Multivariate Analysis of Complications After Simultaneous Pancreas and Kidney Transplantation

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ABSTRACT

Objective. Identification of factors that have an impact on postoperative complications after simultaneous pancreas and kidney transplantation (SPKTx) could help overcome limitations of this kind of treatment.

Methods. Postoperative complications among 112 SPKTx recipients were divided into 3 groups: related to transplanted pancreas (n = 66), related to transplanted kidney (n = 23) and general surgical complications (n = 31) 120 refers to complications among 112 recipients. According to the modified Clavien-Dindo scale, complications were classified according to their severity for each group. Risk factors for complication development related to donor, recipient, surgical technique, and immunosuppression were included to establish the multivariable model using logistic regression.

Results. Multiple regression analysis showed the following independent factors influenced mortal complications due to transplanted pancreas: age of donor (OR, 1.07; $P < .04$), duration of vascular pancreas anastomosis above 35 minutes (OR, 3.94; $P < .04$) and duration of recipient dialysis above 24 months before transplantation (OR, 0.14; $P < .01$). Area under receiver operating characteristic curve for this model was 0.8.

Conclusion. To improve results, the following modification of identified risk factors should be assumed: selection of donor in term of age, shortening of the second warm ischemia time, and adjustment of the waiting list to avoid prolongation of recipient dialysis before SPKTx.

ACCORDING to UNOS/IPTR, a 20% decrease in pancreas transplantation was observed in 2010 compared with 2004 [1]. The declining trend also was noticed in 2011 [2]. One possible explanation of this tendency could be the cost of surgical complications after this type of transplantation. It was estimated that a patient with a surgical complication after pancreas transplantation would cost an additional $17,363 [3,4]. Pancreas transplantation was characterized as having the highest complication and reoperation rates compared with the other solid organ transplants [3,5]. The reoperation rate has been reported from 11.6% to 43%, in contrast with a 2% to 5% relaparotomy rate after general surgical operations [6–10]. When a recipient requires relaparotomy, the cost of pancreas transplantation almost doubled [5]. Within this context, the identification of risk factors that influence the development of surgical complications was crucial. This knowledge could help

to modify donor and recipient selection criteria to avoid the high-risk situations and change post-transplant management in these cases.

The aim of this study was to identify factors that have influence on postoperative complications after simultaneous pancreas and kidney transplantation (SPKTx).

MATERIALS AND METHODS

Postoperative complications related to transplanted kidney among 112 SPKTx recipients who received their grafts from February 1988 to

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July 2010 were analyzed. The indications for transplantation were end-stage renal disease and diabetes type 1. Characteristics of donors and SPKTx recipients are shown in Table 1. For all recipients, the transplanted pancreas was placed at the right iliac fossa intraperitoneally with vascular anastomoses to the iliac vessels. Twelve patients (19%) had portoenteric drainage. Among 100 recipients with systemic-enteric drainage, 24 had transplanted pancreatic segment using four-anastomoses technique [11]. Kidney grafts were placed at the left iliac fossa extraperitoneally. Vascular anastomoses were performed on the iliac vessels with subsequent anastomosis between the end ureter to urinary bladder. Twenty-five (22.3%) recipients received segmental transplant, and immunosuppression consisted of ATG, azathioprine, cyclosporine, and steroids. Twenty-five of 112 (22.3%) recipients were prescribed daclizimab, cyclosporine, and mycophenolate mofetil. ATG, mycophenolate mofetil, tacrolimus, and steroids were administered to 64 of 112 patients (57.1%). Severity of complication was classified according to the Clavien-Dindo scale, adjusted for SPKTx transplant [12,13]. The suffix "g" was introduced and it refers to graft removal (Table 2). Postoperative complications among 112 SPKTx recipients were divided into 3 groups: related to transplanted pancreas (66 complications), related to transplanted kidney (23 complications), and related to neither transplanted pancreas nor kidney (renamed "general surgical," 31 complications). If the recipient developed more than 1 complication, the higher-grade complication was used. According to the modified Clavien-Dindo scale, each recipient with a complication was classified according to his/her severity and for each complication group (Table 3). There were 4 groups of risk factors related to donor (age, gender, cause of death [traumatic vs nontraumatic]), recipient (age, gender, duration of diabetes, type and duration of renal replacement therapy), perioperative (type and time of pancreatic and kidney graft anastomosis, type of enteric anastomosis, total ischemia time), and immunosuppression (tacrolimus vs cyclosporine; monoclonal vs polyclonal antibodies). Body index mass (BMI) of donor and recipients was not incorporated because BMI values above 25 kg/m^2 were not considered for pancreas harvesting

Table 1. Characteristics of Organ Donors and SPKTx Recipients

Gender of recipients (male/female)	69/43 (61.6%/38.4%)
Age of recipient at SPKTx (y)	38 (24–59)*
Duration of diabetes before transplantation (y)	24 (9–44)*
Duration of renal replacement therapy before transplantation (mo)	14 (0–102)*
Renal replacement therapy before SPKTx	
Hemodialysis	69 (61.6%)
Peritoneal dialysis	18 (16.1%)
Preemptive kidney transplantation	25 (22.3%)
Mean vascular anastomosis time of transplanted pancreas (min)	39 (20–95)
Mean vascular anastomosis time of transplanted kidney (min)	33 (15–72)
Mean total ischemia time of transplanted pancreas (min)	517 (183–860)
Mean total ischemia time of transplanted kidney (min)	576 (165–1099)
Cause of donor death	
Traumatic	53
Nontraumatic	41
Gender of donor (male/female)	67/27 (57.1%/42.9%)
Age of donors (y)	28.5 (17–53)

*Values given as median (minimum–maximum).

Table 2. Modified Clavien-Dindo Scale of Complication Severity After Simultaneous Pancreas and Kidney Transplantation

Severity of Complication	Definition
I	No complication
II	Pharmacological treatment
III	Invasive intervention (radiological, endoscopic, operative)
IIIA	• invasive intervention general anesthesia not required
IIIB	• invasive intervention general anesthesia required
IV	Life- or graft-threatening complication
IVA	• failure of the graft
IVB	• death

If the graft was removed the suffix "g" was added to the grade of complication severity.

and transplantation. Impacts of risk factors (independent variables) on severity of complication grades (dependent variables) were analyzed. In the case of missing data, variable discretization was performed. Separate categories were created for missing values A risk-adjusted model using multivariable logistic regression was built in backward selection. The area under the receiver operating characteristic curve for the model was calculated for internal validation according to recommended standards [14]. All statistical analysis was performed using STATISTICA 12 PL (Statsoft Polska, Kraków, Polska).

RESULTS

Mortality due to transplanted pancreas, kidney, and general surgery complications were 12,5%, 1,7%, and 1,7% respectively. It was possible to build the model only for mortal complications related to transplanted pancreas (grade IVB). The constructed model included: donor age (odds ratio [OR], 1.07; confidence interval [CI], 1.0–1.13; $P < .04$), duration of vascular pancreas anastomosis above 35 minutes (OR, 3.94; CI, 1.08–14.36; $P < .04$) and duration of recipient dialysis above 24 months prior to SPKTx (OR, 0.14; CI 0.03–0.62; $P < .01$). The following model was built:

$$\text{Logit P} = -4,08 + 0,064 \times \text{donor age} + 1.37 \times \text{time of transplanted pancreas vascular anastomosis above 35 minutes} - 1.93 \times \text{duration of dialysis therapy below 24 months.}$$

The area under receiver operating characteristic curve for this model was 0.8 (Fig 1).

DISCUSSION

SPKTx is the most commonly performed multiorgan transplantation, however it is characterized by a high rate of surgical complications. To describe problem of surgical complications variuos methodological approaches were applied [15–17]. In this study, the modified Claven-Dindo scale was used. In this scale the severity of complication was described by the most efficient treatment of particular complication. This scale has been widely known but rarely