

Extension of the Organ Pool in Kidney Transplantation: First Year Experience of the Israel Transplant Center

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Abstract

Background: Over a 12 month period, the Israel Transplant Center doubled the number of donors by assigning a nurse coordinator to each of 22 hospitals around the country and by using kidneys from elderly donors.

Objective: To evaluate the impact of our "marginal donors" policy on the results immediately following transplantation.

Methods: Between October 1997 and September 1998, 140 cadaveric kidney transplantations from 72 donors were performed in Israel. We defined two groups of recipients: patients with immediate graft function and patients with either delayed graft function requiring >1 week of dialysis post-transplant or with primary graft non-function. We compared the following parameters between groups: donor and recipient age and gender, cause of donor's death, length of stay in the intensive care unit, vasopressor dosage and creatinine levels before harvesting, cold ischemic time, and the number of recipient grafts.

Results: There were 102 recipients (72.8%) with immediate graft function and 38 with either PNF (n=13, 9.3%) or DGF (n=25, 17.9%). On regression analysis, donor age >50 year and retransplantation were significant risk factors for PNF or DGF (odds ratio 4.4 and 2.8, respectively). Of the 56 kidneys from donors >50 years old, 21 (37.5%) developed either PNF (n=9) or DGF (n=12).

Conclusions: We conclude that kidneys from donors over age 50 are at increased risk for graft non-function or delayed function. Better assessment of functional capacity of kidneys from "aged" donors may help to choose appropriate donors from that pool.

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With the increasing gap between the lists of people awaiting transplantation and the number of those who receive transplants, there is a trend toward extending the age limits and other criteria for organ donation [1,2]. Such policies, however, may compromise results after transplantation. Loss of functional nephron mass due to aging may explain the worse outcome of kidney grafts from elderly donors. In addition, diseases that are highly prevalent at this age group (atherosclerosis, hypertension and diabetes) also contribute to glomerulosclerosis and decreased renal blood flow [3]. The UNOS registry large database [4] and most single centers [5-7] have reported poorer outcomes in recipients of kidneys from older donors than from younger donors. Nevertheless, several centers have documented good results with the use of kidneys from elderly donors [2,8,9].

In Israel, a country with a population of 5.5 million, the donation rate in 1996 was 5 donors/10⁶ per year. This low rate, paralleled by an increase in the number of patients on dialysis, led the Israel Transplant Center to adopt the "Spanish Model" for organ donation [10]. Following this model, we assigned a nurse coordinator to each of the 22 hospitals around the country and increased our use of kidneys from elderly donors. This study summarizes the first year national experience with kidney transplantation after implementation of our new policy of extending the age limit for donors. We also evaluate the impact of that action on results immediately after transplant.

Patients and Methods

Between October 1997 and September 1998, 140 kidney transplants from 72 donors were performed, including 2 from non-heart-beating donors and 4 from donors of a single kidney. Mean donor age was 38.8 years (range 3-75); 25 were females and 47 were males [Table 1]. The causes of brain death among donors included head injury (n=32), stroke or intracranial bleed (n=34), and brain

PNF = primary graft non-function
DGF = delayed graft function

Table 1. Donor and recipient characteristics

Donors		Recipients	
Age (yr)	38.8 (3–75)	Age (yr)	40.8 (1–72)
Sex	25 F, 47 M	Sex	77 F, 63 M
Cause of death		Graft No.	
Trauma	32	1st	113
CVA	34	2nd	22
Other	6	3rd	4
		4th	1
ICU stay (days)	3 (1–28)		
Creatinine (mg/dl)	0.97 (0.6–1.9)		
Cold ischemia (h)	19.75 (10–45)		

anoxia (n=6). The mean creatinine level immediately before harvesting was 0.97 mg/dl (0.6–1.9 mg/dl). Mean cold ischemia time was 19.75 hours. Recipients' mean age was 40.8 years (range 1–72); 77 were females and 63 were males. In 113 cases, patients were undergoing a primary transplant; another 22 were recipients of a second graft, 4 were recipients of a third graft, and one patient received a fourth graft.

The allocation of kidneys was based on a national computerized scoring system that included the following variables: recipient and donor age, waiting time on the list, HLA match, panel reactive antibodies score, and the number of grafts. Kidneys from elderly donors (above age 60) were preferably given to elderly recipients, and kidneys from young donors (<18 years old) were offered first to children. Data were collected prospectively on all donors and recipients and stored in the Israel Transplant Center database. This study specifically analyzed immediate graft function; therefore we used the recipient's first 3 months follow-up data.

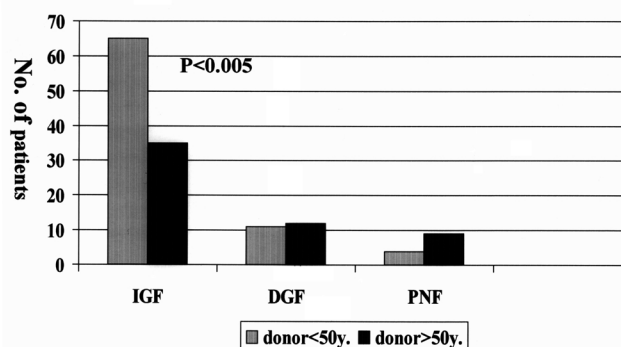
We defined two groups of recipients: patients with immediate graft function, and those with delayed graft function requiring more than a week of dialysis or with primary non-function. The two groups were compared for donor and recipient age and gender, cause of death of the donor, length of stay in the intensive care unit, maximal vasopressor dosage and creatinine level before harvesting, cold ischemia time, and recipient's number of grafts.

In addition, we compared immediate graft function between patients aged ≥ 50 and those <50 and analyzed the outcome of all pairs of kidneys in order to specifically detect donor risk factor for graft dysfunction. Univariate analysis was performed using Chi-square analysis and Student's *t*-test, and variables with a $P < 0.3$ were then entered into a stepwise logistic regression analysis.

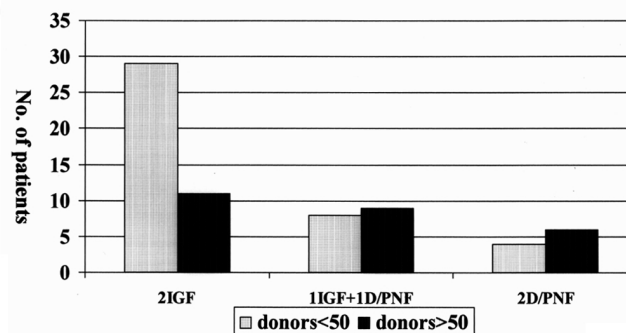
Results

There were 102 (72.8%) recipients with immediate graft function and 38 with either PNF (n=13, 9.3%) or DGF (n=25, 17.9%). Two of the four recipients of kidneys from non-heart-beating donors developed DGF. On univariate analysis, significant risk factors for PNF or DGF were recipient's age ($P < 0.01$), donor's age ($P < 0.001$), vasopressor dose ($P < 0.01$), and retransplantation ($P < 0.01$). On regression analysis, donor's age ≥ 50 (odds ratio 4.4)

Graft function by donor age

**Figure 1.** Graft function by age.

Analysis by pairs of kidneys

**Figure 2.** Analysis by pairs of kidneys.

and retransplantation (odds ratio 2.8) were significant risk factors.

When the four kidneys from non-heart-beating donors were excluded, 21 of the 56 recipients of kidneys from donors ≥ 50 years (37.5%) developed either PNF (n=9) or DGF (n=12). In contrast, 15 of 80 recipients of kidneys from donors aged <50 (18.7%) had DGF (n=11) or PNF (n=4) ($P < 0.01$) [Figure 1]. Of 26 pairs of kidneys from donors ≥ 50 years, 6 pairs (23%) developed PNF or DGF versus only 4 of 41 pairs (9.7%) of kidneys from donors <50 years ($P < 0.05$) [Figure 2]. Fourteen of 18 kidneys from donors >60 years old were transplanted into patients of the same age group. Nine of these 14 kidneys (64%) developed PNF (n=4) or DGF (n=5).

Patient and graft 3 month survival rates were 96.5% and 86.4%, respectively. The rate of graft loss due to PNF was 16% among patients who received kidneys from donors aged ≥ 50 , versus 5% among those with kidneys from donors <50 years old.

Discussion

The rate of brain death from cerebrovascular accident is relatively high among patients older than 50 years compared to the younger age group, and in recent years a larger proportion of donors has come from this age popula-

tion. In Spain, the use of organs from elderly donors has led to a significant increase in the number of transplants; the proportion of donor brain deaths due to stroke reached 60% in 1996 [11]. In addition, in their recent experience 50% of all donors were older than 50 [11]. A similar trend was seen in our series, with intracerebral bleeding or infarction accounting for 47% of brain deaths among donors.

Such expansion of the donor pool, however, does have a price. According to the UNOS registry data, increasing donor age is associated with a higher incidence of first day anuria, dialysis requirement, and discharge serum creatinine [4]. The worst 5 year graft survival rate (39%) in this report was noted in zero HLA-A, B, DR matched kidneys from elderly donors (>60 years). Our study, as well as other single-center studies, also found a similar poor outcome with kidneys from elderly donors compared to younger donors [5–7]. No less important is that a large proportion of kidneys from that donor pool has a delayed graft function, which is a known risk factor for a later graft dysfunction or loss [12]. Lewis et al. [7] reported a 45% rate of delayed function when using kidneys from donors aged over 55. We too noted a relatively high incidence of primary non-function (16%) and delayed graft function (21%) among recipients of “aged” kidneys, which might have been worsened by our policy to transplant these kidneys into age-matched recipients. Moreover, “aged” kidneys transplanted into young recipients implied sub-optimal function and inferior long-term graft survival (56% in 5 years) [13]. Interestingly, the difference in results between cadaveric transplants and those from living relatives is much more marked when using elderly donors. In fact, some authors reported comparable long-term graft survivals with living related kidneys from young and from old donors [8,14,15]. This observation implicates the role of other mechanisms in graft injury, such as changes that occur during warm ischemia and cold preservation, in addition to the anatomic and functional changes of aging. With elderly kidney donors, therefore, it is particularly crucial to prevent significant hypotension and to shorten cold ischemia time.

Despite the poorer outcome with kidneys from elderly donors, acceptable long-term graft function and survival may be achieved, particularly in recipients of grafts with immediate function [16]. A careful selection of appropriate candidates from that donor pool, by excluding donors with significant proteinuria (>0.5 g/24 hour), calculated creatinine clearance of less than 60 ml/min, or abnormal ultrasonographic findings, achieved excellent results [17].

In conclusion, our study, which summarizes initial experience of the national transplant center’s new program, shows that extension of the age limit permits a significant increase in the number of transplants. Unselective use of kidneys from elderly donors, however, is associated with increased risk for delayed and primary graft non-function after cadaveric kidney transplantation. Therefore, we

suggest that when using “marginal” kidneys, it is essential to minimize additional risks for graft dysfunction by shortening cold ischemia time and selecting stable, not necessarily elderly recipients for a first graft. A more careful functional assessment of kidneys from “aged” donors by measuring protein excretion and calculating creatinine clearance may help to select appropriate donors from this age group.

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