbeat. From our data base of recipients of kidneys from donors with a heartbeat, 122 randomly identified patients were matched on a one-to-one basis with the patients. Data were collected prospectively during routine follow-up at our institution, and complete follow-up information was available for each patient.

Institutional approval was obtained in accordance with the guide-

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**TABLE 1.** STUDIES OF KIDNEY TRANSPLANTATION FROM DONORS WITHOUT A HEARTBEAT.

REFERENCE	NO. OF TRANSPLANTATIONS FROM DONORS WITHOUT A HEARTBEAT	FIRST YEAR OF PROGRAM	DURATION OF STUDY	STUDY DESIGN	MATCHED PATIENTS	GRAFT SURVIVAL		
						TIME AFTER TRANSPLAN- TATION	DONORS WITH A HEARTBEAT	DONORS WITHOUT A HEARTBEAT
			yr			yr	percent	
Wijnen et al. <sup>5</sup>	57	1980	12	Multicenter	Yes	5	55	54
Current study*	122	1985	15	Single center	Yes	5 10	83 77	84 79
Gonzalez Segura et al. <sup>6†</sup>	52	1985	10	Single center	No	5 9	77 66	68 50
Pacholczyk et al. <sup>7</sup>	76	1986	9	Single center	Yes	1	90	82
Balupuri et al. <sup>8</sup>	47	1988	10	Single center	No	5	83	88
Casavilla et al. <sup>9‡</sup>	24	1989	4	Single center	No	1		86, 82
Sanchez-Fructuoso et al. <sup>1</sup>	95	1989	10	Single center	No	5	84	83
Metcalfe et al. <sup>10*</sup>	72	1992	8	Single center	Yes	5	81	75
Orloff et al. <sup>11</sup>	19	1992	2	Single center	No	1	76	
Cho et al. <sup>12</sup>	229	1994	2	Multicenter	No	1	86	83

\*Data from patients who died with a functioning graft were censored.

†The survival rates were estimated by Kaplan–Meier analysis.

‡In this study, donors without a heartbeat were stratified according to whether the donation was “uncontrolled” or “controlled”; graft survival was 86 percent and 82 percent, respectively. Uncontrolled donations involve donors who have died without warning and for whom there is little time to prepare for the donation; in controlled donations, there is more time to organize the donation.<sup>13</sup>

lines of the Swiss Academy of Medical Sciences. Potential recipients of a kidney graft were informed at the time of their acceptance for the waiting list that they might receive an organ from an alternative donor, such as an elderly donor or a donor without a heartbeat, in order to reduce waiting time. With regard to consent from the family of the donor, legislation allowing presumed consent has been enacted in the state of Zurich. Therefore, until 1995, when the Maastricht protocol was established, a few organs from donors without a heartbeat were procured, with presumed consent. Since then, informed consent has routinely been obtained from every donor's next of kin.

**Donors and Recipients**

A standardized protocol for the transplantation of kidneys from donors without a heartbeat has been used at our institution since this transplantation program was initiated, in 1985. Our initial protocol was similar to the Maastricht protocol (Table 2),<sup>14</sup> established in 1995, with the exception of the waiting period after cardiac arrest. During the first decade of the study, from 1985 until 1995, organ retrieval was initiated 5 minutes after cardiopulmonary arrest; after 1995, organ retrieval was performed according to the Maastricht protocol, which requires a waiting period of 10 minutes after cardiopulmonary arrest. All 122 kidney donors who had a heartbeat fulfilled the criteria for brain death.

To conduct this matched-pair study, we randomly matched each recipient of a kidney graft from a donor without a heartbeat to a patient from our data base of recipients of kidneys from donors with a heartbeat. The two groups of recipients were matched according to sex, age (within 5 years), and the calendar period of transplantation (within 12 months).

All recipients were chosen according to our local allocation system, which considers HLA matching, age matching, and recipients'

waiting time. Beginning in 1989, only primary transplantations were performed with organs from donors without a heartbeat, because of the failure of two such grafts in patients who underwent transplantation at the beginning of the program. The recipients of grafts from donors with a beating heart were treated with standard triple-immunosuppressive therapy consisting of prednisone, cyclosporine (Sandimmune, Novartis), and azathioprine (Imurek, Wellcome); azathioprine was replaced by mycophenolate mofetil (CellCept, Roche) in patients who underwent transplantation after 1996. In the recipients of grafts from donors without a heartbeat, immunosuppression was induced with intravenous antithymocyte globulin (ATG, Fresenius), with overlapping therapy consisting of oral cyclosporine beginning 10 days after surgery.<sup>15</sup> Except for the use of antithymocyte globulin in the latter group, the immunosuppressive regimen in the two groups was identical.

Delayed graft function was defined as the need for dialysis during the first week after transplantation, with subsequent recovery of renal function. Primary nonfunction was defined as the absence of renal function during follow-up. When the initial function of the graft was impaired, surveillance biopsy was performed weekly to permit detection of acute episodes of rejection.<sup>16</sup> Each episode of acute rejection during a period of delayed graft function was confirmed by biopsy and was graded according to the Banff criteria.<sup>17</sup>

**Data Collection and Statistical Analysis**

Data were prospectively collected and stored in a data base. Patients who died were considered either to have had a failed graft or (in the case of those who died of other causes) to have had a functioning graft. Graft survival was recorded for all the patients, including those who died with a functioning graft. In some analyses, data on patients who died with a functioning graft were censored.

To evaluate the natural course of the transplanted grafts, we con-

**TABLE 2. KEY POINTS OF THE MAASTRICHT PROTOCOL REGARDING THE USE OF ORGANS FROM DONORS WITHOUT A HEARTBEAT.\***

Diagnosis of death by physicians independent of procurement team
Waiting time of 10 minutes after cessation of cardiac massage and artificial ventilation
Protocol approved by the local medical ethics committee
Categorization of donor†
I: Dead on arrival
II: Unsuccessful resuscitation
III: Cardiac arrest awaited
IV: Cardiac arrest in a brain-dead donor

\*Information is from Kootstra.<sup>14</sup>

†Categories I and II comprise “uncontrolled” donations, in which donors have died without warning, and there is very little time in which to prepare for organ donation. Categories III and IV comprise “controlled” donations, in which there is more time to organize the process of donation.<sup>13</sup>

ducted analyses that included patients whose data were censored after they died with a functioning graft, unless otherwise indicated. Categorical variables were analyzed with the use of the chi-square test or, when appropriate, Fisher’s exact test. Continuous variables were analyzed with the use of the Mann–Whitney U test; the results are expressed as means ±SD, unless otherwise stated. Rates of graft survival were computed by the Kaplan–Meier method, and comparisons among groups were calculated with the use of the log-rank test. A P value of less than 0.05 was considered to indicate statistical significance. Variables that were significant in the univariate analysis were included in a Cox proportional-hazards analysis performed to identify independent risk factors for graft failure.

## RESULTS

### Characteristics of the Donors and Recipients

The characteristics of the donors without a heartbeat and of those with a heartbeat were not significantly different except with respect to the cause of death, the duration of warm ischemia, and the use of diuresis in the hour before organ harvesting (Table 3). The distribution of the 122 donors without a heartbeat ac-

**TABLE 3. CHARACTERISTICS OF THE DONORS AND RECIPIENTS.\***

CHARACTERISTIC	GRAFTS FROM DONORS WITHOUT A HEARTBEAT (N=122)	GRAFTS FROM DONORS WITH A HEARTBEAT (N=122)	P VALUE
<b>Donor</b>			
Age — yr	37.4±13	37.5±18	0.98
Diuresis in the hour before organ retrieval — ml	141.6±146	273.7±314	<0.001
Serum creatinine — mg/dl†	1.1±0.5	1.0±0.4	0.09
Duration of warm ischemia — min‡			<0.001
Mean	29.2±8.9	0.7±1.7	
Range	10–60	0–2	
Duration of cold ischemia — hr§			0.10
Mean	16.8±5.5	14.7±6.1	
Range	4–35	2.5–30	
Cause of death — no. (%)			
Trauma	98 (80.3)	52 (42.6)	<0.001
Cerebrovascular event	19 (15.6)	62 (50.8)	<0.001
Other	5 (4.1)	8 (6.6)	0.57
Type of donation — no. (%)¶			
Controlled	66 (54.1)	NA	
Uncontrolled	56 (45.9)	NA	
<b>Recipient</b>			
Age — yr	50.8±18.5	45.3±13.3	0.12
Male sex — no. (%)	74 (60.7)	70 (57.4)	0.69
Panel-reactive antibodies >50% — no. (%)	9 (7.4)	10 (8.2)	0.99
Repeated grafting — no. (%)	12 (9.8)	12 (9.8)	1.00
Duration of dialysis — min	37.7±34.6	38.0±33.7	0.94
Type of dialysis — no. (%)			
Hemodialysis	92 (75.4)	95 (77.9)	0.76
Continuous ambulatory peritoneal dialysis	30 (24.6)	27 (22.1)	0.76
HLA mismatches — no.	3.3±0.9	3.1±1.2	0.14

\*Plus-minus values are means ±SD. NA denotes not applicable.

†To convert the values for creatinine to micromoles per liter, multiply by 88.4.

‡The duration of warm ischemia in donors without a heartbeat was considered the interval from the moment of cardiac arrest until the start of the hypothermic flush-out.

§The duration of cold ischemia was considered the time from the start of preservation of the organ to its removal from cold storage.

¶The type of donation from donors without a heartbeat was defined according to the Maastricht protocol.<sup>14</sup>

according to the categories in the Maastricht protocol<sup>14</sup> was as follows. In no case was an organ procured from a donor who was dead on arrival at the hospital (Maastricht protocol category I). In the case of 56 donors (46 percent), resuscitation after cardiac arrest was unsuccessful (category II). In these 56 cases, resuscitation efforts had been performed for a minimum of 30 minutes, in accordance with the guidelines of the Swiss Academy of Medical Sciences. Cardiac arrest was awaited in 57 patients (47 percent) (category III), and cardiac arrest occurred before brain death could be diagnosed in 9 (7 percent) (category IV). For donors in category III, the decision to continue life-support measures was made by physicians who acted strictly independently of the transplantation team. The mean hospitalization time from admission until organ procurement was  $28.1 \pm 26.4$  hours for the “controlled” donations (involving donors in category III or IV) and  $5.4 \pm 3.0$  hours for the “uncontrolled” donations (involving donors in category I or II).

The characteristics of the recipients (including age, sex, number of previous transplantations, and 12-month period of transplantation) did not differ between those who received kidneys from donors without a heartbeat and those who received kidneys from

donors with a heartbeat. The number of immunologically sensitized patients with panel-reactive antibody values greater than 50 percent was also similar in these two groups. Likewise, variables for which the two groups were not matched, such as the duration of dialysis before transplantation, the type of dialysis (hemodialysis or continuous ambulatory peritoneal dialysis), and the average number of HLA mismatches, were also not significantly different in the two groups (Table 3).

**Outcomes of the Grafts**

Primary nonfunction occurred in both groups; the incidence was 5.7 percent among the kidneys from donors without a heartbeat and 4.9 percent among those from donors with a heartbeat ( $P=0.99$ ) (Table 4). Delayed graft function occurred more frequently with the kidneys from donors without a heartbeat than with those from donors with a heartbeat (48.4 percent vs. 23.8 percent,  $P<0.001$ ). The higher incidence of delayed graft function in the former group was reflected in their higher serum creatinine levels on postoperative day 7 (4.0 mg per deciliter [ $354 \mu\text{mol per liter}$ ] vs. 2.6 mg per deciliter [ $230 \mu\text{mol per liter}$ ],  $P<0.001$ ). However, the serum creatinine levels

**TABLE 4. OUTCOMES AFTER TRANSPLANTATION.\***

OUTCOME	GRAFTS FROM DONORS WITHOUT A HEARTBEAT (N=122)	GRAFTS FROM DONORS WITH A HEARTBEAT (N=122)	P VALUE
<b>Short-term outcomes</b>			
Delayed graft function — no. (%)	59 (48.4)	29 (23.8)	<0.001
Primary nonfunction — no. (%)	7 (5.7)	6 (4.9)	0.99
Acute rejection — no. (%)	53 (43.4)	67 (54.9)	0.10
Serum creatinine — mg/dl†			
7 days after transplantation	$4.0 \pm 2.5$	$2.6 \pm 2.0$	<0.001
1 mo after transplantation	$1.8 \pm 1.0$	$1.8 \pm 1.0$	0.90
1 yr after transplantation	$1.5 \pm 0.6$	$1.6 \pm 0.7$	0.11
Graft survival at 1 yr — %			
Kaplan–Meier estimate	85.8	86.5	0.92‡
After censoring of data from those who died with a functioning graft	91.7	90.7	0.98‡
<b>Long-term outcomes</b>			
Graft survival at 5 yr — %			
Kaplan–Meier estimate	74.2	76.0	
After censoring of data from those who died with a functioning graft	83.7	82.3	
Graft survival at 10 yr — %			
Kaplan–Meier estimate	63.6	60.9	
After censoring of data from those who died with a functioning graft	78.7	76.7	

\*Plus-minus values are means  $\pm$ SD.

†To convert the values for creatinine to micromoles per liter, multiply by 88.4.

‡The P values for graft survival were calculated by the log-rank test with use of the Kaplan–Meier estimates of survival.

among patients with a functioning graft were similar in the two groups at one month (1.8 mg per deciliter [ $159 \mu\text{mol}$  per liter] in both groups,  $P=0.90$ ) and at one year (1.5 mg per deciliter [ $133 \mu\text{mol}$  per liter] and 1.6 mg per deciliter [ $141 \mu\text{mol}$  per liter] in those with a graft from a donor without a heartbeat and those with a graft from a donor with a heartbeat, respectively;  $P=0.11$ ).

The median follow-up for the analysis of graft survival was 8.7 years (range, 1.4 to 15.2). Thirteen of the 122 patients in each group (10.7 percent) died with a functioning graft during follow-up. There was no significant difference in the rate of graft survival between kidneys from donors without a heartbeat and those from donors with a heartbeat one year after transplantation (91.6 percent and 90.6 percent, respectively) (Fig. 1). The rates of graft survival calculated 5 and 10 years after transplantation were 83.7 percent and 78.8 percent, respectively, in patients who received kidneys from donors without a heartbeat and 82.3 percent and 76.7 percent, respectively, in those who received kidneys from donors with a heartbeat ( $P=0.98$  by Kaplan–Meier survival analysis) (Fig. 1A). In an analysis of the patients whose data were not censored because of death with a functioning graft, the long-term graft survival was found to be similar in the two groups ( $P=0.92$ ) (Fig. 1B).

Univariate analysis with the log-rank test revealed that delayed graft function had a significant adverse effect on the survival of grafts from donors with a heartbeat ( $P=0.006$  for the comparison with grafts without delayed function), whereas this effect was not noted in the grafts from donors without a heartbeat ( $P=0.15$ ). According to the univariate analysis, significant risk factors for graft loss among the patients in the latter group were a panel-reactive antibody value above 50 percent ( $P=0.028$  for the comparison with a value  $\leq 50$  percent), acute rejection ( $P=0.01$  for the comparison with the absence of such rejection), and corticosteroid-resistant rejection ( $P=0.006$  for the comparison with the absence of such rejection). Acute rejection was also a risk factor for the loss of grafts from donors with a heartbeat ( $P=0.029$  for the comparison with grafts not affected by acute rejection). The following variables had no significant influence on graft survival in either group: trauma or cerebrovascular disease as the cause of death in the donor, the age of the donor (range, 4 to 73 years among those with a heartbeat and 15 to 61 years among those without a heartbeat), diuresis during the hour before death, the age of the recipient (range, 12 to 71 years among those who received a graft from a donor without a heartbeat and 14 to 75 years among those who received a graft from a donor with a heartbeat), sex, and number of HLA mismatches. The duration of cold ischemia did not correlate with graft outcome

in either group (grafts from donors without a heartbeat: mean, 17 hours; range, 4 to 35;  $P=0.47$  for the comparison between long [ $>24$  hours] and short periods of cold ischemia; grafts from donors with a heartbeat: mean, 15 hours; range, 3 to 30;  $P=0.97$ ). The duration of warm ischemia among the grafts from donors without a heartbeat ( $29 \pm 9$  minutes; range, 10 to 60) had no significant effect on the survival of the grafts ( $P=0.56$  for the comparison between long [ $>30$  minutes] and short periods of warm ischemia). Finally, the survival of grafts from donors without a heartbeat was not significantly influenced by the Maastricht protocol category<sup>14</sup> of the donation (“controlled” or “uncontrolled,”  $P=0.69$ ).

The multivariate analysis conducted to identify independent risk factors revealed a strong and significant association between delayed graft function and decreased graft survival in the grafts that had been obtained from donors with a heartbeat ( $P=0.03$  for the comparison between grafts with delayed function and those without delayed function) but not among the grafts from donors without a heartbeat ( $P=0.28$ ). In the latter group, risk factors for graft failure that reached statistical significance in the Cox regression analysis were panel-reactive antibody values above 50 percent ( $P=0.03$  for the comparison with values  $\leq 50$  percent) and episodes of corticosteroid-resistant rejection ( $P<0.001$  for the comparison with the absence of such episodes) (Table 5).

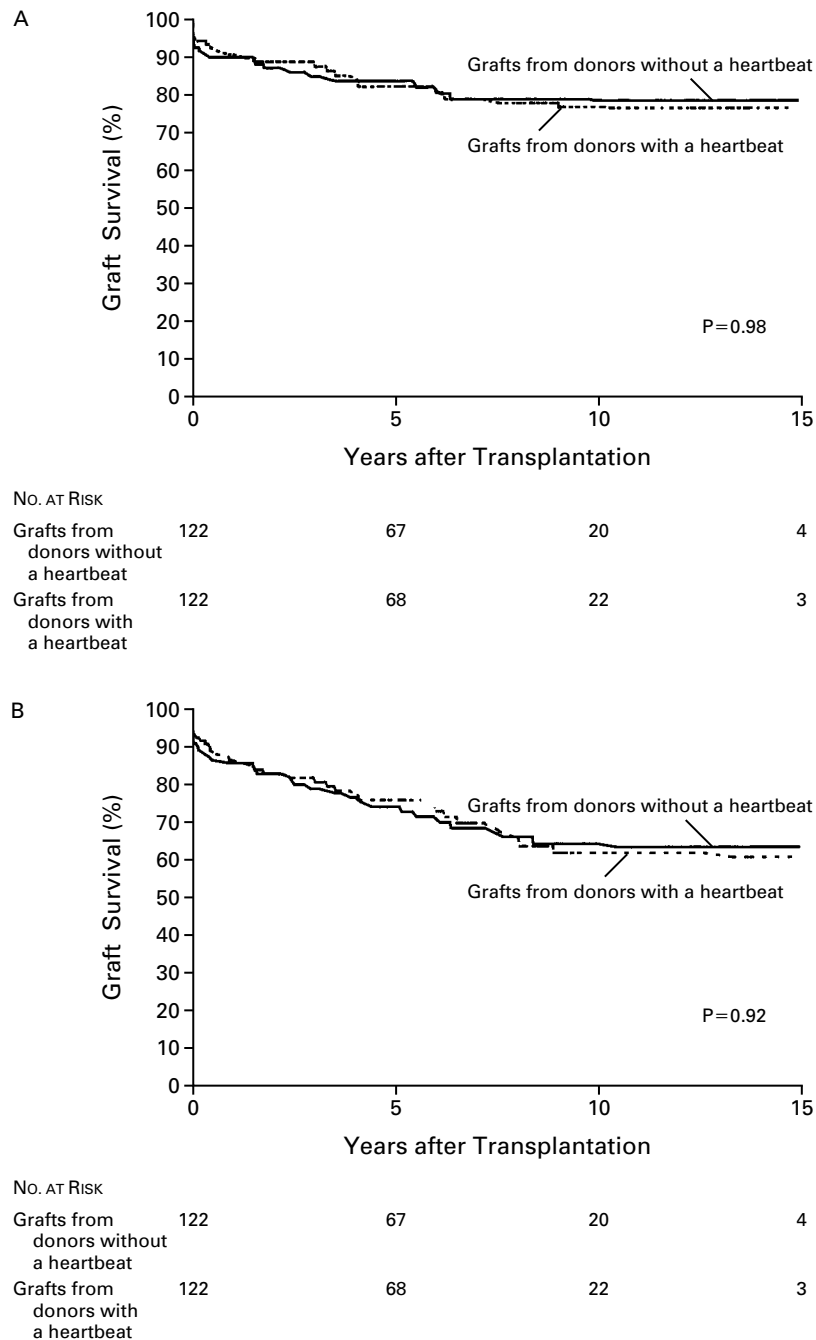
## DISCUSSION

In this single-center, matched-pair study, we found that although the incidence of delayed graft function affecting kidneys from donors without a heartbeat was approximately double that affecting kidneys from donors with a heartbeat, the two groups had similar, low rates of primary nonfunction and similar long-term outcomes. These data support the concept that kidneys from donors without a heartbeat can routinely be included in kidney-transplantation programs, thus decreasing waiting times and mortality rates among patients who are waiting for organs.<sup>18</sup>

The numbers of patients awaiting organs and the waiting periods before transplantation have increased dramatically during the past decade.<sup>19</sup> This situation has triggered interest in seeking alternative strategies for enlarging the donor pool — for example, by retrieving organs from living unrelated donors, elderly brain-dead donors, or donors without a heartbeat. Validation of these alternative approaches is critical if they are to be appropriately recommended by those who make transplantation policy.

Despite its introduction into clinical practice in the early 1980s, the use of organs from donors without a heartbeat has not been popular.<sup>20</sup> Numerous issues of concern have been raised about this type of dona-

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**Figure 1.** Rates of Long-Term Graft Survival after Transplantation of Kidneys from Donors without a Heartbeat and Donors with a Heartbeat.

Kaplan–Meier analysis was used to estimate the rates of survival, and the log-rank test was used to calculate the P values. Panel A shows the results of analysis after data from patients who died with a functioning graft were censored. Panel B shows the results of analysis before these data were censored.

**TABLE 5.** RISK FACTORS FOR GRAFT FAILURE, ACCORDING TO THE COX REGRESSION ANALYSIS.\*

CHARACTERISTIC	GRAFTS FROM DONORS WITHOUT A HEARTBEAT		GRAFTS FROM DONORS WITH A HEARTBEAT	
	HAZARD RATIO (95% CI)	P VALUE	HAZARD RATIO (95% CI)	P VALUE
Delayed graft function	1.6 (0.7–4.0)	0.28	2.9 (1.1–7.4)	0.03
Panel-reactive antibodies >50%	4.2 (1.2–15.2)	0.03	0.8 (0.2–3.1)	0.77
Corticosteroid-resistant rejection	4.9 (2.0–12.2)	< 0.001	1.3 (0.5–3.1)	0.56

\*CI denotes confidence interval. P values are for the comparison with grafts without the given characteristic (delayed graft function or corticosteroid-resistant rejection) with antibody values of less than or equal to 50 percent.

tion, with medical and ethical issues central among them. The poor long-term survival expected of such grafts as a consequence of the high incidence of delayed graft function has been mentioned repeatedly.<sup>21,22</sup> The controversy has been sustained by opposing voices that suggest good outcomes with grafts from donors without a heartbeat (Table 1). The absence of properly designed studies with long-term follow-up, particularly the lack of appropriate comparison groups of patients, has prevented the discussion about this type of donation from moving beyond speculation. In addition, multicenter analyses of transplantation programs that make use of organs from donors without a heartbeat suffer from “center effects,” since policies regarding the medical and ethical management of donors without a heartbeat vary among institutions and have varied over time.<sup>23</sup>

The present study is based on the experience at a single center and extends the analysis of outcome beyond a 10-year follow-up period. A standard protocol was used for all the transplantations, and follow-up was complete for all the donors and recipients. Since a randomized trial was not feasible, a matched-pair design using a large data base of patients who received kidneys from donors with a heartbeat at the same center seemed appropriate. As in previous reports,<sup>1,12</sup> delayed graft function was more frequent among the recipients of grafts from donors without a heartbeat than among other recipients. However, delayed graft function had no significant negative effect on long-term organ survival in the former group. These results are in contrast to the negative effects of delayed function on graft survival in the recipients of kidneys from donors with a heartbeat. These negative effects have been noted in several other series.<sup>24–26</sup>

In patients with anuria who have delayed graft function, episodes of rejection may be missed because there is a lack of clinical monitoring. Therefore, our protocol included routine biopsy of nonfunctional re-

nal grafts both from donors with a heartbeat and donors without a heartbeat so that rejection would not be missed and left untreated.<sup>27</sup> This approach is particularly crucial for recipients of grafts from donors without a heartbeat, since the incidence of delayed graft function is higher in this group than in recipients of grafts from donors with a heartbeat. We also used a distinct protocol for the induction of immunosuppression in patients who received renal transplants from donors without a heartbeat. Because of the nephrotoxic effects of cyclosporine, we used antithymocyte globulin for the first 10 days after transplantation in these patients, so as to avoid additional damage to the transplanted kidney. The decision not to use macrolides such as cyclosporine or tacrolimus for the induction of immunosuppression in these patients is further supported by the recent suggestion that the nephrotoxic effect of these drugs is augmented by coexisting ischemic injury.<sup>28</sup> In contrast, antithymocyte globulin contains antibodies to many proinflammatory molecules and may therefore contribute to the attenuation of ischemia–reperfusion injury<sup>29</sup> — a property that might be particularly important in the transplantation of organs from donors without a heartbeat.

The type of donor — either controlled or uncontrolled, as defined by the Maastricht protocol<sup>14</sup> — has been reported to be a crucial variable affecting the survival of grafts from donors without a heartbeat.<sup>1</sup> However, this variable did not influence the outcome of kidney transplantation from donors without a heartbeat in our study. The duration of warm ischemia in our cohort was less than 60 minutes, indicating that uncontrolled donors without a heartbeat who have a short warm-ischemia time can be a useful source of grafts. The cause of the donor’s death and the donor’s and recipient’s ages also had no significant influence on long-term graft survival in our study, in contrast to previous studies.<sup>12</sup> Previous recommendations for

limiting the use of organs from donors without a heartbeat should be reconsidered.

In situ cooling of the kidneys by intraaortic infusion of cold preservation solution, as performed by many investigators,<sup>8,10</sup> was not included in our protocol of organ harvesting. In situ cooling is often started before the consent of the potential donor's family has been obtained. This practice has triggered serious ethical debate,<sup>20</sup> rendering the use of organs from donors without a heartbeat unpopular and often unacceptable. Our study shows that excellent results can be obtained without the use of this questionable technique. We also show that a waiting time of 10 minutes after cardiopulmonary arrest, as proposed in the Maastricht protocol,<sup>14</sup> does not appear to influence the long-term survival of kidneys from donors without a heartbeat. If these points are considered, ethical concerns regarding the use of grafts from donors without a heartbeat may diminish, and our results may provide a new basis for the reevaluation of this source of organs by transplantation centers and by legislative bodies that have thus far proscribed the use of organs from donors without a heartbeat.

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