Relationship Between Individual Components of the Extended-Criteria Donor Definition and the First Post-transplant Kidney Graft Resistance Index, Measured by Doppler Sonography

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ABSTRACT

Background. Despite an increasing utilization of kidneys procured from expanded-criteria donors, little is known about the effects of particular expanded-criteria donors definition components, that is, hypertension, increased creatinine prior to procurement, and cerebrovascular cause of death on the kidney graft Doppler parameters measured shortly after transplantation, whose increased values are associated with unfavorable outcomes. Hence, we analyzed the relationship between expanded-criteria donors components and resistance index values measured within 2 to 3 days post-transplant.

Material and Methods. The initial post-transplant resistance index value was measured in 676 consecutive successful first cadaveric kidney graft recipients without delayed graft function or early acute rejection episode. We analyzed resistance index values in 460 patients transplanted with organs from donors <50 years and in 216 recipients with organs from donors >50 years old.

Results. In general, expanded-criteria donors status did not influence the initial resistance index values in the whole study group. Unexpectedly, in older donor groups, both the occurrence of donor hypertension and cerebrovascular cause of death resulted in significantly lower resistance index values in kidney graft recipients (0.73 ± 0.10 vs 0.76 ± 0.11 in the non-hypertension group, $P = .013$ and 0.74 ± 0.11 vs 0.78 ± 0.10 in the non-cerebrovascular cause of death group, $P = .015$, respectively). In the Cox proportional regression model for graft survival, cerebrovascular cause of death was increasing the risk of graft loss by 55%, while recipient's age had the opposite effect, decreasing the risk of graft loss by 2% per year.

Conclusions. Regardless of the limited influence of expanded-criteria donor status on first post-transplant resistance index value, the long-term observation shows moderate but significantly worse kidney graft survival, mostly as a result of the cerebrovascular cause of donor's death.

As KIDNEY transplantation is an optimal treatment modality for patients with end-stage renal disease, expanding the donor pool by using marginal donors, also referred to as expanded-criteria donors (ECDs), has been adopted at most transplant centers to address the growing organ shortage [1] despite generally worse long-term graft outcomes [2]. Notably, both delayed graft function (DGF) and 1-year graft survival of ECD kidneys could be markedly improved by the shortening of the cold ischemia time and machine perfusion storage [3,4]. According to the current

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ECD definition [5], in addition to donor age the following three criteria are included: donor history of hypertension (HA), cerebrovascular cause of death (CVD), and serum creatinine concentration >1.5 mg/dL prior to organ procurement (HC) (usually because of an acute kidney injury during an intensive care unit [ICU] stay).

Kidney graft resistance index (RI), calculated based on the Doppler spectrum measured in the segmental arteries, is a useful monitoring tool in the early post-transplant period since it mainly reflects the degree of interstitial edema within the graft developed as a consequence of ischemia-reperfusion injury. Significantly higher RI values were noted during acute rejection episodes and DGF, and also due to calcineurin inhibitor toxicity [6,7]. Moreover, several donor factors, including age, hypotension episodes, and lower estimated glomerular filtration rate, were also found to influence first post-transplant RI values [6,8]. Aside from the donor's age and kidney function, little is known about the possible effects of other ECD components, that is, HA and CVD, on the kidney graft Doppler parameters measured days after kidney transplantation. On the other hand, it was shown that increased early RI values are associated with unfavorable long-term kidney graft outcomes [9,10].

Thus, the aim of our study was to analyze the influence of specific donor conditions, covered by the ECD definition, on the value of first post-transplant kidney graft resistance index, measured by Doppler sonography, as well as on the long-term kidney graft outcome. To eliminate the potential factors interfering with RI values, we have analyzed a group of patients who have received their first kidney graft with a satisfactory early graft function and without an early acute rejection episode.

SUBJECTS AND METHODS

The initial post-transplant RI value was measured in 1350 consecutive deceased donor kidney graft recipients, operated in our center between January 1999 and December 2015. Patients with primary graft non-function, early acute rejection episodes, or DGF were excluded from this study.

ECD status was defined based on the common criteria [5]. Donor data were prospectively collected from original medical records obtained from the country transplant coordinate institution Poltransplant.

Procured organs were preserved in cold hypothermic storage using a solution from the University of Wisconsin. Until 2011, there was no authorized ECD organ-sharing policy, so organs were allocated at the physician's discretion based on recipient and donor age, the recipient's distance to the transplant center, an expected cold ischemia time, and other medical conditions. Since 2012, when the old-to-old program was launched in Poland, it has been mandatory for organs procured from donors older than 65 to be transplanted into recipients older than 60.

In all of the recipients until 2005, the ultrasound-Doppler intrarenal RI value was initially measured on the second or third post-transplant day with an Acuson 2.5–4.0 MHz micro-convex-array transducer machine (Aspen, Mountain View, Calif, United States), and since then with a Siemens machine (Sonoline Antares, Mountain View, Calif, United States), equipped with a 2.5–4.0 MHz convex-array transducer. In each patient, after visualization of 3 to 5 segmental arteries (localized in both kidney poles and the central region), the Doppler spectrum was recorded, averaged, and analyzed. During the examination, patients were asked to refrain from forced inspiration since this could modify the intra-abdominal pressure. The peak systolic velocity (V_{max}) and end-diastolic velocity (V_{min}) were measured, then the RI value was calculated as [$RI = 1 - (V_{min}/V_{max})$].

Statistical analysis was performed using the Statistica 12.0 PL for Windows software package (StatSoft Polska, Kraków, Poland) and MedCalc 14.12.0 (Mariakerke, Belgium). The distribution of quantitative variables was shown by mean values ± standard deviation (SD), and of qualitative variables by absolute and relative frequencies. Statistical significance of between-group differences was evaluated by analysis of variance (ANOVA) (quantitative variables) and by χ^2 test (qualitative variables). Graft survival was compared using the Kaplan-Meier method and log-rank test. Multivariate regression analysis was performed for first post-transplant RI values, including individual components of the ECD definition as potential explanatory variables in the whole study group (model I) and among recipients of ECD kidneys (model II). Multivariable Cox proportional hazard analysis was performed for factors (components of the ECD definition) significantly influencing graft survival. In all of the statistical tests, a P value below .05 was considered statistically significant.

RESULTS

Study Group

We analyzed first RI values in a cohort of 676 first-transplanted patients without early acute rejection or delayed graft function, composed of 460 patients with organs from donors younger than 50 years, and 216 patients transplanted with organs from donors of 50 years or older. Within the study cohort, there were recipients of 123 ECD organs and 553 non-ECD organs. When comparing ECD subgroups and non-ECD subgroups, there were expected differences regarding the criteria of ECD definition; for example, ECDs were significantly older, had a greater prevalence of hypertension, and more frequently died of cerebrovascular causes. The percentage of donors with an acute kidney injury suffered during an ICU stay was almost twice as high in ECDs. In addition, the recipients of ECD kidneys were also significantly older and had higher body mass index (BMI) values (Table 1).

Of note, the majority (74%) of hypertensive donors died of CVD. There was no such difference with regard to the coexistence of HC and CVD (43.7% vs 56.3% in non-CVD groups).

Donors who died of CVD were significantly older (48.7 years vs 36.8 years in non-CVD groups, $P < .001$), and the oldest was the subgroup of hypertensive donors with CVD (52.9 years).

ECD Components and First RI Values

In general, ECD status did not influence the initial RI values in the whole study group ($P = .8$), per se. In kidneys procured from younger donors, only HC corresponded with significantly higher RI values after transplantation (0.76 ± 0.12 vs 0.73 ± 0.11 in non-HC groups, $P = .03$) (Fig 1A), which was not observed in the older donor groups (Fig 1B) (despite