

# What Is the Influence of Both Risk Donor and Risk Receiver on Simultaneous Pancreas-Kidney Transplantation?

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### ABSTRACT

Introduction. Some factors affect the pancreas of a marginal donor, and although their influence on graft survival has been determined, there is an increasing consensus to accept marginal organs in a controlled manner to increase the pool of organs. Certain factors related to the recipient have also been proposed as having negative influence on graft prognosis. The objective of this study was to analyze the influence of these factors on the results of our simultaneous pancreas-kidney (SPK) transplantation series.

Materials and Methods. Retrospective analysis of 126 SPK transplants. Donors and recipients were stratified in an optimal group (<2 expanded donor criteria) and a risk group ( $\geq 2$  criteria). A pancreatic graft survival analysis was performed using a Kaplan-Meier test and log-rank test. Prognostic variables on graft survival were studied by Cox regression. Postoperative complications (graded by Clavien classification) were compared by  $\chi^2$  test or Fisher test.

Results. Median survival of pancreas was 66 months, with no significant difference between groups (P > .05). Multivariate analysis showed risk factors to be donor age, cold ischemia time, donor body mass index, receipt body mass index, and receipt panel-reactive antibody.

Conclusions. In our series, the use of pancreatic grafts from donors with expanded criteria is safe and has increased the pool of grafts. Different variables, both donor and recipient, influence the survival of the pancreatic graft and should be taken into account in organ distribution systems.

THE INCIDENCE and prevalence of diabetes mellitus have grown significantly throughout the world. Nowadays, it constitutes a global pandemic [1]. Its natural evolution involves vascular complications with high morbidity and mortality. In fact, diabetes is the leading cause of kidney disease in the developed world. Pancreas transplantation is an established therapeutic option that can restore normoglycemia and protect from chronic complications of the diabetes [2,3]. Nonetheless, pancreas transplantation traditionally follows the most conservative donor criteria, with a clear disparity between demand and organ procurement. This fact has stimulated the use of those socalled "marginal" or "expanded criteria donors" as an alternative in recent years. Multiple factors have been

0041-1345/18 https://doi.org/10.1016/j.transproceed.2017.09.065 shown to decrease the survival of the pancreatic graft [4–7]. However, several studies have obtained satisfactory results in pancreases implanted from expanded criteria donors [7–10]. In addition, factors related to the recipient can confer a potential risk of short- and long-term complications [11,12], but the influence of these on survival and post-operative results, as well as the combination with donor prognostic factors, has been less studied.

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#### DONOR AND RECIPIENT RISK FACTORS

The aim of the present study was to compare postoperative results and graft survival of pancreas transplantation according to the stratification in both donor and recipient risk groups.

#### MATERIALS AND METHODS

A retrospective analysis was performed on the 126 simultaneous pancreas-kidney transplantations (SPKs) performed in our center by the same surgical team from 2000 to 2015. Six cases were excluded from analysis due to lack of data or loss of patient control. In all recipients, an enteric drainage technique was used. The criteria of expanded criteria donor used in this study were those defined for Spanish National Transplantation Organization: age >45 years; body mass index (BMI) > 30; personal or familiar history of mellitus diabetes; donation after cardiac death or hemodynamic instability; death by cardiovascular accident; previous splenectomy; cold ischemia time (CIT) over 12 hours; maintained hypernatremia; stay in intensive care unit more than 3 days; and positive serology for human immunodeficiency virus, hepatitis B virus, or hepatitis C virus. We considered as risk donors those who had at least 2 risk criteria and optimal donors those with none or only a single risk factor. Criteria of risk recipients used in our study were age over 50 years; coronary artery disease or peripheral vasculopathy; motor neuropathy; overweight or obesity (BMI >25); HLA mismatches >3; panel-reactive antibody >20%; peritoneal dialysis; and diabetes mellitus disease evolution over 15 years. Likewise, we considered as risk recipients those with at least 2 risk criteria, and optimal recipients those with 1 or no risk factors.

Graft loss was defined as return to exogenous insulin or graft explant. Pancreatic graft survival according to the stratification into donor and recipient risk groups (optimal donor and recipient group; expanded criteria donor; risk recipient group) was calculated and compared using Kaplan-Meier test and log-rank test. The association between graft survival and risk variables were determined using univariate and multivariate Cox regression analysis.

Postoperative complications studied were recipient mortality; surgical reoperation; serious postsurgical complications, defined as Clavien > III (excluded deaths, Clavien V); and premature loss of graft function (into first 90 days from transplantation).

#### RESULTS

Baseline features of donors and recipients are shown in Tables 1 and 2. One-year global cumulative survival in the series was 87%. There was no statistically significant differences in graft survival rates over 90 days in log-rank test between groups (P > .05), depending on donor type (optimal or expanded criteria), recipient type (optimal or risk recipient), or the combination of expanded criteria donor plus risk recipient versus the rest of donor and recipient combinations (Fig 1). Donor factors with influence in graft survival beyond 90 days independently were age >45 years (hazard ratio [HR] 1.020; 95% confidence interval [CI] 1.003–1.045; P = .017), BMI >25 (HR 1.012; 95% CI 1.002-1.040; P = .044), and CIT >12 hours (HR 1.451; 95% CI 1.102–1.689, P = .004). Within the recipient factors that influenced in pancreatic graft survival independently beyond 90 days, we only found the presence of a reactive panel of antibodies >20% as a risk factor (HR 15.452; 95% CI 2.210–109.220; P = .006). In

Table 1. Demographic Features of Donors of 120 Simultaneous Pancreas and Kidney Transplants

| Feature                 | Value                            |
|-------------------------|----------------------------------|
| Age (y)                 | 27.88 ± 9.59                     |
| Body mass index         | $22.87\pm2.73$                   |
| ICU stay                | $3.23\pm4.48$                    |
| Ischemia time (h)       | $10.91 \pm 2.37$                 |
| рН                      | $7.40\pm0.87$                    |
| Creatinine              | $0.84 \pm 0.40$                  |
| Sodium                  | $147.45\pm8.33$                  |
| Potassium               | $\textbf{3.8} \pm \textbf{0.62}$ |
| Glycemia                | $154.17 \pm 54.87$               |
| Hemodynamic instability | 98 (83%)                         |
| Hematocrit              | $33\pm7$                         |
| Amylase                 | $109 \pm 130$                    |
| Death cause (stroke)    | 46 (38%)                         |
| Local donor             | 13 (11%)                         |
| PDRI                    | 1.08 (±0.31)                     |
| 0.64-0.85               | 36 (28.59%)                      |
| 0.86-1.15               | 43 (34.12%)                      |
| 1.16–1.56               | 27 (21.42%)                      |
| 1.57–2.11               | 12 (9.52%)                       |
| 2.12–2.86               | 8 (6.35%)                        |
|                         |                                  |

Data values are expressed in median  $\pm$  standard deviation.

Abbreviations: BMI, body mass index; ICU, intensive care unit; PDRI, pancreatic donor risk index.

multivariate Cox analysis, donor and recipient factors associated with pancreas graft survival over 90 days were donor age >45 years (HR 1.057; 95% CI 1.003–1.113; P = .037), CIT >12 hours (HR 2.572; 95% CI 1.1342–5.837; P = .024), donor BMI >25 (HR 1.010; 95% CI 1.001–1.032; P = .044),

Table 2. Demographic Features of Pancreas and Kidney Transplant Recipients

| Feature                              | Value                              |
|--------------------------------------|------------------------------------|
| Age (y)                              | $39\pm7.30$                        |
| Body mass index (kg/m <sup>2</sup> ) | $\textbf{22.96} \pm \textbf{2.91}$ |
| Sex                                  |                                    |
| Female                               | 21 (17.5%)                         |
| Male                                 | 99 (82.5%)                         |
| Duration of diabetes                 |                                    |
| >15 y                                | 83/120 (69.16%)                    |
| <15 y                                | 37/120 (30.84%)                    |
| Peritoneal dialysis hemodialysis     | 28/120 (23.33%)                    |
|                                      | 92/120 (76.66%)                    |
| HLA mismatches (DR $+$ A $+$ B)      |                                    |
| >3                                   | 99/120 (82.5%)                     |
| <u>≤</u> 3                           | 21/120 (17.5%)                     |
| Antibody reaction test               | 2/120> 20% (1.66%)                 |
|                                      | 118/120 < 20% (98.33%)             |
| Mismatch gender donor/recipient      |                                    |
| Yes                                  | 55/120 (45.83%)                    |
| No                                   | 65/120 (54.16%)                    |
| Mismatch BMI                         |                                    |
| >10 kg/m <sup>2</sup>                | 12/120 (10%)                       |
| <10 kg/m <sup>2</sup>                | 108/120 (90%)                      |
| Peripheral vasculopathy              | 38/120 (31.66%)                    |

Data values are expressed in median  $\pm$  standard deviation. Abbreviation: BML body mass index.

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