Crucial Role of Extended Criteria Donors in Deceased Donor Single Kidney Transplantation to Face Chronic Shortage in the Heart of the Mediterranean Basin: A Single-Center Experience

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ABSTRACT

Background. The gap between organ availability and patients on the waiting list for deceased donor kidney transplants has resulted in the wide use of extended criteria donors (ECDs). We aimed to compare the surgical outcomes of single kidney transplantation (KT) performed at our institute with standard criteria donor (SCD) or ECD grafts, according to the Organ Procurement and Transplantation Network definition. Patients and methods. Our retrospective analysis studied 115 adult recipients of KT from January 2016 to July 2018, with kidney grafts procured from adult donors after brain or circulatory death, performed at our institute. Among the 2 recipients' groups, we compared the incidence of early graft loss, delayed graft function, hospitalization, and surgical complications. We compared the evaluation of time to early graft loss with Kaplan-Meier estimators and curves; the hypothesis of no difference in time to graft loss between the 2 groups was tested using the log-rank statistics.

Results. Of the 103 deceased donor kidney transplants during the study period, 129 grafts were used after the regional network sharing allocation. More frequently, ECDs had a greater body mass index than SCDs (25.2 ± 3.9 vs 27.7 ± 5.0, $P = .005$) and type II diabetes mellitus (0% vs 18%, $P = .002$). KT recipients who received an ECD graft (73, 63.5%) were older (59.8 ± 9.8 vs 45.2 ± 15.4, $P < .001$) and presented a higher rate of delayed graft function (56% vs 24%, $P = .001$). Post-transplant graft loss did not differ among the 2 groups.

Conclusion. Based on clinical experience in a single transplant center, ECD use for KTs is crucial in facing the organ shortage, without impairing post-deceased donor kidney transplant outcomes.

KIDNEY transplantation (KT) is the gold standard treatment for end-stage kidney disease, but limited organ availability requires an optimization of extended criteria donor (ECD) graft allocation and a precise and rigorous analysis of postoperative clinical outcomes [1,2]. We aimed to compare the results of transplants performed using organs procured from standard criteria donors (SCDs, Group A) and those from ECDs (Group B) to identify incidence of early graft loss, delayed graft function (DGF), length of hospital stay, and early clinical complications.

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PATIENTS AND METHODS

This retrospective analysis studied 115 adult recipients of KT performed at IRCCS ISMETT from January 2016 to July 2018, with kidney grafts procured from adult deceased brain donors (DBDs) and deceased after circulatory death (DCD) donors. We excluded patients who underwent dual KT and/or combined solid organ transplantation, a recipient who underwent KT with a graft procured from a DBD affected with thrombotic microangiopathy, and recipients of a living donor transplant. Deceased donor kidney grafts were classified as ECDs, according to the Organ Procurement and Transplantation Network definition, if they met either of the following conditions: donor age equal to or more than 60 years or donor age 50 to 59 years, with at least 2 of the following criteria:

serum creatinine more than 1.5 mg/dL, death due to cerebrovascular accident, or history of hypertension. Donor and recipient characteristics were compared between the 2 recipient groups. Kidney with prolonged ischemia time (> 20 hours) as a result of extraregional donors, while awaiting cross-match results and recipient preoperative dialysis, and DCD kidney were preserved at 4°C with hypothermic machine perfusion (HMP) (Kidney Assist, Organ Assist, Groningen, The Netherlands), with a fixed systolic perfusion pressure of 25 mm Hg. Duration of HMP and perfusion parameters such as flow, renal resistance, and pressure were recorded.

The primary endpoints of this study were the incidence of early graft loss at 6 months, after KT, DGF, overall and intensive care
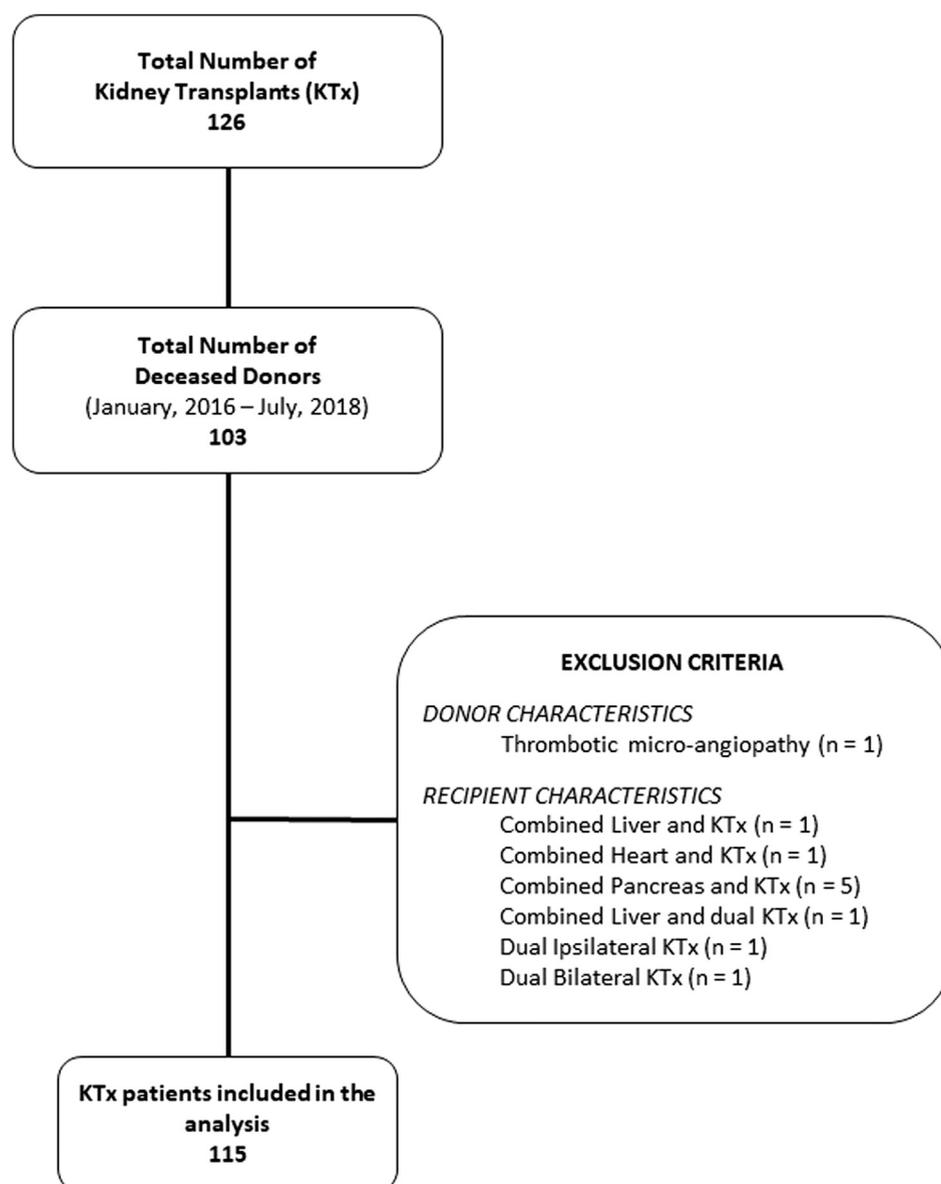

Fig 1. Strengthening Reporting of Observational Studies in Epidemiology (STROBE) flow diagram of cases included in, and excluded from, the study.

Table 1. List of the Distribution of the Donor and Recipient Characteristics Between the 2 Groups of Patients According to the ECD Graft Used

	Group A	Group B	P
N	42	73	
Donor characteristics			
Hepatitis C virus infection	2 (5)	4 (5)	1.000
Donation after cardiac death donors	0 (0)	3 (4)	.298
Sex, male	26 (62)	41 (56)	.563
Age (years), mean ± std. dev.	36.4 ± 13.9	65.2 ± 7.7	< .001
Arterial hypertension	2 (5)	51 (70)	< .001
Body mass index (kg/m^2), mean ± std. dev.	25.2 ± 3.9	27.7 ± 5.0	.005
Type II diabetes mellitus, n (%)	0 (0)	13 (18)	.002
Creatinine (mg/dL), mean ± std. dev.	0.9 ± 0.8	1.2 ± 0.7	.040
Causes of death			.002
Cerebrovascular, n (%)	21 (50)	59 (81)	
Trauma, n (%)	11 (26)	4 (5)	
Hypoxia, n (%)	8 (19)	8 (11)	
Other, n (%)	2 (5)	2 (3)	
Infectious risk			.220
Bacteremia, n (%)	2 (5)	3 (4)	
HBcAb+, n (%)	1 (2)	8 (11)	
HBsAg+, n (%)	0 (0)	1 (1)	
Hepatitis C virus infection, n (%)	1 (2)	0 (0)	
Hepatitis C virus infection and HBcAb+, n (%)	0 (0)	3 (4)	
Oncologic risk, n (%)	2 (5)	5 (7)	1.000
Surgical Procedures	2 (5)	2 (3)	.622
Machine perfusion reconditioning (%)			
Cold ischemia time (hours), mean ± std. dev.	16 ± 8	19 ± 7	.074
Warm ischemia time (min), mean ± std. dev.	41 ± 20	35 ± 14	.109
Length of Surgery (min), mean ± std. dev.	263.3 ± 69.4	274.9 ± 60.1	.351
Recipient Characteristics			
Sex, male	32 (76)	49 (67)	.397
Age (years), mean ± std. dev.	45.2 ± 15.4	59.8 ± 9.8	< .001
Body mass index (kg/m^2), mean ± std. dev.	23.8 ± 4.2	25.4 ± 3.6	.032
Previous kidney transplantation, n (%)	2 (5)	8 (11)	.322
Postoperative Outcomes			
Length of stay (days), mean [min., max.]	8.0 [7.0, 12.2]	11.0 [8.0, 19.0]	.017
Length of stay > 40 days, n (%)	2 (5)	2 (3)	.622
ICU length of stay, days, median [IQR]			.082
1 day	6 (14)	11 (15)	
2 or more days	8 (19)	4 (5)	
Hospital readmission within 30 days, n (%)	11 (26)	18 (25)	1.000
Operating room readmission, n (%)	6 (14)	12 (16)	1.000
Delayed graft function, n (%)	10 (24)	41 (56)	.001
Acute rejection, n (%)	2 (5)	9 (12)	.323
Graft loss at 6 months, n (%)	2 (5)	6 (8)	.487
Urinary leakage, n (%)	1 (2)	3 (4)	1.000
Urinary stenosis, n (%)	0 (0)	3 (4)	.298

ECD, extended criteria donor; ICU, intensive care unit; IQR, interquartile range.

units (ICUs) length of stay, operating room readmission, hospital readmission (within 30 days), biopsy-proven acute cellular, humoral and vascular rejection episodes, and postoperative complications.

Statistical Analysis

Data are expressed as mean and standard deviation or as median and interquartile range when not approximately normal. Differences between groups were tested using the Student t test or the Kruskal-Wallis test, as appropriate. Time to graft loss was evaluated by means of Kaplan-Meier estimators and curves; the hypothesis of no difference in time to graft loss between the 2 groups was tested using log-rank statistics. All analyses and graphics were done in the R statistical computing environment, version 3.5.1 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 126 deceased donor kidney transplants were performed at our institute in the study period. We excluded patients who underwent dual KT and/or combined solid organ transplantation (10, 7.9%) and a recipient who

underwent KT with a graft procured from a DBD affected with thrombotic microangiopathy, resulting in a patient cohort of 115 (Fig 1). In 10 cases, patients had already received a kidney transplant, without a statistically significant discrepancy between Group A and B (Table 1).

ECDs had a greater body mass index than SCDs (25.2 ± 3.9 vs 27.7 ± 5.0, $P = .005$) and more frequently had a history of type II diabetes mellitus (0% vs 18%, $P = .002$).

In KT recipients who received an SCD graft (Group A: 42, 36.5%) the length of hospital stay was lower ($P = .017$). KT recipients who received an ECD graft (Group B: 73, 63.5%) were older (59.8 ± 9.8 vs 45.2 ± 15.4, $P < .001$) and experienced a higher incidence of DGF (56% vs 24%, $P = .001$). Two DCD kidneys were type III and 1 type II according to the Maastricht classification. Two DCD kidneys were reconditioned with HMP after procurement, and during transport until the transplant, 1 DCD and 4 DBD kidneys were placed in HMP upon arrival at our institute. Mean perfusion time was 15 hours; mean renal resistance was 0.22 ru. No differences were found in terms of machine perfusion reconditioning, cold and warm ischemia times, and length of surgical procedures during KT.

Recipients in the ECD group were older (59.8 ± 9.8 vs 45.2 ± 15.4, $P < .001$) and presented a higher rate of DGF (56% vs 24%, $P = .001$). The rate of acute rejection episodes (5% vs 12%, $P = .323$), urinary leakage (2% vs 4%, $P = 1$), and stenosis (0% vs 4%, $P = .298$) did not differ among the 2 groups. Furthermore, no differences were detected in terms of hospital length of stay > 40 days, ICU length of stay, operating room readmission (14% vs 16%), and hospital readmission within 30 days (26% vs 25%). Post-transplant early graft loss was similar in the 2 groups, $P = .727$ (Fig 2).

DISCUSSION

In recent years, the demand for organs for KT has progressively increased, widening the already existing imbalance between supply and demand. The number of KTs performed has remained constant in these years. The average waiting time in Italy in 2017 was 2.1 years for transplant and 3.2 years for the patients still on the list. Since the average waiting time is long, and considering the patients have end-stage kidney disease and in almost all cases undergo dialysis, every year there are a certain number of patients who die while on the waiting list (1.7% in 2017) or drop off the list for another reason (2.5% in 2017). These data explain why in Italy, and especially in regions such as Sicily, there is a serious imbalance between those who need a transplant and the number of organs available.

In Sicily, the rate of deceased donation is the lower (8.4 donors per million per year) than in other Italian regions (21 donors per million per year). In order to optimize resources, nonaccepted kidneys in the region of origin (surplus) are proposed to other regions by the National Transplant Center. In 51% of cases, these surpluses are ECD and are allocated by transplant centers, other than the regional referral centers, using a stripe pattern with regional macroarea prioritization. In addition, in 2015, the National Transplant Center established a national program through the sharing of protocols and procedures that regulate DCD programs and the policies of perfusion machine system applications with the precise aim of increasing the number of donors available and, as a result, the number of organ transplants [3,4]. From January 2016 to April 2018, data on donation, allocation, and transplantation, collected by the National Transplant Center and crossed with those reported in the national dataset as a dedicated Web function, have
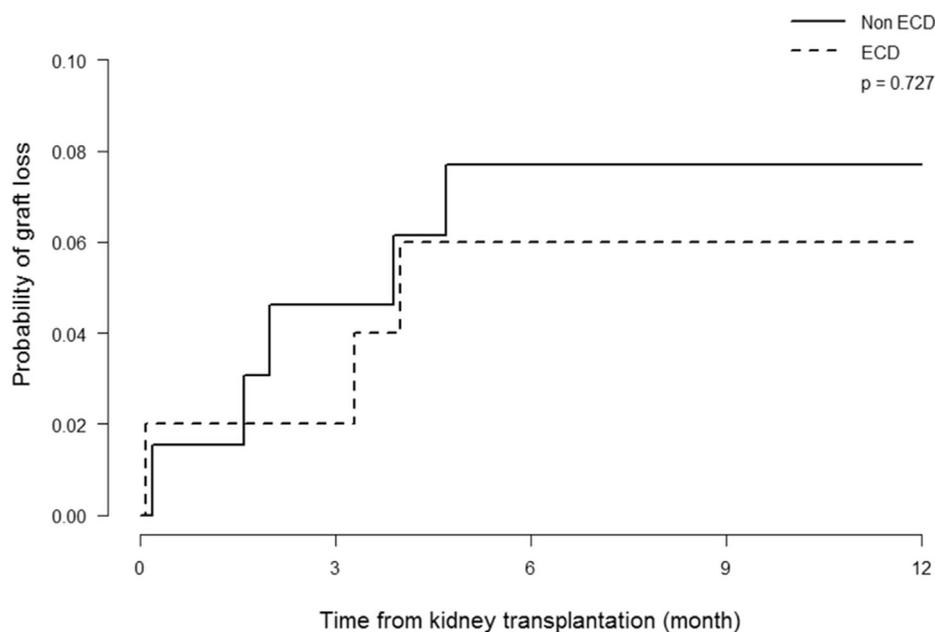

Fig 2. Time to graft loss was evaluated by means of Kaplan-Meier estimators and curves.

revealed a significant increase in transplant activity and in the number of ICUs and transplant centers involved [5].

Therefore, it is necessary for organ donation increasing by promotion of the practice of living donor transplantation, especially in countries like Italy where this still is of marginal importance (less than 10% of the total in the decade 2000-2010) and considering as usable donors those without optimal characteristics [6]. Ojo et al showed that patients receiving an ECD transplant lived on average 5 years longer than recipients with the same characteristics but who remained on the waiting list and who continued dialysis treatment. This study therefore concluded that it is convenient to accept an organ from a marginal donor instead of continuing dialysis therapy [7,8].

At our institute, through what has been defined in the literature as a tailored approach, we have tried to make the best use of the kidneys procured from ECDs, also with the aim of responding to organ shortages, and have managed to obtain satisfactory results, with a significantly decreased likelihood of early graft loss, suggesting that this approach is a better model for allocating kidney grafts [9]. It is necessary to widen the analysis of the allocation system, as well as prospectively collect data to quantify the true impact of ECDs in the long-term follow-up setting.

CONCLUSION

Based on clinical experience in a single transplant center, ECDs for KT are crucial in facing the chronic organ shortage in a Mediterranean area with a very low rate of deceased donation, without impairing post-KT early outcomes.

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