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Kidney Transplants from Elderly Donors: The Experience of a Reference Center in Croatia

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Abstract

Objectives: **Our country Croatia is among the global leaders regarding deceased donation rates, yet we are facing organ shortage and concurrently a sharp decline in our acceptance rates for kidney offers. To reevaluate our organ acceptance policy, we retrospectively analyzed the factors that influenced the posttransplant outcomes of kidneys from elderly deceased donors at our center during a 20-year period and the changes to our organ acceptance criteria during Eurotransplant membership.**

Materials and Methods: **We studied all kidney transplants from donors ≥60 years old during the two 5-year episodes of Eurotransplant membership from 2007 to 2017 (period II and period III) and compared those data to data from the decade before Eurotransplant membership (period I, 1997-2007). Differences in acceptance rates and reasons for the decline of kidney offers between the two 5-year periods of Eurotransplant membership were analyzed.**

Results: **In period I, 14.1% of all kidney allografts were obtained from donors ≥60 years old; in period II and period III the rates were nearly 2-fold higher (27.0% and 25.7%, respectively; *P* = .007 and *P* = .008). During the first 5-year period of Eurotransplant membership (period II), we accepted significantly more grafts from marginal donors with a higher number of human leukocyte antigen mismatches compared with period I. Consequently, the 3-month survival rate of kidneys from donors ≥60 years old dropped from 91.1% to as low as 74.2% (*P* = .034). After application of more-stringent human leukocyte antigen matching, especially in human leukocyte antigen DR, and more-stringent donor acceptance criteria in period III, graft survival improved to 91.1%.**

Conclusions: **Our experience indicates that careful selection of kidneys from elderly deceased donors and allocation to human leukocyte antigen-matched recipients is important to improve transplant outcomes.**

Key words: *Graft survival, Histocompatibility, Kidney allograft*

Introduction

The development of a successful deceased donation program placed Croatia among the leading countries in the world for deceased organ donation and transplant rates, and yet transplant centers remain confronted with organ shortages.[1,2] High transplant rates had reduced the number of wait-listed candidates to only 29 candidates per million population in 2014; thereafter, the wait list increased and reached 59 candidates per million population in 2019.[3-5] Meanwhile, the acceptance rate of deceased donor kidney offers has declined at Croatian transplant centers due to poor quality of potential organs. To reevaluate our organ acceptance policy, we analyzed kidney transplants from elderly donors performed at our center, with special attention to posttransplant outcome and the reasons for the refusal of kidney offers during the two 5-year episodes of Eurotransplant (ET) membership (since August 2007). We hypothesized that the increased use of kidneys from marginal donors had a negative effect on posttransplant outcomes and induced constraints in our organ acceptance policy. We analyzed our data to identify factors that mainly influenced graft survival from marginal donors and to evaluate the possibility of extending our organ

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acceptance criteria. Such transplant centers' experiences may be helpful in the design of corrective measures to improve organ allocation strategies.

Materials and Methods

For this retrospective study, data on all kidney transplants at the Reference Center in Croatia were obtained from local and national databases as well as from the Collaborative Transplant Study database (www.ctstransplant.org) to which all transplant data from our center have been reported since 1985. The work of the CTS is approved by the ethics committee of the Medical Faculty of Heidelberg University (No. 083/2005) and the study was performed in accordance with the World Medical Association Declaration of Helsinki Ethical Principles. We compared the kidney transplants performed in patients ≥15 years old after our center obtained ET membership and during the decade before, with patient follow-up until August 2019.

From August 1997 to July 2017, there were 451 kidney transplants performed at our center; 92.2% (n = 416) were from brain-dead donors, and 7.8% (n = 35) were from living related donors. Ninety-five patients (21.1%) of this cohort received grafts from donors ≥60 years old. We divided them into 3 groups according to the period of kidney transplant: the decade before the ET membership (period I, August 1997 to July 2007) and the first and second 5-year periods of ET membership (period II, August 2007 to July 2012; and period III, August 2012 to July 2017). Period I is longer because of low annual transplant rates. Data for all consecutive transplants from deceased donors ≥60 years old were included in this study. Transplants from living donors were excluded from the analysis because we had not performed kidney transplants from living donors ≥60 years old in period II and period III; therefore, the overall number of analyzed patients who received kidneys from donors ≥60 years old was 87.

We used the database and patient records to compare outcomes from the 3 periods for recipients of grafts from donors ≥60 years old, including graft function within 24 hours, posttransplant need for dialysis, surgical complications, acute rejection (defined as at least 1 rejection treatment within 3 months after transplant), renal function at 6 months, loss of graft function, and death, by considering recipient presensitization status and the number of human leukocyte antigen (HLA) A, B, and DR mismatches between recipient and donor pairs. Additionally, we compared the first 5-year period of ET membership with the second 5-year period of membership with regard to the acceptance rates and reasons for refusal of kidney offers by our transplant team. For all 3 periods, we assigned organ quality on the basis of reported donor data by direct communication with the donor coordinator and/or by donor report and kidney report forms. On rare occasions, a pretransplant biopsy had been performed to evaluate the usability of the graft.

Survival rates were computed with the Kaplan-Meier method. For statistical analysis, we used the software package Statistica 13 (TIBCO Software Inc.). $P < .05$ was considered significant.

Results

Demographics of all kidney transplants from August 1997 and July 2017

Among a total of 451 kidney transplants performed from August 1997 to July 2017, 92.2% were from deceased donors. Ninety-five patients (21.1%) received kidneys from donors ≥60 years old, of which 87 (91.6%) were deceased and 8 (8.4%) were living relatives (7 parents, 1 sister). Demographic data on all 451 transplants stratified by the 3 analysis periods are shown in Table 1. From period I to period III, the median of donor age increased from 46 to 54 years and the median recipient age from 46 to 59 years. Compared with the decade before ET membership (period I), the number of kidney transplants increased by 35% during the two 5-year periods of ET membership (period II and period III). Between period I and II we observed a more than 2-fold rise of kidney transplants from deceased donors ≥60 years old (from 11.9% to as high as 27.2%; $P < .001$), whereas no further rise was observed in period III (26.1%; $P = .002$, vs period I).

Characteristics of kidney transplants from deceased donors 60 years old and older

The 87 consecutive kidney transplants from deceased donors ≥60 years old with a mean follow-up time of 6.9 years were analyzed in detail. Most of them were single-kidney transplants, except there were 2 double-kidney transplants in period II and 1 double-kidney transplant in period III. The changes in the demographic and baseline characteristics of recipients

Table 1. Demographic Data for 451 Kidney Transplants at Rijeka Transplant Center, Croatia, August 1997 to July 2017

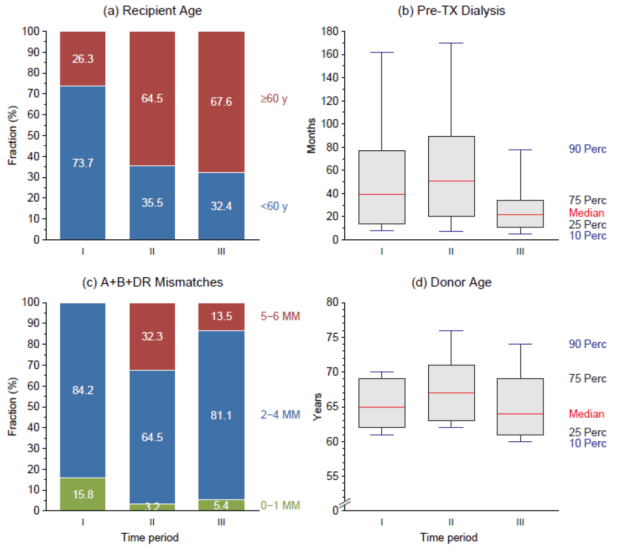
Characteristic	Period I (n = 192)	Period II (n = 115)	Period III (n = 144)	*P*		
				Period I vs II	Period I vs III	Period II vs III
Transplant				1	.84	.82
First transplant	178 (92.7%)	107 (93.0%)	132 (91.7%)			
Retransplant	14 (7.3%)	8 (7.0%)	12 (8.3%)			
Donor type				<.001*	<.001*	1
DD	160 (83.3%)	114 (99.1%)	142 (98.6%)			
LD	32 (16.7%)	1 (0.9%)	2 (1.4%)			
Recipient sex				.91	.018*	.028
Female	85 (44.3%)	52 (45.2%)	45 (31.2%)			
Male	107 (57.3%)	63 (54.8%)	99 (68.8%)			
Recipient age, median (range), y	46 (16-72)	56 (15-77)	59 (16-80)	<.001*	<.001*	.088
Recipient age group, No. (%)				<.001*	<.001*	.13
≥60 y	32 (16.7%)	45 (39.1%)	70 (48.6%)			
<60 y	160 (83.3%)	70 (60.9%)	74 (51.4%)			
Donor sex, No. (%)				.024*	.37	.21
Female	73 (38.0%)	59 (51.3%)	62 (43.1%)			
Male	119 (62.0%)	56 (48.7%)	82 (56.9%)			
Donor age, median (range), y	46 (6-70)	53 (4-79)	54 (0-76)	<.001*	<.001*	.82
DD age group, No. (%)				<.001*	.002*	.89
≥60 y	19 (11.9%)	31 (27.2%)	37 (26.1%)			
<60 y	141 (88.1%)	83 (72.8%)	105 (73.9%)			
DD age group whose recipients were <60 y old				<.001*	<.001*	1
Donor age ≥60 y, No. DD (%)	14 (73.7%)	11 (15.9%)	12 (16.7%)			
Donor age <60 y, No. DD (%)	5 (26.3%)	58 (84.1%)	60 (83.3%)			

Abbreviations: DD, deceased donor; LD, living donor

Period I is the decade before Eurotransplant membership (August 1997 to July 2007); period II is the first 5 years of Eurotransplant membership (August 2007 to July 2012); period III is the second 5-year period of membership (August 2012 to July 2017). *P* values were calculated with the Fisher exact test and the Mann-Whitney U test. *Significant difference.

of these kidneys during the 3 periods are shown in Table 2 and Figure 1. During the 3 periods, diabetes mellitus was observed to have been more frequent as the main cause of end-stage kidney disease (0%, 6.5%, and 13.5%, respectively, for periods I, II, and III) versus glomerulonephritis and interstitial nephritis/pyelonephritis (31.6%, 25.8%, and 13.5%; and 31.6%, 16.1%, 8.1%; respectively). The proportion of patients without specified cause of end-stage kidney disease increased (5.3%, 19.4%, and 35.1%, respectively), probably because of a higher incidence of hypertension/nephrosclerosis that usually was not confirmed with biopsy. Compared with the low rate of 26.3% in the decade before ET membership (period I), more kidneys from donors ≥60 years old were transplanted to patients ≥60 years old during the 2 ET membership periods (period II, 64.5%; period III, 67.6%; $P = .019$ and $P = .005$, respectively). The median recipient age increased from 52 years in period I to 63 years in period II and period III ($P = .010$ and $P = .002$, respectively) (Table 2, Figure 1). The median pretransplant dialysis time increased from 39 months (range, 4-192 months) in period I to 50 months (range, 4-228 months) in period II; however, this dropped to 21 months (range, 1-191 months) during period III ($P = .006$, vs period II) (Figure 1). The percentage of

Figure 1. Kidney Transplants from Deceased Donors 60 Years Old and Older at Rijeka Transplant Center, Croatia, August 1997 to July 2017



Abbreviations: HLA, human leukocyte antigen; MM, mismatch; TX, transplant

(a) A significantly higher proportion of recipients who were ≥60 years old underwent kidney transplant during Eurotransplant membership (period II and period III, August 2007 to July 2017) compared with period I (August 1997 to July 2007) ($P = .019$ and $P = .005$, respectively). **(b)** Compared with period II, kidney recipients had a significantly shorter median pretransplant dialysis time (21 months) in period III (August 2012 to July 2017) ($P = .006$). **(c)** The HLA-A+B+DR MM rate was higher in period II (August 2007 to 2012) than in period I ($P = .004$). **(d)** The highest values for median and absolute donor age were observed in period II (August 2007 to July 2012).

kidney recipients who were less-optimal candidates for transplant dramatically increased in period II and period III compared with period I (P = .022 and P = .019, respectively). Induction therapy was applied to 42.1% of kidney recipients from donors ≥60 years old in the period before ET membership (period I, antilymphocyte globulin) and to all recipients in the following two 5-year periods (period II and period III, 92.6% of recipients received anti-interleukin 2 receptor antagonists and 7.4% received antilymphocyte globulin). In the decade before ET membership (period I), the initial regimen included an antimetabolite in all patients (63% azathioprine, 37% mycophenolate), steroids in 95% of patients, and cyclosporine in 90% of patients. In period II, all recipients were treated with mycophenolate, corticosteroids, and tacrolimus, except for 1 patient who received cyclosporine. In the most recent period (period III), the initial regimen included mycophenolate in 91.9% of patients, steroids in 86.5%, tacrolimus in 94.6%, and mechanistic target of rapamycin inhibitors in 13.5%.

Kidney transplants from marginal donors became more frequent during the ET membership (period II and period III). The highest median and absolute age (67 and 79 years, respectively) and the highest rate of arterial hypertension, as well as death due to cerebrovascular accident, among donors ≥60 years old were registered in period II (54.8% and 77.4%, respectively), and the highest rate of diabetes mellitus was in period III (16.2%) (Table 2). We observed a strong increase in the rate of shipped kidneys, from 36.8% in period I to 54.8% in period II and 78.4% in period III (compared with period I; P = .003). The duration of median cold ischemia time remained similar during the 3 periods (15, 15, and 16 hours, respectively).

The proportion of transplants with a higher number of HLA mismatches increased significantly in period II, reaching a median of 4 mismatches (compared with period I; P = .004) (Figure 1). For HLA mismatches of separate loci, the HLA-DR mismatch rate was significantly higher in transplants during period II (compared with period I and III; P = .016 and P < .001, respectively) (Table 2). During all 3 periods, most of the recipients had a lymphocytotoxic panel reactivity of ≤5%, and no recipient had a lymphocytotoxic panel reactivity of ≥50% in the latest pretransplant serum (Table 2).

Table 2. Demographic, Baseline, and Immunological Characteristics of 87 Kidney Transplants from Deceased Donors 60 Years Old and Older at Rijeka Transplant Center, Croatia, August 1997 to July 2017

Characteristic	Period I (n = 19)	Period II (n = 31)	Period III (n = 37)	*P*		
				Period I vs II	Period I vs III	Period II vs III
Recipient sex, No. (%)				.26	.39	1
Female	10 (52.6%)	11 (35.5%)	14 (37.8%)			
Male	9 (47.4%)	20 (64.5%)	23 (62.2%)			
Recipient age, median (range), y	52 (34-72)	63 (45-77)	63 (40-79)	.010*	.002*	.68
Donor sex, No. (%)				.39	1	.47
Female	10 (52.6%)	12 (38.7%)	18 (48.6%)			
Male	9 (47.4%)	19 (61.3%)	19 (51.4%)			
Donor age, median (range), y	65 (60-70)	67 (60-79)	64 (60-76)	.096	.49	.034*
Donor comorbidity, No. (%)				.007*	.008*	.19
Hypertension	3 (15.8%)	17 (54.8%)	15 (40.5%)			
Diabetes mellitus	0	1 (3.2%)	6 (16.2%)			
HLA A, B, and DR MM, No. (%)				.004*	.14	.15
0-1 MM	3 (15.8%)	1 (3.2%)	2 (5.4%)			
2-4 MM	16 (84.2%)	20 (64.5%)	30 (81.1%)			
5-6 MM	0	10 (32.3%)	5 (13.5%)			
HLA-DR MM, No. (%)				.016*	.28	<.001*
0 MM	9 (47.4%)	5 (16.1%)	11 (29.7%)			
1 MM	9 (47.4%)	15 (48.4%)	25 (67.6%)			
2 MM	1 (5.2%)	11 (35.5%)	1 (2.7%)			
PRA, No. (%)				.83	.21	.39
0%	16 (84.2%)	27 (87.10%)	34 (91.9%)			
1% to 9%	1 (5.3%)	2 (6.5%)	3 (8.1%)			
10% to 49%	2 (10.5%)	2 (6.5%)	0			

Abbreviations: HLA, human leukocyte antigen; MM, mismatch; PRA, panel reactive lymphocytotoxic antibodies

Period I is the decade before Eurotransplant membership (August 1997 to July 2007); period II is the first 5 years of Eurotransplant membership (August 2007 to July 2012); period III is the second 5-year period of membership (August 2012 to July 2017). *P* values were calculated with the Fisher exact test and the Mann-Whitney U test. *Significant difference.

Outcome of kidney transplants from deceased donors 60 years old and older by human leukocyte antigen mismatch and transplant period

The outcomes of 87 patients who received grafts from deceased donors ≥60 years old during the 3 periods are shown in Table 3. The mortality rate at year 2 after transplant was similar for all 3 transplant periods: 10.5% (n = 2) in period I, 12.9% (n = 4) in period II, and 10.8% (n = 4) in period III. Cardiovascular disease or sudden death and sepsis were the most common causes of death. However, kidney transplants that had been performed during the first 5 years of ET membership (period II) had a strikingly higher incidence of surgical complications (67.8%) versus the other 2 periods (period I, 26.3%; period III, 40.5%; $P = .006$ and $P = .034$, respectively). In 58.1% of the patients, complications occurred either during the transplant procedure or within the first 3 months after transplant, and these were most often observed to be vascular (n = 6) and urinary complications (n = 6). There were 3 patients with early graft loss, all caused by vascular complications (2 in period II and 1 in period III). In addition to a higher incidence of surgical complications, the worst graft function and lowest graft survival at posttransplant month 3 (74.2% in period II vs. 91.1% in period I and period III; $P = .034$), especially in cases with a poor HLA-DR match, were also observed during period II. Kaplan-Meier graft survival is illustrated in Figure 2. The highest rate of patients who required blood transfusion during the early postoperative period was observed with 38.7% in the first period of ET membership (period II) compared with the rates of 21.1% and 32.4% in period I and period III, respectively ($P = .23$ and $P = .62$, respectively). In the decade before ET membership (period I), most of the kidneys had been procured from local donors; thereafter the rate of kidney shipment to our center significantly increased (36.8% in period I vs 78.4% in period III; $P = .003$) but the duration of cold ischemia time remained similar.

Compared with the decade before ET membership, despite a significantly higher rate of HLA mismatches and HLA-DR mismatches between donor and recipient pairs during the first 5 years of ET membership (period II) ($P = .004$ and $P = .016$, respectively) (Table 2), fewer patients received antirejection treatment within the first 3 months

Table 3. Outcomes of 87 Kidney Transplants from Deceased Donors 60 Years Old and Older at Rijeka Transplant Center, Croatia, August 1997 to July 2017

Characteristic	Period I (n = 19)	Period II (n = 31)	Period III (n = 37)	*P*		
				Period I vs II	Period I vs III	Period II vs III
Graft function within 24 h, No. (%)				1	.11	.073
Yes	8 (50.0%)	16 (51.6%)	27 (75.0%)			
No	8 (50.0%)	15 (48.4%)	9 (25.0%)			
No data	3	0	1			
Acute tubular necrosis, No. (%)				1	.28	.35
Yes	12 (80.0%)	23 (79.3%)	31 (91.2%)			
No	3 (20.0%)	6 (20.7%)	3 (8.8%)			
No data	4	2	3			
Posttransplant dialysis, No. (%)				1	.16	.054
Yes	6 (40.0%)	12 (42.9%)	7 (18.9%)			
No	9 (60.0%)	16 (57.1%)	30 (81.1%)			
No data	4	3	0			
Antirejection treatment within 3 mo, No. (%)				.033*	<.001*	.002*
Yes	7 (53.8%)	6 (19.4%)	2 (5.4%)			
No	6 (46.2%)	25 (80.6%)	35 (94.6%)			
No data	6	0	0			
Surgical complications, No. (%)				.006*	.35	.034*
None	14 (73.7%)	10 (32.3%)	22 (59.5%)			
Early	3 (15.8%)	18 (58.1%)	10 (27.0%)			
Late	2 (10.5%)	3 (9.7%)	5 (13.5%)			
Graft function at 6 mo as serum creatinine, No. (%)				.083	.20	.22
<130 µmol/L	11 (57.9%)	8 (25.8%)	14 (37.8%)			
130-259 µmol/L	6 (31.6%)	13 (41.9%)	18 (48.6%)			
260-400 µmol/L	1 (5.3%)	2 (6.5%)	0 (0.0%)			
Graft lost (including death)	1 (5.3%)	8 (25.8%)	5 (13.5%)			

Period I is the decade before Eurotransplant membership (August 1997 to July 2007); period II is the first 5 years of Eurotransplant membership (August 2007 to July 2012); period III is the second 5-year period of membership (August 2012 to July 2017). *P* values were calculated with the Fisher exact test. *Significant difference.

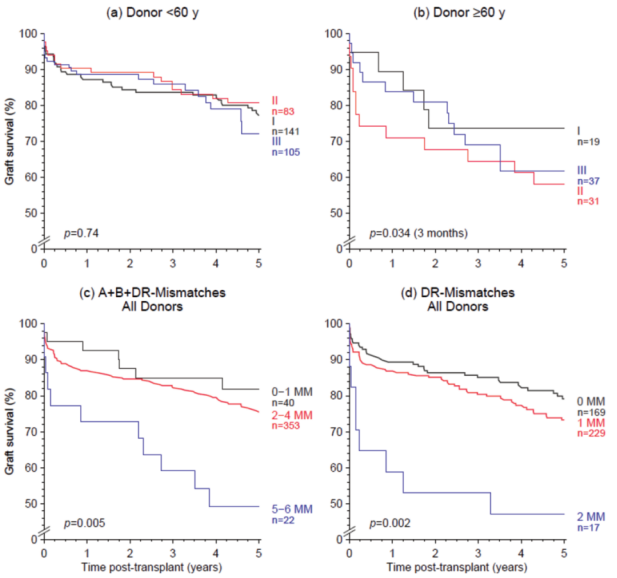
(P = .033) (Table 3). During ET membership, a more potent initial immunosuppressive protocol that included induction therapy had been applied to all recipients of kidneys from donors ≥60 years old. With improved HLA-matching during period III, the need for antirejection treatment within the first 3 months had decreased further, especially in patients without HLA-DR mismatch (compared with period II; P = .002). When all 451 kidney transplants from 1997 to 2017 were analyzed, 5 to 6 HLA-A+B+DR mismatches, as well as 2 HLA-DR mismatches, had a strong negative influence on graft survival (compared with 0 to 4 HLA-A+B+DR mismatches and 0 to 1 HLA-DR mismatches; P = .005 and P = .002, respectively) (Figure 2). During the first 5-year period of ET membership (period II), we observed the best graft survival in recipients of kidneys with no HLA-DR mismatches (91.2% at 5 years; P < .001, vs 1 to 2 HLA-DR mismatches).

Changes in organ acceptance criteria in period III and the associated consequences for kidney transplants from donors 60 years old and older

Compared with the first 5-year period of ET membership (period II), we observed that the criteria for donor acceptance and HLA matching were more stringent in the second 5-year period of ET membership (period III). Our center refused 39.4% (n = 74) of kidney offers in the first period of ET membership (period II). In period III, we accepted more kidneys for transplant; however, the rate of refusal was 57.7% (n = 198), which was 46.4% higher versus period II (P < .001), and the acceptance rate of kidneys from donors ≥60 years old decreased significantly from 37.3% to 23.9% (P = .024). The main reasons for refusal were poor donor or organ quality (37.8% in period II vs 58.1% in period III; P = .003), followed by recipient reasons (nonimmunological and immunological) and incompatible age/size match.

In our analyses of kidney transplants from donors ≥60 years old, compared with period I, we observed in period II an increase in the rate of patients with impaired graft function (serum creatinine ≥130 μmol/L) as well as graft loss at 6 months posttransplant, which, however, showed a trend of improvement in period III (P = .083) (Table 3). Furthermore, in period III, there was a trend toward a higher graft function rate within the first 24 hours after transplant and significantly fewer surgical complications versus period II (P = .034). Kaplan-Meier analysis confirmed the improvement of graft survival from donors ≥60 years old in period III, especially during the year 1 after transplant (Figure 2). Insufficient follow-up of more recent transplants in period III (August 2012 to July 2017) is the most likely reason that we did not observe long-term improvement.

Figure 2. Graft Survival of Deceased Donor Kidney Transplants



Abbreviations: HLA, human leukocyte antigen; MM, mismatch

Graft survival by **(a, b)** donor age group, **(c)** HLA-A+B+DR, and **(d)** HLA-DR MM for deceased donor kidney transplants performed during the 3 transplant periods from August 1997 to July 2017 at Rijeka Transplant Center, Croatia. **(b)** The extended acceptance criteria applied for deceased donor organs, recipients, and HLA mismatch were observed to have a negative influence on graft survival, and the negative trend was especially pronounced in recipients of grafts from donors ≥60 years old during the first posttransplant year of period II (August 2007 to July 2012). Graft survival was worse for transplants with **(c)** 5-6 HLA-A+B+DR MM and **(d)** 2 HLA-DR MM. Global log-rank P values are shown.

Discussion

Our present study compared kidney transplants from donors ≥60 years old at our center during the decade before and after obtaining ET membership, with a goal to discover the most important factors for successful posttransplant outcomes and thereby to increase the number of acceptable kidneys for transplant. Our intention was to improve patient survival by the development of a successful deceased donation program in Croatia and a broader range of acceptance criteria for donor organs and kidney recipients. Compared with the pre-ET decade (period I), we performed 35% more kidney transplants during the two 5-year periods of ET membership (2007-2017), more frequently from deceased donors ≥60 years old,

but none from living donors ≥60 years old. We noticed worse graft survival during the first period of ET membership (period II), and kidney transplants from elderly donors have been associated with less successful posttransplant outcomes.[6-12] This led to a 46.4% lower acceptance of organs during the subsequent second 5-year period of ET membership (period III). Many of these refused organs were allocated and transplanted to recipients at other ET centers with less-restrictive criteria for kidneys from older or marginal donors.[6,7,13-15] Living related kidney transplants, including transplants from elderly donors, have shown better outcomes compared with deceased donor transplants.[4,16,17] In our study cohort, patient and graft survival rates after kidney transplant from living related donors ≥60 years old (n = 8 in period I) were 100% at 1 year, and all recipients, except for 1 patient who died with a functional graft and 2 patients for whom follow-up was incomplete, had well-functioning grafts during the follow-up period of 13 to19 years.

Especially in Europe, there has been an increase in the use of kidneys from donors ≥60 years old.[5] At our center, during the 20-year period of study, 21.1% of kidney transplants were from donors ≥60 years old, with a more than 2-fold increase between the pre-ET decade and the first 5-year period of ET membership. An even higher proportion of transplanted kidneys from donors ≥60 years old was reported to the Collaborative Transplant Study database by European centers, with an increase from 21% in the period 2000-2001 to 42% in the period 2016-2017.[12] In our study, the median donor age was 54 years in the second 5-year period of ET membership (period III) with a parallel increase of the median recipient age to 59 years, and the proportion of renal transplant recipients ≥60 years old reaching 48.6%. In ET countries, the median age of deceased kidney donors rose from 46 years in 2000 to 55 years in 2018, and the median age reached 59 years in Croatia.[5]

Dialysis vintage has also been associated with worse posttransplant outcomes, although data in the literature are inconsistent.[18] In our study, patients who underwent kidney transplant during the first 5-year period of ET membership (period II, 2007-2012) had a very long median pretransplant dialysis time of 50 months, with dialysis vintage up to 19 years. According to the ET point score system for organ allocation, these patients with more comorbidities received high scores during organ allocation based on the long dialysis vintage (wait time) that outweighed the scores for HLA compatibility. In the whole collective of 451 kidney transplants from the period 1997-2017, 5 to 6 HLA-A+B+DR mismatches and 2 HLA-DR mismatches had a strong negative influence on graft survival. The importance of HLA-matching in kidney transplants from elderly donors has been emphasized in previous studies.[11,19,20]

There were no significant differences in donor sex, recipient HLA sensitization, and retransplant rate. The rate of kidney shipment to our center increased from 36.8% during period I to 54.8% and 78.4% during period II and period III, respectively. We had no highly sensitized recipient with PRA ≥50%, and cold ischemia duration remained similar for all the periods of study, which enabled us to differentiate the other factors that negatively influenced graft survival rates.[7,21] The risk of graft failure has been shown to increase with a longer cold ischemia time, especially in kidney transplants from older donors and for donation after circulatory death; nevertheless, successful outcomes of kidney transplants with prolonged cold ischemia times have been reported.[22-24] In the first 5-year period of ET membership (period II), we observed a high incidence of surgical complications in as many as 67.8% of the patients, which occurred in 58.1% of the patients within the first 3 months after transplant and were linked to an increased need for blood transfusion. The implant of organs from elderly deceased donors is more difficult because of organ and recipient characteristics, and surgical complications represent important causes of morbidity, inferior graft survival, and mortality.[10,25,26]

Altogether, graft survival was negatively influenced by donor and recipient characteristics as well as by poorly HLA-matched kidney transplants during the first 5-year period of ET membership. The 3-month survival rate of kidneys from deceased donors ≥60 years old dropped from 91.1% during period I to as low as 74.2% during period II; however, after better organ selection and allocation, we observed that the kidney survival rate improved to 91.1% during period III. Immunological factors may combine with poor quality factors of organs and thereby exacerbate inferior outcomes.[7,21] We applied more-stringent criteria during period III and accepted better HLA-matched organs from selected older donors. This differs from the ET Senior Program, which disregards HLA matching in an

effort to shorten the cold ischemic period.[27,28] The higher stringency of our policy resulted in a 46.4% greater rate of refusal in period III compared with period II, primarily for kidneys of less-optimal quality from donors ≥60 years old with poor HLA match, but with significantly better posttransplant outcome, including a lower incidence of rejection episodes within the first 3 months after transplant, a lower rate of surgical complications, better graft function, and less need for posttransplant dialysis, whereas the total number of transplants increased. Early posttransplant graft function and less need for posttransplant dialysis have been associated with better graft survival.[7,29-32]

Our low annual transplant rate and short follow-up time for transplant patients during the last period are limitations of our study, and caution is warranted. However, these data were from a transplant center with long-term experience (the first transplant center in Croatia), and this center remains the reference center for kidney transplant in Croatia. The comparison of data before and after obtaining ET membership allowed the evaluation of factors with greatest influence on kidney graft survival, which would not have been possible otherwise. We used predefined and standardized protocols to analyze the data from all consecutive kidney transplants from donors ≥60 years old and to treat and monitor all recipients. Careful follow-up of patients and access to robust data records at our single transplant center were the major strengths. This is the first study of recipients of kidneys from donors ≥60 years old in Croatia that analyzed the consequences of changes in organ acceptance criteria after accession to ET. The limitations of our study were its retrospective design and the single-center venue, and substantial variations have been reported for the transplant outcomes from older donors in different regions.[6,33,34]

Unfortunately, the information on the outcome of kidney transplants at other transplant centers after the refusal of these organs by our center is incomplete, and yet feedback remains a critical element to facilitate performance improvements. Kidney transplant data submission to international registries, such as the Collaborative Transplant Study database, the ET, and the future European Registry (https://edith.project.eu), remains important because the availability of transplant outcome data for the early and long-term periods allows monitoring of adverse developments and refinement of donor and recipient selection criteria. Kidneys from well-selected donors ≥60 years old are a valuable addition to the pool of organs, which may lead to an increase in transplant rates, a reduction of the wait list, and improvement in rates of graft and patient survival. Selected, less-optimal organs should be preferentially allocated to the best HLA-matched recipient within local range, to facilitate (1) robust estimates of organ quality, (2) ease of access to comprehensive data on donor characteristics and treatment history, and (3) reduction in the duration of cold ischemic periods. Better HLA matching, eg, for HLA-DR, which significantly reduces the risks of excessive immunosuppression, immunological rejection, comorbidity, and death, appears to be an effective method to improve posttransplant outcomes, especially in recipients of kidneys from donors ≥60 years old.

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