Factors Influencing Long-Term Survival of Kidney Grafts Transplanted From Deceased Donors—Analysis Based on a Single-Center Experience

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ABSTRACT

Background. Kidney transplantation is a routine procedure in the treatment of patients with kidney failure and requires collaboration of experts from different disciplines. Improvements in the procedure result from numerous factors.

Methods. The analyzed group consisted of 150 patients divided into 2 equal subgroups: long-term (>15 years) and short-term (<6 years) graft survival. The following factors were taken into consideration: graft survival time, HLA mismatches, recipient sex, sex compatibility, panel reactive antibodies (PRA), cold ischemia time (CIT), and cause of kidney insufficiency. Factors were analyzed in groups with the use of Student *t* and chi-square tests, Kruskal-Wallis analysis of variance (ANOVA), and multifactorial ANOVA.

Results. Basic statistical analysis revealed no significance between long-term and short-term survival groups in HLA mismatches, recipient sex, or sex compatibility. There was a very significant difference in CIT. ANOVA revealed no statistical difference between groups in recipient sex, sex compatibility, or recipient disease. There were more patients in the group with long-term survival with lower PRA. There were more women in the group with long-term survival who received kidneys from men. Multifactorial analysis revealed no interactions or independent influence of the selected factors.

Conclusions. CIT was a strong independent factor influencing graft survival. Recipient sex and cause of kidney insufficiency seemed to have no impact. Lower PRA was positively correlated with long-term survival. Women who received kidneys from men lived longer with functioning grafts.

KIDNEY transplantation is a routine procedure in the treatment of patients with kidney failure and requires collaboration of experts from different disciplines. Improvements in the procedure result from numerous factors, such as increased clinical experience of transplantation teams, diagnostic methods, immunosuppression, and individualized therapy. In our center, kidney transplantation has been performed since 1982. We currently manage ~420 transplant patients, and 99% of the harvested organs come from deceased heart-beating donors. Fewer than 20 kidney transplantations have been performed from living donors, including several grafts harvested by means of laparoscopic procedure. One-year graft survival rates are >95% in many centers [1] (94% in ours), but improvement of long-term function remains a challenge, although more common use of new developments in molecular immunology and computational biology—HLA and non-HLA matching, individual omics-wide molecular diagnostics, extracorporeal therapies, and drug developments—allow for precise

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individual decision making and treatment. There is also a general trend toward a reduction in the influence of HLA mismatch and increased attention to the importance of other factors shown to affect post-transplantation outcomes, such as cold ischemia time (CIT), duration of dialysis, donor and recipient ages, and comorbidity, which are considered for kidney allocation and successful outcome [2]. In the face of organ shortages, uncommon factors should be also taken into consideration, such as pre-transplantation physical function [3], cause of disqualification by other centers [4], and genetic predictors [5].

METHODS

The analyzed group consisted of 150 patients divided into 2 subgroups: 1) long-term graft survival (>15 years), 75 patients; and 2) short-term graft survival (<6 years), 75 patients. Mean donor age was 48.3 ± 12.4 years, and mean recipient age was 41.6 ± 12.8 years. The following factors were considered: graft survival time, HLA mismatches (MM), recipient sex, sex compatibility, panel reactive antibodies (PRA), CIT, and recipient disease (ie, cause of kidney insufficiency: glomerulonephritis, autosomal dominant polycystic kidney disease, arterial hypertension, or other. Factors were analyzed in groups with the use of Student *t* and chi-square tests (Table 1). Ranged parameters with >2 subgroups were analyzed with the use of Kruskal-Wallis analysis of variance (ANOVA; KWA) and multifactorial ANOVA (MA; Table 2). Sex compatibility was analyzed in 2 ways: 1) sex compatibility: yes or no answer for chi-square tests; and 2) sex incompatibility: with the use of KWA, man to woman/woman to man donation was considered to diversify possible results. CIT was analyzed as quantitative data for Student *t* test as well as qualitative data in specified ranges to make additional KWA calculations in those groups.

RESULTS

Graft survival time differed in both groups ($P < .05$; Table 1), which was the basis of main group division. Basic Student *t* and chi-square statistical analysis revealed no significance between long-term and short-term survival groups in MM (Table 1), recipient sex (Table 1) or sex compatibility ($P > .05$; Table 1). There was a very significant difference in CIT between groups (Table 1).

KWA in the long- versus short-term graft survival groups revealed no statistical differences between groups in following qualitative data: recipient sex (Table 1), sex compatibility (Table 1), and recipient disease (Table 2). There was a statistical difference in PRA ranges: There were more patients with lower PRA in the group with long-term survival (Table 2). There was a statistical difference between PRA range 1 versus 3 and (borderline) 2 versus 3 within the sex incompatibility groups: There were more women in the group with long-term survival who received kidneys from men (Table 2). Correlation in the whole group was mainly affected by cases with CIT <30 hours; in the group with CIT >30 hours this predominance was not observed. There was a statistical difference between CIT ranges 1 and 2 versus 3, 4, and 5: There were more patients in the group with long-term survival with shorter CIT (Table 2).

Finally, multifactorial analysis was calculated to emphasize interactions between selected factors (Table 3). Analysis revealed no statistical differences.

DISCUSSION

The analyzed groups with long- and short-term graft survivals were quite homogeneous in terms of MM, recipient sex, and sex compatibility (Table 1). Graft survival was not significantly affected by those factors, which indirectly could emphasize importance of other factors. However, our analysis is coherent with similar studies where male donor–to–male recipient transplants had lower graft failure, particularly better than female to male [6]. In larger groups, the significance of MM on graft survival in all donor type groups has been presented [6]. Other studies show that the highest relative hazards for graft failure were observed for female recipients of male-donor kidneys and male recipients of female-donor kidneys in situations where the recipient was >30 kg larger than the donor [7].

Although CIT ≤16 hours seems to have limited impact on living-donor outcomes [8], CIT >26 hours is associated with a significantly impaired survival of extended-criteria and cardiac-death grafts [9]. The main findings are that the consequences of prolonged CIT are mainly identifiable in the early post-transplantation period as delayed graft function, especially in expanded-criteria donors, and possibly in an increased acute rejection rate. Some data suggest that the risk of death is proportionally increased for each additional hour of cold ischemia time (hazard ratio, 1.018) and that CIT must be taken into account to increase graft and patient survivals [10]. On the other hand there are studies suggesting that the effects of CIT on the long-term outcome of renal transplants in the form of impaired graft function and graft survival are less evident [11,12].

There were no differences in the present study in cause of kidney failure between the long- versus short-term survival groups, although the analyzed group was too small to reveal

Table 1. Group Analysis–Factors I

Graft Survival	Graft Survival (mo)	HLA Mismatches	Recipient Sex	Sex Compatibility (No/Yes)	Cold Ischemia Time (h)
Long	227.20 ± 37.9	3.00 ± 1.14	36 M, 39 F	29 N, 46 Y	16.60 ± 4.83
Short	41.25 ± 15.49	3.60 ± 1.28	45 M, 30 K	38 N, 37 Y	27.92 ± 9.47
Test	*t*	χ^2	χ^2; KWA	χ^2; KWA	*t*
P value	<.01	.4893	.1404 (NS)	.1394 (NS)	<.000001

Abbreviation: KWA, Kruskal-Wallis analysis of variance; NS, not significant.