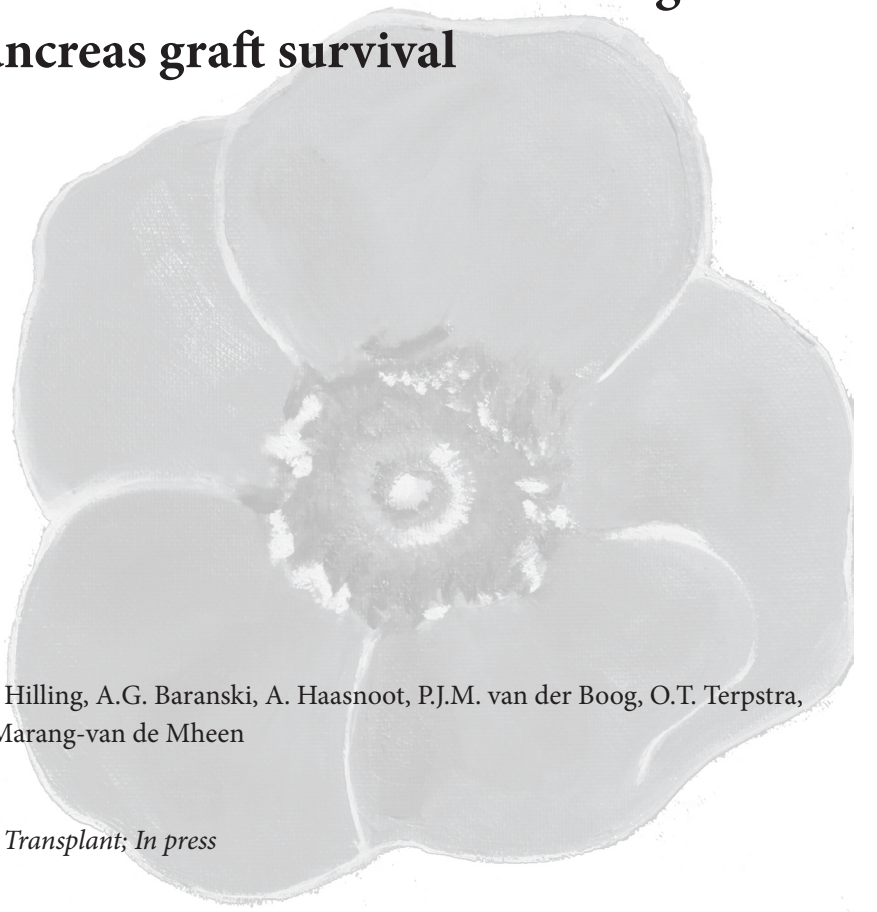
Part I

Pancreas transplantation

Chapter 2

Contribution of donor and recipient characteristics to short- and long-term pancreas graft survival



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ABSTRACT

Background

Many donor and recipient factors are known to affect pancreas graft survival. However, their relative importance in explaining differences in graft survival is unknown. Purpose of this study was to retrospectively evaluate the impact of donor and recipient factors on pancreas graft survival, and compare their contribution in explaining graft survival differences.

Methods and Materials

Patient records of all 170 pancreas transplantations (158 Simultaneous Pancreas-Kidney; 12 Pancreas-after-kidney) in the period 1997-2008 were reviewed retrospectively to assess recipient factors before/during transplantation, and to assess graft survival. Eurotransplant reports were reviewed to assess donor factors.

Results

Death-censored 1-year graft survival was 88.4% and 82.3% at 3 years. Several factors significantly influenced graft survival: female recipient gender (Hazard Ratio (HR) 2.81[1.10-7.14]), enteric graft drainage (HR 2.85[1.15-7.05]), and donor-recipient match on BMI (HR 2.46[1.01-6.02]). None of the donor factors significantly affected survival. Similar results were found for 1-year survival, except for enteric graft drainage and donor-recipient BMI matching. In total, donor factors explained 3.6% and recipient factors 10.0% of the variance in graft survival. Donor factors were more important for 1-year survival (3.1%), but still less important than recipient factors which explained 6.4%.

Conclusion

Recipient factors are more important in explaining differences in pancreas graft survival than donor factors.

BACKGROUND

Pancreas transplantation is able to correct metabolic abnormalities in patients with type 1 diabetes mellitus, prevent or delay secondary complications, and in simultaneous pancreas kidney (SPK) transplants is also a treatment for diabetic nephropathy (1-3). Outcomes have improved in recent years due to improved procurement and transplantation techniques, immunosuppression regimes and more emphasis on donor management and careful recipient selection (4-7).

Many donor characteristics have been reported to influence pancreas graft survival (8-14). This led the Eurotransplant Pancreas Advisory Committee to define a pancreas donor quality score, (comparable to the SOFT score in liver transplantation (15)) based on nine clinical parameters: the "Preprocurement Pancreas Allocation Suitability Score" (P-PASS) (16). They reported that pancreata from suboptimal donors (P-PASS > 17) had a significantly higher graft failure rate within the 1st year after transplantation (17). However, this effect may be partly explained by differences in recipient factors that affect survival, which were not taken into account. Other studies have shown that recipient characteristics, surgical techniques and other transplantation features such as ischemia times have an influence on graft survival (2,4,10,18,19). This raises the question on how the impact of donor characteristics relates to that of the recipient: are both equally important? To our knowledge, no studies so far have examined the contribution of donor and recipient factors to graft survival.

Another issue that may affect survival is whether donor and recipient are properly matched. ABO blood group matching and to a lesser extent HLA matching are known to improve pancreas graft survival and have become part of routine practice (10,20-22). However, donor-recipient matching on other factors (e.g. age) could also influence pancreas graft survival, as it is shown that kidneys of older donors give better outcomes in older than in younger recipients (23). This could also be true for pancreas graft survival, but has not been examined.

The purpose of the present study was to retrospectively evaluate the impact of donor and recipient factors on 1-year and overall pancreas graft survival, and to compare their contribution in explaining graft survival differences between pancreas recipients.

METHODS AND MATERIALS

Patients

Between January 1997 and September 2008 a total of 170 pancreas transplantations (158 SPK and 12 Pancreas After Kidney (PAK) transplantations) were performed at the Leiden University Medical Center in the Netherlands, with the number of transplantations

increasing from 9 per year in 1997 to 22 per year in 2007. All patients were insulin dependent diabetes mellitus type I. Patients undergoing SPK transplantation also had kidney insufficiency due to end-stage diabetic nephropathy. PAK recipients had previously received a kidney transplant (1 patient) or lost the pancreas graft after a previous SPK transplantation (11 patients). Pancreas Transplantation Alone was not performed in this period.

Donors

All donor pancreata were procured from multi-organ donations after brain death (DBD). Abdominal organs were mobilised and flushed "in situ" via the abdominal aorta with either cold University of Wisconsin (UW) or Histidine Tryptophane Ketoglutarate (HTK) organ preservation solution. Subsequently, the pancreata were procured "en bloc" with the spleen and stapled loop of the duodenum. In case of SPK transplantation, the kidney was procured with the ureter, renal vein and renal artery. Directly after procurement, the pancreata were packed and stored according to Eurotransplant guidelines and transported to our center (24,25).

Technical aspects

The procedure of SPK transplantation has been described previously (26,27). In short: a midline incision was made with both organs placed intraperitoneally. The kidney was placed in the left iliac fossa, with the renal vessels anastomosed end-to-side to the common or external iliac vessels. The pancreas was placed in the right iliac fossa, and the portal vein of the pancreas allograft was anastomosed end-to-side to the recipient's inferior vena cava or to the common or external right iliac vein. In most cases, the superior mesenteric and splenic arteries were reconstructed using a donor iliac artery Y graft. If the iliac artery could not be used (e.g. due to atherosclerosis), the brachiocephalic trunk or aortic arch of the donor were used for the arterial reconstruction. In some cases, no vascular reconstruction was performed due to anatomical abnormalities of the arterial vascularization of the pancreas allograft. Therefore, the pancreas graft was procured with the celiac trunk and the superior mesenteric artery together on the aorta patch. Arterial anastomosis in all pancreas grafts were performed end-to-side with one of the right common or external iliac arteries of the recipient. PAK transplantation was performed in a similar fashion. Pancreas transplants were either enteric (ED, n = 31) or bladder drained (BD, n = 139), with BD patients undergoing elective pancreas conversion 6 – 12 months after transplantation, as described previously (26,27).

Perioperative management

Prophylactic intravenous antibiotics were given for 24 hr perioperatively, consisting of benzylpenicillin 1x106 U four times per day, gentamycin 1.5 mg/kg once per

day, metrodinazol 500 mg three times per day and ceftazolin 1000 mg three times per day. Until the end of 2007, the immunosuppression regime consisted of prednisone, tacrolimus/cyclosporine and mycophenolate mofetil as maintenance immunosuppression and antithymocyt globulin (ATG) or daclizumab as induction treatment. Since the end of 2007, patients received a steroid-free regime with tacrolimus and mycophenolate mofetil as maintenance therapy and campath (preoperatively and the first postoperative day 15 mg subcutaneously) as induction treatment. Episodes of acute rejection are treated with solumedrol. Steroid-resistant rejections are subsequently treated with ATG.

Definitions and methods

Eurotransplant donor reports were reviewed retrospectively to assess donor characteristics included in the P-PASS score as well as other characteristics known to affect survival. Donor P-PASS scores were calculated as described by Vinkers et al. (16) from the following characteristics: age, Body Mass Index (BMI), intensive care unit (ICU) stay, cardiac arrest, last sodium, last amylase or lipase blood levels before procurement, and vasopressor dosage before procurement. Both the P-PASS score and the included individual characteristics were assessed. In addition, we collected data on the following donor factors known to affect graft survival: gender, ABO blood group, Human leukocyte antigen (HLA) type, Cytomegalovirus (CMV) infection, cause of death, hypotensive periods before procurement (Systolic Blood Pressure < 90 mm Hg and/or Diastolic Blood Pressure < 60 mm Hg) smoking and preservation fluid (7,10-12,21,22,28-32). Furthermore, patient records were reviewed retrospectively to assess graft survival, and the following recipient characteristics given their reported impact on graft survival (2,4,10,11,18,19,21,22,26,31-33):

- Preoperative recipient characteristics: age at transplantation, gender, BMI, ABO blood group, HLA type, duration and type of diabetes, duration and modality of dialysis, time on waiting list, preoperative anticoagulant therapy, positive anti-CMV antibody, last systolic and diastolic blood pressure before transplantation and last total cholesterol in blood before transplantation.
- Other (operative) factors: type of transplant (SPK or PAK), primary drainage (bladder or enteric), warm and cold ischemia time and postoperative anticoagulant therapy in addition to fraxiparine (GlaxoSmithKline inc, London, United Kingdom) 0.3 ml once per day, which was given to all patients postoperatively as prophylaxis.

All of these characteristics were assessed for each transplant, shortly before transplantation. In this way, recipient characteristics of patients receiving multiple transplants were not counted twice. Follow-up of graft survival was based on the last visit of the patient to the hospital or the outpatient clinic (or date of death in case of deceased patients). Mean duration of follow-up was 3.1 years, range [0 – 11 years].

Graft loss was defined as removal of the graft or return to exogenous insulin therapy. Patients who deceased with a functioning graft were censored at the time of death.

Statistical analysis

We calculated 1-year and overall survival rates for pancreas graft survival using the Kaplan-Meier method. Cox proportional hazard analysis was used to assess which donor and recipient factors significantly affected 1-year and overall pancreas graft survival. First, univariate analysis was performed for each of the following variables:

1. Donor factors: P-PASS score (> 17 versus <17), age, body mass index (BMI), length of ICU stay, last sodium blood level before procurement, last amylase blood level before procurement, last lipase blood level before procurement, cardiac arrest (yes/no), vasopressin use before procurement (yes/no), gender, cause of death (CVA or other), hypotensive periods (yes/no), smoking (yes/no), and preservation fluid (UW versus other)
2. Recipient factors: age at transplantation, gender, BMI, duration of diabetes, type of diabetes (type 1 or type 2), duration of dialysis, dialysis modality (hemo dialysis versus peritoneal dialysis), time on waiting list, pre- and postoperative anticoagulant therapy (yes/no), last systolic and diastolic blood pressure before transplantation, last total cholesterol before transplantation, type of drainage (bladder or enteric), type of transplant (SPK or PAK), warm and cold ischemia time.
3. Donor-recipient matching: age, gender, BMI, ABO blood group (yes/no, no meaning ABO compatible but non-identical), HLA type (yes/no), positive anti-CMV antibody (yes/no). For age and BMI, we assessed whether donor and recipient matched (yes/no) for either age group (<30, 30-40, >40 years) or BMI group (<20, 20-25, >25). These categories were chosen since these were used in the P-PASS score. For HLA, we assessed whether donor and recipient matched (yes/no) for HLA group (<5, >5 loci).

The adjusted R2 (% variance explained by the model) (34) was calculated for each variable and used as a measure of the importance of each variable in explaining the variance in graft survival.

Since the effect on graft survival in univariate analysis may be confounded by other factors, a multivariate analysis was performed, including only variables significantly influencing graft survival in univariate analysis. To assess the relative importance of donor factors versus recipient factors versus donor-recipient matching, we included the variables in separate blocks of donor factors, versus recipient factors versus donor-recipient matching. In case that none of the factors in a particular block showed a significant effect on graft survival in univariate analysis, we included the factor explaining the highest percentage of variance. The adjusted R2 (% variance explained by the model) was calculated for each block and used as a measure of the

importance of each block in explaining the variance in graft survival. In this way, we were able to compare the contribution of donor factors, relative to recipient factors and donor-recipient matching.

A P value of less than 0.05 was considered statistically significant in all analyses.

RESULTS

Donor and recipient characteristics of the 170 pancreas transplantations performed during the period 1997-2008 are listed in Table 1. In accordance with Eurotransplant

Table 1. Characteristics of 170 pancreas transplantations in the Leiden University Medical Center (1997-2008)

	SPK transplants (n=158)	PAK transplants (n=12)	All transplants (n=170)
Donor characteristic		**Mean ± SD or N (%)**	
P-PASS score			
< 17	81 (51.3%)	7 (58.3%)	88 (51.8%)
17+	40 (25.3%)	5 (41.7%)	45 (26.5%)
missing	37 (23.4%)	0 (0.0%)	37 (21.8%)
Age (years) [1]	32.8 ± 12.1	30.6 ± 14.5	32.7 ± 12.2
Body mass index (kg/m2) [1]	23.1 ± 3.2	24.0 ± 2.4	23.1 ± 3.2
ICU stay (days) [a, 1]	2.5 ± 2.6	2.7 ± 4.1	2.5 ± 2.7
Last sodium blood level before procurement (mEq/l) [1]	144.7 ± 7.3	146.7 ± 6.5	144.9 ± 7.2
Last amylase blood level before procurement (U/l) [b, 1]	147.7 ± 168.1	178.8 ± 180.8	150.0 ± 168.7
Last lipase blood level before procurement (U/l) [c, 1]	50.4 ± 66.4	46.3 ± 50.0	49.7 ± 63.6
Cardiac arrest [d, 1]	15 (9.6%)	3 (25.0%)	18 (10.7%)
Vasopressin use before procurement [1]	125 (79.1%)	9 (75.0%)	134 (78.8%)
Male gender	76 (48.1%)	5 (41.7%)	81 (47.6%)
Smoking [f]	58 (39.5%)	5 (45.5%)	63 (39.9%)
Cytomegalovirus infection	67 (42.2%)	1 (8.5%)	68 (40.0%)
Cause of death			
CVA	86 (54.4%)	6 (50.0%)	92 (54.1%)
Other	72 (45.6%)	6 (50.0%)	78 (45.9%)
Hypotension [2]	50 (31.6%)	5 (41.7%)	55 (32.4%)
Hypotension duration (min) [d]	8.0 ± 20.6	10.8 ± 14.4	8.2 ± 20.2
Preservation fluid			
UW	149 (94.3%)	12 (100%)	161 (94.7%)
Other	9 (5.7%)	0 (0%)	9 (5.3%)
Recipient characteristic			
Age (years)	41.5 ± 7.4	43.4 ± 4.6	41.6 ± 7.3
Male gender	92 (58.2%)	4 (33.3%)	96 (56.5%)
Body mass index (kg/m^2)	23.5 ± 3.1	23.8 ± 2.2	23.6 ± 3.1
Duration of Diabetes (years) [f]	29.2 ± 7.3	32.6 ± 5.6	29.4 ± 7.3
Dialysis preoperative [g]	100 (63.3%)	0 (0%)	100 (58.8%)
Duration of dialysis (months) [g]	1.2 ± 1.4	0.0 ± 0.0	1.2 ± 1.4
Modality of dialysis [g]			
Haemodialysis	35 (35.0%)	0 (0%)	35 (35.0%)
Peritoneal dialysis	65 (65.0%)	0 (0%)	65 (65.0%)
Time on waiting list (months)	15.9 ± 8.3	16.9 ± 13.3	16.0 ± 8.7
Positive anti-CMV antibody	63 (39.9%)	4 (33.3%)	67 (39.4%)

Preoperative anticoagulant therapy	44 (27.8%)	7 (58.3%)	51 (30.0%)
Last Systolic Blood Pressure preoperative (mmHg)	150.6 ± 24.9	149.3 ± 12.3	150.5 ± 24.2
Last Diastolic Blood Pressure preoperative (mmHg)	84.8 ± 12.2	83.7 ± 8.1	84.8 ± 11.9
Last Total cholesterol blood level preoperative (mmol/l) [h]	4.6 ± 1.2	4.7 ± 1.1	4.6 ± 1.2
Warm ischemia time pancreas (minutes) [j]	29.2 ± 7.7	28.9 ± 6.0	29.2 ± 7.6
Cold ischemia time pancreas (hours) [k]	12.9 ± 3.3	11.0 ± 2.8	12.8 ± 3.3
Drainage			
Enteric	28 (17.7%)	3 (25.0%)	31 (18.2%)
Bladder	130 (82.3%)	9 (75.0%)	139 (81.8%)
Postoperative anticoagulant therapy [3]	29 (18.4%)	7 (58.3%)	36 (21.2%)
Donor – recipient matching			
Matching on age (<30, 30-40, >40 years)	53 (33.5%)	3 (25.0%)	56 (32.9%)
Matching on gender (male, female)	115 (72.8%)	11 (91.7%)	126 (74.1%)
Matching on BMI (<20, 20-25, >25 kg/m^2)	77 (48.7%)	8 (66.7%)	85 (50.0%)
ABO blood group mismatch (ABO compatible, but non-identical) [h, 4]	6 (3.8%)	1 (8.3%)	7 (4.1%)
Donor-recipient HLA type mismatch (> 5 loci)	81 (51.3%)	5 (41.7%)	86 (50.6%)

[a] Data missing for 35 donors (35 SPK), [b] Data missing for 6 donors (6 SPK), [c] Data missing for 125 donors (120 SPK, 5 PAK), [d] Data missing for 2 donors (2 SPK), [e] Data missing for 12 donors (11 SPK, 1 PAK), [f] Data missing for 1 donor (1 PAK), [g] Data missing for 2 donors (1 SPK, 1 PAK), [h] Data missing for 1 donor (1 SPK), [j] Data missing for 3 donors (3 SPK), [k] Data missing for 7 donors (6 SPK, 1 PAK)

[1] Characteristics of the P-PASS: Preprocurement Pancreas Allocation Suitability Score
[2] Hypotension: last measured blood pressure before transplantation, Systolic Blood Pressure (SBP) <90 mm Hg and/or Diastolic Blood Pressure (DBP) <60 mm Hg
[3] Started independently of preoperative anticoagulant therapy
[4] Mismatches were 5 donor O, recipient B; 1 donor A, recipient AB; 1 donor B, recipient AB

regulations for pancreas allocation, donor age did not exceed 50 years and donor BMI did not exceed 30 kg/m2. Most grafts were matched on gender (74.1%) but not so much on age (32.9%) and BMI (50.0%). Death censored graft survival was 88.4% at 1 year, 82.3% at 3 years and 80.9% at 5 years. In total, 31 (18.2%) of the pancreas grafts were lost at some point during follow-up. Graft loss was due to thrombosis (n = 17), rejection (n = 5) or to an unknown cause (but patient returning to insulin dependence) (n = 9), comparable to other studies (35). 71% of the graft loss due to thrombosis were lost within 2 weeks, 82% were lost after 1 year and 100% after 2,5 years. For rejection, 20% was lost within 2 weeks, the remaining 80% was lost between 1,5 and 7 years after transplantation. 56% of the grafts lost due to an unknown cause was lost after 1 year, 100% was lost after 2,5 years.

Univariate analysis showed that several factors significantly increased the probability of graft loss and thus reduced graft survival: female gender, recipient total cholesterol, enteric graft drainage, and donor-recipient match on BMI (Table 2). In multivariate analysis, only enteric graft drainage and donor-recipient match on BMI remained as independent predictors of graft survival (Table 3). Because no donor

factors were found to significantly influence graft survival in univariate analysis, the last donor serum amylase before procurement was added as a variable in the multivariate analysis since this factor explained the highest percentage of variance (Table 4). Similar results were then shown, with female gender as an additional variable significantly reducing pancreas graft survival. Taken together, this model explained 11.6% of 1-year graft survival and 15.5% of overall graft survival.

When we excluded the PAK transplants from our analysis, similar results were found, except that enteric graft drainage was no longer a significant predictor for pancreas graft survival (even though results were in the same direction). Further exploration of the results regarding donor-recipient BMI match showed that pancreas graft survival was better in recipients with higher BMI than the donor, compared with recipients receiving a graft from a donor with similar BMI (BMI match). Graft survival in recipients with lower BMI than the donor was similar as in recipients with matching donor-BMI (data not shown).

The included donor characteristics explained 3.1% of the variance in 1-year graft survival and 3.6% of overall survival. Recipient characteristics were more important and explained 6.4% of the variance in 1-year survival and 10.0% of overall survival. Donor-recipient matching explained 2.6% of the variance in 1-year and 2.6% of overall survival. These results suggest that donor characteristics are approximately equally important for short-term and long-term graft survival, but that recipient factors remain most important in explaining the variance in graft survival.

DISCUSSION

The present study has shown that both donor and recipient characteristics as well as donor-recipient matching influence graft survival. Pancreas graft survival was reduced in female patients, who receive a graft from a donor with a similar BMI, with enteric graft drainage. While donor factors were equally important in explaining differences in short- and long-term pancreas graft survival, recipient factors remain most important and explain the largest proportion of the variance in both 1-year and overall survival.

In the Netherlands, the Leiden University Medical Center is the largest center performing pancreas transplantations. In 2007, 87% of all pancreas transplantations in the Netherlands were performed in our center (36). Even though all pancreas transplantations performed in our centre during the period 1997-2008 were included in the present study, thereby including all eligible patients, our results might (in theory) be influenced by selection. If pancreata from suboptimal donors (P-PASS > 17) were accepted only for the best, most optimal recipients, this may only slightly reduce survival rates, given the importance of recipient factors. Such selection would underestimate the effect of the P-PASS score on pancreas graft survival as the reduction in survival would have been larger when these pancreata were accepted randomly

Table 2. Univariate analysis of the impact of donor and recipient factors on 1-year and overall pancreas graft survival (Leiden University Medical Center, 1997-2008).

	1-year follow-up			Overall follow-up		
	Hazard Ratio	**95% CI**	**% variance**	**Hazard Ratio**	**95% CI**	**% variance**
Donor						
P-PASS > 17 vs < 17 a	1.86	0.72 – 4.81	2.14	1.59	0.67 – 3.77	1.11
missing vs < 17 a	0.49	0.11 – 2.27	2.14	0.78	0.28 – 2.15	1.11
Age (years)	1.04	1.00 – 1.08	1.97	1.02	0.99 – 1.05	0.80
Body mass index (kg/m2)	1.00	0.87 – 1.15	0.00	0.98	0.87 – 1.10	0.07
ICU stay (days)	1.11	0.98 – 1.26	1.64	1.08	0.95 – 1.23	0.89
Last sodium blood level before procurement (mEq/l)	0.97	0.91 – 1.04	0.47	0.98	0.93 – 1.03	0.35
Last amylase blood level before procurement (U/l)	0.99	0.99 – 1.00	3.06	1.00	0.99 – 1.00	3.88
Last lipase blood level before procurement (U/l)	1.00	0.99 – 1.01	0.99	1.00	0.99 – 1.01	0.51
Cardiac arrest (yes vs no)		Model could not be fitted			Model could not be fitted	
Vasopressin use before procurement (yes vs no)	0.99	0.33 – 2.97	0.00	0.82	0.33 – 2.04	0.10
Gender (female vs male)	1.62	0.64 – 4.10	0.62	1.53	0.70 – 3.34	0.68
Smoking (yes vs no)	1.78	0.69 – 4.61	0.88	1.48	1.66 – 3.30	0.57
Cause of death (CVA vs other)	1.91	0.73 – 5.03	1.07	1.29	0.60 – 2.77	0.25
Hypotensive period (yes vs no)	0.74	0.27 – 2.04	0.21	0.65	0.27 – 1.53	0.62
Preservation fluid (UW vs other)	0.43	0.10 – 1.88	0.59	0.57	0.14 – 2.42	0.29
Recipient						
Age (years)	1.00	0.94 – 1.07	0.01	1.00	0.95 – 1.05	0.01
Gender (female vs male)	**2.88**	**1.09 – 7.58**	**2.91**	**3.30**	**1.45 – 7.55**	**5.13**
Body Mass Index (kg/m2)	0.92	0.79 – 1.07	0.70	0.93	0.82 – 1.06	0.70
Duration of diabetes prior to transplantation (years)	1.03	0.97 – 1.10	0.67	1.00	0.95 – 1.05	0.01
Preoperative dialysis (yes vs no)	1.36	0.51 – 3.62	0.23	1.41	0.61 – 3.25	0.40
Duration of dialysis prior to transplantation (years)	1.00	0.71 – 1.40	0.00	1.08	0.84 – 1.40	0.20
Dialysis modality (hemo vs peritoneal dialysis)	0.16	0.02 – 1.23	4.98	0.65	0.23 – 1.82	0.72
Time on waiting list (months)	0.16	0.02 – 1.23	4.98	0.65	0.23 – 1.82	0.72
Preoperative anticoagulant therapy (yes vs no)	0.44	0.13 – 1.51	1.18	0.68	0.28 – 1.69	0.43
Systolic Blood Pressure (mmHg)	1.00	0.98 – 1.02	0.03	1.00	0.99 – 1.02	0.04
Diastolic Blood Pressure (mmHg)	1.00	0.96 – 1.04	0.00	1.00	0.97 – 1.04	0.02

Total cholesterol (mmol/l)	1.40	0.98 – 1.99	1.91	**1.41**	**1.05 – 1.91**	**2.80**
Type of drainage of the pancreas (ED vs BD)	**2.88**	**1.13 – 7.33**	**2.52**	**2.60**	**1.12 – 6.03**	**2.50**
Type of transplant (PAK vs SPK)	1.53	0.35 – 6.60	0.17	1.20	0.28 – 5.09	0.03
Warm ischemia time (minutes)	1.01	0.95 – 1.07	0.01	1.00	0.96 – 1.05	0.00
Cold ischemia time (hours)	0.88	0.75 – 1.04	1.56	0.94	0.83 – 1.07	0.53
Postoperative anticoagulant therapy (yes vs no)b	0.99	0.33 – 3.00	0.00	0.73	0.25 – 2.12	0.21
Match Donor - Recipient						
ABO blood group match (yes vs no)		Model could not be fitted		1.22	0.17 – 8.99	0.02
HLA match (>5 vs < 5 loci)	1.36	0.55 – 3.39	0.26	1.48	0.68 – 3.18	0.59
CMV infection match (yes vs no)	1.14	0.45 – 2.91	0.05	1.00	0.46 – 2.16	0.00
Age (<30, 30-40, >40 years; match vs no match)	1.88	0.76 – 4.62	1.07	1.22	0.56 – 2.66	0.14
Gender (male, female; match vs no match)	1.30	0.43 – 3.91	0.13	1.69	0.64 – 4.46	0.72
BMI (<20, 20-25, >25 kg/m2; match vs no match)	**3.97**	**1.32 – 11.97**	**4.28**	**3.12**	**1.32 – 7.38**	**4.43**

Hazard Ratio's in bold indicate significant differences
[a] P-PASS: Preprocurement Pancreas Allocation Suitability Score. This score is based on 9 donor characteristics: age, Body Mass Index, ICU stay, cardiac arrest, last sodium and amylase or lipase before procurement, vasopressor dosage before procurement (14).
[b] Started postoperatively independently of preoperative anticoagulant u

Table 3. Multivariate analysis of the impact of donor and recipient factors on 1-year and overall pancreas graft survival (Leiden University Medical Center, 1997-2008). Factors with a significant effect in the univariate analysis were included.

	1-year follow-up			Overall follow-up		
	Hazard Ratio	**95% CI**	**% variance**	**Hazard Ratio**	**95% CI**	**% variance**
Donor						
Recipient						
Gender (female vs male)	2.44	0.92 – 6.47		2.36	0.98 – 5.66	
Type of drainage of the pancreas (ED vs BD)	**2.65**	**1.04 – 6.80**		**2.96**	**1.23 – 7.14**	
Total cholesterol (mmol/l)	-	-		1.32	0.95 – 1.83	
			5.2%			8.4%
Match Donor - Recipient						
BMI (<20, 20-25, >25 kg/m2; match vs no match)	**3.64**	**1.20 – 11.04**		**2.94**	**1.22 – 7.04**	
			3.7%			3.8%
Total % variance explained			8.7%			11.9%

Hazard Ratio's in bold indicate significant differences

Table 4. Multivariate analysis of the impact of donor and recipient factors on 1-year and overall pancreas graft survival (Leiden University Medical Center, 1997-2008). Factors with a significant effect in the univariate analysis were included, as well as donor factor explaining most of the variance.

	1-year follow-up			Overall follow-up		
	Hazard Ratio	**95% CI**	**% variance**	**Hazard Ratio**	**95% CI**	**% variance**
Donor						
Last amylase blood level before procurement (U/l)	1.00	0.99 – 1.00		1.00	0.99 – 1.00	
			3.1%			3.6%
Recipient						
Gender (female vs male)	**2.89**	**1.00 – 8.34**		**2.81**	**1.10 – 7.14**	
Type of drainage of the pancreas (ED vs BD)	2.57	0.98 – 6.77		**2.85**	**1.15 – 7.05**	
Total cholesterol (mmol/l)	-	-		1.28	0.91 – 1.80	
			6.4%			10.0%
Match Donor - Recipient						
BMI (<20, 20-25, >25 kg/m2; match vs no match)	3.00	0.98 – 9.23		**2.46**	**1.01 – 6.02**	
			2.6%			2.6%
Total % variance explained			11.6%			15.5%

Hazard Ratio's in bold indicate significant differences

and thus also for less optimal recipients. However, given Eurotransplant allocation procedures, the surgeon decides whether quality of the graft is acceptable, after which it offered to the first patient on the waiting list. It therefore seems unlikely that our results were influenced to a great extent by such selection.

The donor and recipient characteristics found to influence pancreas graft survival in the present study have also been found in other studies (2,9,17,26). With respect to operative factors, it was found that our routinely used two-step approach of primary BD followed by elective ED after 6-12 months, with the aim to prevent short-term disadvantages of enteric drained grafts and long-term (urological) complications of related to bladder drainage, resulted in better graft survival consistent with previously shown results (26).

Matching donor and recipients on age has been shown to influence kidney graft survival (23,37). However, we did not find this for pancreas transplantation in our study. Donor-recipient matching on BMI on the other hand, was shown to increase graft loss, which to our knowledge has not been described before. Pancreas graft survival was shown to be better in recipients with higher BMI than the donor, compared to patients who received a graft from a donor with a similar BMI. Mean recipient BMI was 23.6 and only 6 recipients had a BMI higher than 30. A possible explanation may be that both recipients with high BMI and recipients with a very low BMI have worse outcomes than recipients with an average BMI, similar to the effects of BMI on cardiovascular mortality found in the general population (38-40). Graft survival in these patients is reduced particularly if these patients receive a graft from a donor with a similarly high or low (matched) BMI. These results should be tested and explained in further research.

Our method of quantifying the impact of donor versus recipient factors has not been shown before. Recipient factors were shown to be more important for graft survival than donor factors. The advantage of this method is that besides the assessment of which factors significantly influence pancreas graft survival, their importance in terms of their contribution to graft survival can also be established. Optimizing recipient factors thus seem more important for long-term survival than optimizing donor factors. This seems logical when considering that pancreas donors are highly selected, prior to procurement and transplantation. Because of this selection, the variation in donor factors (e.g. age) is much smaller than in recipient factors and would thus have a smaller effect in explaining differences in pancreas graft survival. Recipients on the other hand are selected to a smaller extent, in particular in more recent years in which pancreas transplantation is also offered to more high-risk patients (e.g. older patients with comorbidity) so that they differ far more in various characteristics that may influence survival. Further research may lead to improvement of this model by including other factors, which may result in a higher explained variance in survival.

In conclusion, even though both donor factors and donor-recipient matching explain part of the differences in short-term and long-term pancreas graft survival, recipient factors remain most important and explain the largest proportion of the variance in both 1-year and overall survival. Hence, emphasis should be placed in optimizing these recipient factors to improve graft survival after pancreas transplantation. Surgeons may thus choose to first optimize recipients factors, e.g. by treating comorbidity or cholesterol levels before transplanting the patient, to obtain better graft survival after transplantation.

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