Risk factors and outcome in clinical pancreas transplantation

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Center Volume Is Associated With Outcome After Pancreas Transplantation Within the Eurotransplant Region

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Introduction: Outcome after surgery depends on several factors, among these, the annual volume-outcome relationship. This might also be the case in a highly complex field as pancreas transplantation. No study has investigated this relationship in a European setting.

Methods: All consecutive pancreas transplantations from January 2008 until December 2013 were included. Donor-, recipient-, and transplant-related factors were analyzed for their association with patient and graft survivals. Centers were classified in equally sized groups as being low volume (<5 transplantations on average each year in the 5 preceding years), medium volume (5-13/year), or high volume (≥13/year).

Results: In the study period, 1276 pancreas transplantations were included. Unadjusted 1-year patient survival was associated with center volume and was best in high volume centers, compared with medium and low volume: 96.5%, 94% and 92.3%, respectively (p = 0.017). Pancreas donor risk index (PDRI) was highest in high volume centers: 1.38 versus 1.21 in medium and 1.25 in low volume centers ($p < 0.001$). Pancreas graft survival at 1 year did not differ significantly between volume categories: 86%, 83.2%, and 81.6%, respectively (p = 0.114). After multivariate Cox-regression analysis, higher PDRI (hazard ratio [HR], 1.60; $p < 0.001$), retransplantation (HR, 1.91; p = 0.002) and higher recipient body mass index (HR, 1.04; p = 0.024) were risk factors for pancreas graft failure. High center volume was protective for graft failure (HR, 0.70; p = 0.037) compared with low center volume.

Conclusions: Patient and graft survival after pancreas transplantation are superior in higher volume centers. High volume centers have good results, even though they transplant organs with the highest PDRI.

INTRODUCTION

Pancreas transplantation is the only definitive treatment for patients with type 1 diabetes mellitus. This can be as a simultaneous pancreas kidney transplantation (SPK) in case of end-stage renal disease (ESRD) or as a solitary pancreas transplant (pancreas after kidney [PAK], pancreas transplant alone [PTA]) in case of life-threatening hypoglycemic unawareness.[1-3] Even though the number of patients on the waiting list is relatively stable since 2009, optimal usage of scarce number of potential pancreas allografts is still highly important.[4] Apart from donor, recipient and transplant factors influencing outcome after transplantation,[5,6] center factors may also play a significant role.

The Dutch Institute for Clinical Auditing has been working on valid outcome measures in 18 domains of health care, most of them in oncological surgery. Eurotransplant is a non-profit organization that facilitates patient-oriented allocation and cross-border exchange of deceased donor organs. Active for transplant centers and their associated tissue typing laboratories and donor hospitals in 8 countries, Eurotransplant ensures an optimal use of donor organs. To be able to develop allocation policies based on state-of-the-art medical knowledge, Eurotransplant collects donor, recipient, and center data, as well as outcome data after transplantation. Information on center-related outcome, provided that they represent valid and useful outcome measures, should be publicly available: to centers, to improve their results; to patients, to make a well-founded decision on a preferred center; and to politicians, to design legitimate healthcare policies. This information can be derived from organizations, such as the Dutch Institute for Clinical Auditing or Eurotransplant or from single-center reports.

With this information, efforts are being put into concentrating "high complex, low volume" care in The Netherlands.[7] Especially oncology care is subject of this ongoing change. Transplantation has been the subject of concentration of care by the government longer and especially pancreas transplantation, with currently only 2 of 8 transplant centers with an active pancreas transplantation program. The question rises whether this concentration is justified and if the volume outcome relationship also exists in the field of pancreas transplantation, as has been stated before.[8,9] Recently, a German study advocated for an extensive analysis of volume-outcome after transplantation.[10] In 2014, within Eurotransplant there were 37 centers with an active pancreas transplant program, performing a total of 199 vascularized pancreas transplants, thus averaging an annual number of pancreas transplantations of a little over 5 each year.[4]

The aim of this study is to investigate the effect of center volume on outcome after pancreas transplantation in the Eurotransplant region.

Design

All consecutive vascularized pancreas transplantations that were performed in Eurotransplant centers from January 1, 2008, until December 31, 2013, were analyzed. Donor, procurement, recipient, and transplant data that were derived from the standard Eurotransplant database are shown in Table 1. Follow-up data were collected through the Eurotransplant registry. The Eurotransplant registry data were extracted at October 6, 2015. Graft survival was death censored. A frequently used definition of graft failure is that graft failure has occurred, when the recipient had returned to exogenous insulin therapy. This was the definition that the authors applied to all patients that were transplanted at the Leiden University Medical Center. For all other centers, it was unknown which definition was used, so the definition of pancreas graft failure was left up to the discretion of the transplant centers. When graft failure and death occurred at the same day or a graft had not been reported as failed before recipient death, this was not considered graft failure, and these cases were censored. The procurement surgeon determined organ quality (good, acceptable, poor) based on macroscopic evaluation; however, exact criteria were unknown.

Center volume for each year was defined as the total transplant volume of the 5 preceding years, based on standard Eurotransplant data reports (i.e., factor center volume for 2008 was based on average volume from 2003 to 2007, for 2009 based on 2004 to 2008, and so on).[11] Volume calculations were not performed for centers before their entry in the Eurotransplant collaboration. Croatia entered Eurotransplant in 2007, therefore, only transplants in 2013 (volume based on 2008-2012) were included in the center volume-survival analysis. Hungary entered in 2013, so was excluded from the center volume-survival analysis. Three equally sized groups were determined (low, medium, and high volume), based on the total volume in the 5 preceding years. Multiorgan transplants were only used to compute the total volume and were excluded from further analysis. Data in all 3 categories were pooled in order not to compromise recipient privacy and in order to not be able to identify individual centers.

Statistical Analysis

Differences between different volume categories were displayed using pooled sample mean and SE. P-values were calculated using 1-way analysis of variance. Missing values were imputed using 20 imputation rounds. Missing survival data were not imputed. Survival analysis for categorical variables was done using Kaplan-Meier estimates and groups were compared using Log-rank tests. Continuous variables were analyzed using Cox proportional hazard models after testing of the proportional hazards assumption.[12] P-values less than 0.05 were considered statistically significant. All significant factors from univariate survival analysis, as well as factors that were different among volume groups were entered in multivariate Cox proportional hazards model. To account for clustering of the data, robust sandwich estimates of the standard errors were used in multivariate analysis.[13] Only complete cases after multiple imputations were analyzed.

Table 1. Demographics, univariate analysis of association with pancreas graft survival [a]

	N (%)	P	X^2
Donors	1276 (100)		
Sex [b] (male)		0.150	2.070
Male	678 (53.1)		
Female	598 (46.9)		
Cause of death [b]		0.076	8.460
Cerebrovascular accident	624 (48.9)		
Trauma	497 (38.9)		
Circulational/Anoxia	115 (9.0)		
CNS tumor	7 (0.5)		
Other	33 (2.6)		
Donor type [b]		0.387	0.749
DBD	1268 (99.4)		
DCD	8 (0.6)		
	Mean (SD)	**P**	**HR**
Age, y [b]	32 (12)	0.006	1.014
Weight, kg	71 (14)	0.218	1.006
Height, cm [b]	173 (12)	0.884	1.001
BMI, kg/m^2 [b]	23 (3)	0.036	1.045
Sodium, mmol/l	147 (9)	0.611	1.004
Creatinine, mg/dl [b]	0.87 (0.58)	0.358	1.089
Amylase, U/l	125 (281)	0.114	1.000
PDRI	1.27 [c]	0.006	1.466
	N (%)	**P**	**X^2**
Transplant			
Perfusion solution		0.036	6.658
UW [d]	339 (26.6)		
HTK	906 (71)		
Other	13 (1.0)		
Unknown	18 (1.4)		
Transplant type [b]		<0.001	61.191
SPK [d]	1148 (90.0)		
PAK	84 (6.6)		
PTA	44 (3.4)		
Retransplantation (yes)	118 (9.2)	<0.001	13.036

Table 1. Demographics, univariate analysis of association with pancreas graft survival [a] (continued)

Transplant year		0.691	3.060
2008	199 (16.4)		
2009	172 (14.2)		
2010	228 (18.8)		
2011	220 (18.1)		
2012	211 (17.4)		
2013	184 (15.2)		
	Mean	**P**	**HR**
Pancreas cold ischemia, h [b]	10.4**	0.610	1.012
	N (%)	**P**	**X^2**
Recipient			
Gender		0.577	0.312
Male	785 (61.5)		
Female	491 (38.5)		
End stage renal disease			
No end stage renal disease (PAK/PTA)	128 (10.0)		
End stage renal disease (SPK)		0.140	0.140
Pre-emptive	218 (19.0)		
Hemodialysis	736 (64.1)		
Peritoneal dialysis	194 (16.9)		
	Mean (SD)	**P**	**HR**
Age, y	44 (9)	0.487	0.995
BMI, kg/m^2	24 [c]	0.025	1.038
Waiting time, y	1.15 (1.3)	0.970	0.998

[a] Kaplan-Meier estimates (Log rank Mantel-Cox) for categorical variables. Cox proportional hazards for continuous variables.
[b] PDRI factor
[c] based on imputed data
[d] favorable factor

Missing Data Imputation

Recipient weight (6.2%), recipient height (6.2%), and pancreas cold ischemia (25.4%) had missing values. Variables that were included in the imputation model were: donor age, sex, weight, height, body mass index (BMI), cause of death, creatinine, DBD versus DCD, pancreas donor risk index (PDRI), and donor country; recipient age, sex, weight, height, dialysis type, waiting time; pancreas cold ischemia time in minutes and hours, total pancreas cold ischemia time (hours), transplant type (SPK, PAK, PTA), center volume, warm ischemic period, transplant center, transplant year, organ quality, perfusion solution. Warm ischemic time, PDRI, creatinine, amylase, lipase, sodium, transplant center, donor country, perfusion solution, and organ quality were used as indicators only. Imputation method

was automatically selected by SPSS (SPSS version 22, IBM, North Castle, NY) based on patterns of missing value analysis. To reduce sampling variability from the imputations, 20 imputation rounds were performed.[14] Results of multiple imputations are shown in Table 2. Recipient BMI and PDRI were calculated based on the imputed values.

Table 2. Imputation of missing data

	Original data			Imputed data [a]		
	n	% missing	Mean (SEM)	n	% missing	Mean (SEM)
Recipient height (cm)	1198	6.2	172 (0.26)	1276	0	172 (0.26)
Recipient weight (kg)	1198	6.2	72 (0.39)	1276	0	72 (0.40)
Pancreas CIT (hr)	952	25.4	10.4 (0.09)	1276	0	10.4 (0.08)

[a] 20 rounds of multiple imputations

RESULTS

In the study period (January 2008 to December 2013), 1276 pancreas transplantations were included in the study. There were 1148 (90%) SPK transplantations, 84 (6.6%) PAK transplantation, and 44 (3.4%) PTA transplantations. During the study and follow-up period, 122 (9.6%) patients were reported deceased and 256 (20.1%) grafts were reported as failed (death-censored). Mean duration of follow-up was 3.2 years. Mean pancreas donor risk index was 1.27. Demographics are shown in Table 1.

Patient and Pancreas Graft Survival

Overall patient survival at 180 days, 1 year, and 3 years was 95.4%, 94.1%, and 91.2%, respectively. Patient death was associated with higher recipient age (hazard ratio [HR], 1.03; $p = 0.006$). Pancreas graft survival (death-censored) at 180 days, 1 year, and 3 years was 85.3%, 83.7%, and 78.8%, respectively. Pancreas graft failure was associated with higher donor age ($p = 0.006$), higher donor BMI ($p = 0.036$), higher PDRI ($p = 0.007$), and high recipient BMI ($p = 0.027$), retransplantation ($p < 0.001$) and the use of histidine tryptophan ketoglutarate (HTK) as perfusion solution ($p = 0.036$). Simultaneous pancreas kidney transplantation ($p < 0.001$) was protective in univariate analysis. Results of univariate analysis on factors associated with pancreas graft failure are shown in Table 1. Year of transplant was not associated with pancreas graft survival ($p = 0.69$).

In a separate subgroup analysis of recipients with ESRD (SPK recipients), the influence of dialysis modality (either pre-emptive transplantation, peritoneal dialysis or hemodialysis) was analyzed for the association with patient and graft survival. In this analysis, patient ($p = 0.235$) and graft survivals ($p = 0.140$) were not associated with dialysis technique.

Analysis of Center Volume on Outcome

For 1214 (95.1%) transplantations, center volume was calculated. Nine transplantations (0.7%) were from Hungary and 53 (4.2%) from Croatia, and these were excluded, because they had too few preceding years in Eurotransplant. Low volume centers (<25 transplantations/5 preceding years) performed 396 (32.6%) transplantations, 425 (35%) were performed in medium volume (25-64 transplantations/5 years) centers and 393 (32.4%) in high volume (≥65 transplantations/5 years) centers. An overview of number of transplantations in each year by center category is shown in Table S1 (SDC, http://links.lww. com/TP/B303). Center demographics are shown in Table 3. The pooled sample mean PDRI of donors transplanted in different categories differed significantly: 1.25 in low volume centers, 1.21 in medium volume centers, and 1.38 in high volume centers ($p < 0.001$). Post hoc testing (Bonferroni corrections) showed that PDRI only differed between high versus low ($p < 0.001$) and high versus medium ($p < 0.001$), not low versus medium ($p = 0.316$). High volume centers transplanted patients with ESRD more frequently in a preemptive setting, compared with low and medium volume ($p < 0.001$). Mean time from waiting list registration to transplantation

Table 3. Demographics in center categories

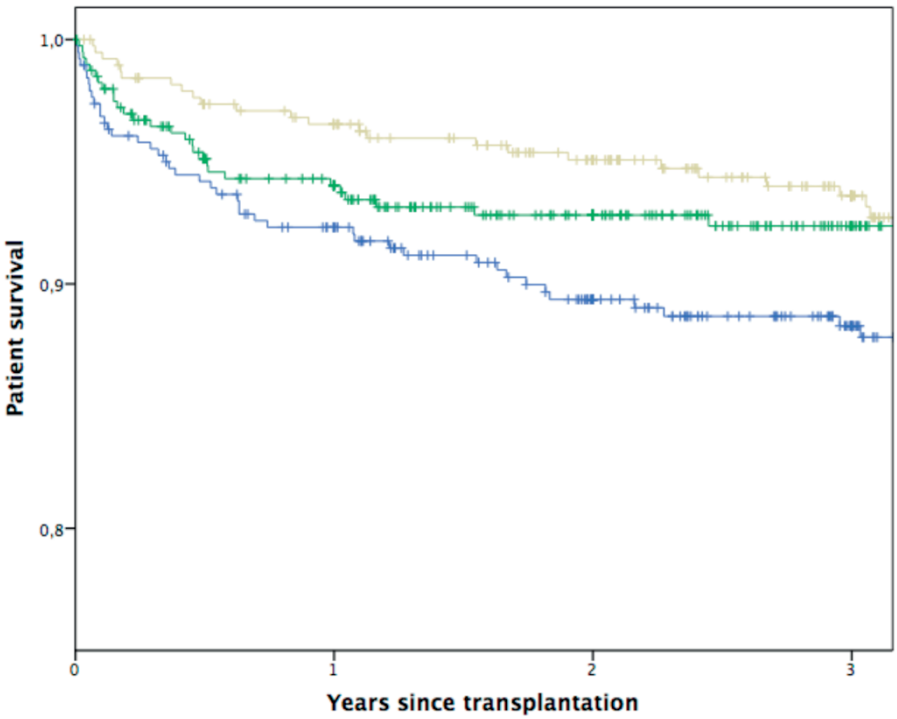
	Low volume [b]	Medium volume [b]	High volume [b]	p [a]
n	396 (32.6%)	425 (35%)	393 (32.4%)	
PDRI	1.25 (0.41)	1.21 (0.41)	1.38 (0.46)	<0.001
PDRI factors				
Donor age, y	33 (11)	30 (12)	35 (13)	<0.001
Donor BMI, kg/m^2	23.6 (2.8)	22.9 (3.2)	23.3 (2.9)	0.005
Pancreas CIT, hr	9.7 (2.6)	10.4 (3.1)	11.2 (2.6)	<0.001
SPK transplantation	361 (91.2%)	375 (88.2%)	353 (89.8%)	0.019
Cause of death (stroke)	196 (49.5%)	194 (45.6%)	210 (53.4%)	0.252
DCD	0 (0%)	0 (0%)	8 (2%)	<0.001
Recipient age, y	44 (8.7)	44 (8.6)	44 (8.7)	0.660
Recipient BMI, kg/m^2	24.2 (4.2)	24.1 (3.8)	24.2 (3.8)	0.593
Sensitized				0.177
6 – 80 % PRA	15 (4%)	28 (6.9%)	21 (5.5%)	
>80% PRA	3 (0.8%)	0 (0%)	3 (0.8%)	
Waiting time, d	586 (434)	649 (497)	583 (532)	0.087
Retransplantations	32 (8.1%)	46 (10.8%)	40 (10.2%)	0.387
End stage renal disease (SPK)				<0.001
Pre-emptive	61 (16.9%)	54 (14.4%)	101 (28.6%)	
Hemodialysis	243 (67.3%)	262 (69.9%)	192 (54.4%)	
Peritoneal dialysis	57 (15.8%)	59 (15.7%)	60 (17.0%)	

[a] One-way ANOVA for continuous variables (mean, SD), X^2 for categorical variables (n, %)

[b] Low volume (<5 transplantations/year), medium volume (5-13/year) or high volume (≥ 13/year).

was not significantly different in 3 volume categories (Table 3). The proportional hazards assumption was not violated (p = 0.350).

Patients transplanted in high volume centers had longest patient survival (p = 0.017) (Figure 1A). Other than age and center volume, no factors were significantly associated with patient survival in univariate analysis. After correcting for recipient age (HR, 1.04; 95% confidence interval [95% CI], 1.02-1.06; p = 0.001) in a multivariate Cox regression analysis, high volume (HR, 0.51; 95% CI, 0.32-0.81, p = 0.004) but not medium volume (HR, 0.65; 95% CI, 0.42-1.00; p = 0.052) was protective compared with low volume. One

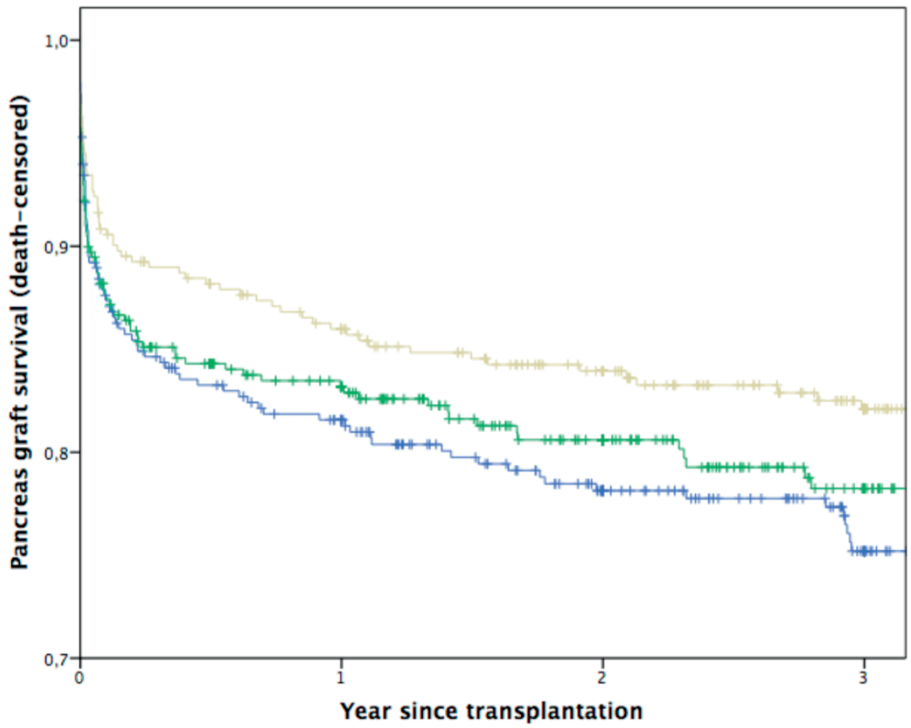


	0 days	180 days	1 year	3 years
Low volume				
N at risk	382	353	332	216
Patient survival	100%	94.2%	92.3%	88.3%
Medium volume				
N at risk	399	353	329	170
Patient survival	100%	95.1%	94.0%	92.4%
High volume				
N at risk	382	360	346	236
Patient survival	100%	97.4%	96.5%	93.6%

Figure 1a Kaplan-Meier estimates for patient survival in different volume categories (p=0.017)

hundred twelve cases (8.8%) were excluded due to missing follow-up data or because they were performed in the first years of Croatian or Hungarian membership of Eurotransplant.

In univariate analysis, graft survival was not significantly different among the 3 categories (p = 0.11) (Figure 1B). Higher PDRI (HR, 1.60; p<0.001), retransplantation (HR, 1.91; p = 0.002), and higher recipient BMI (HR, 1.04; p = 0.024) were independent risk factors for pancreas graft failure after multivariate Cox regression analysis. Perfusion with University of Wisconsin (UW) solution was not protective after multivariate analysis, compared with



	0 days	180 days	1 year	3 years
Low volume				
N at risk	382	300	280	170
Graft survival	100%	83.3%	81.6%	75.2%
Medium volume				
N at risk	399	310	284	139
Graft survival	100%	84.3%	83.2%	78.2%
High volume				
N at risk	382	324	307	203
Graft survival	100%	88.2%	86.0%	82.1%

Figure 1b Kaplan-Meier estimates for pancreas graft survival in different volume categories (p=0.114)

HTK (p = 0.111) or other solutions (p = 0.739). Higher center volume was associated with a lower risk of pancreas graft failure. This effect was statistically significant for low versus high volume (HR, 0.70; p = 0.037), but not for low versus medium volume (HR, 0.89; p = 0.562). Results of multivariate analyses are shown in Table 4a. One hundred thirty (10.2%) cases were excluded from multivariate analysis due to missing follow-up data or because they were performed in the first years of Croatian or Hungarian membership of Eurotransplant.

In a separate subgroup analysis (Table 4b) with only SPK transplants included, PDRI, volume category, and perfusion solution (significant factors from univariate analysis),

Table 4.1. Multivariate analysis of association of risk factors with pancreas graft survival (all transplantations)

	HR (95% CI)	**P**
PDRI	1.60 (1.23 - 2.07)	<0.001
Perfusion solution		
UW	reference	
HTK	1.28 (0.95 - 1.72)	0.111
Other	0.71 (0.09 – 5.40)	0.739
Retransplantation	1.91 (1.26 - 2.91)	0.002
Recipient BMI	1.04 (1.00 - 1.07)	0.024
Center volume		
Low volume	reference	
Medium volume	0.89 (0.59 - 1.33)	0.562
High volume	0.70 (0.50 - 0.98)	0.037

Table 4.2. Multivariate analysis of association of risk factors with pancreas graft survival (SPK transplantations)

	HR (95% CI)	**P**
PDRI	1.94 (1.45 – 2.60)	<0.001
Perfusion solution		
UW	reference	
HTK	1.56 (1.07 – 2.28)	0.021
Other	1.02 (0.13 – 7.93)	0.984
Retransplantation	1.33 (0.84 – 2.13)	0.227
End stage renal disease		
Pre-emptive	reference	
Hemodialysis	0.97 (0.67 – 1.39)	0.85
Peritoneal dialysis	1.47 (0.96 – 2.24)	0.07
Recipient BMI	1.04 (1.00 – 1.07)	0.047
Center volume		
Low volume	reference	
Medium volume	0.91 (0.58 – 1.44)	0.696
High volume	0.69 (0.49 – 0.97)	0.032

recipient BMI, and dialysis category were included in multivariate analysis. In this multivariate analysis, high PDRI was associated with graft failure (HR, 1.94; $p < 0.001$). High volume, as compared to low volume, was protective for graft failure (HR, 0.69; $p = 0.032$), whereas medium volume was not (HR, 0.91; $p = 0.696$). The use of HTK was associated with a higher risk of graft failure compared with UW (HR, 1.56, $p = 0.021$). Whether a recipient was transplanted preemptively or while on dialysis was not associated with pancreas graft survival. Of all 1148 SPK transplantations, 119 (10.4%) were excluded from multivariate analysis due to missing follow-up data or because they were performed in the first years of Croatian or Hungarian membership of Eurotransplant.

DISCUSSION

This study investigates the association of center volume with outcome after pancreas transplantation. We have shown that there is a significant relationship between center volume (defined as volume in 5 preceding years) and outcome, measured both in patient survival years as in pancreas graft survival years.

In this study, center volume was calculated based on the total number of pancreas transplantations in the previous 5 years. The authors have the opinion that 5 years is a reasonable timeframe to maintain an experienced program for pancreas transplantations. The calculations of volume were deliberately performed on data from preceding years, in order not to violate assumptions in analysis of longitudinal data.[11] This allowed us to analyze the influence of volume on outcome, and we excluded the possibility that lower or higher volume was influenced by previous results. This is the preferred method to investigate volume-outcome in any specialty; however, results might have been clouded by the fact that centers were allowed to migrate between the categories. It could thus have been that a center was defined as medium volume in the first year, but was analyzed as being low volume in the following year. This might be considered as a limitation, but the authors consider this as a strength of the study, because this method allowed us to establish the existence of the volume-outcome relationship, without considering the individual center effect. We acknowledge the fact that center volume is a surrogate marker, because true quality depends on multiple factors, such as surgical experience, adequate recipient selection and screening, postoperative care, and long-term follow-up protocols.

Patient survival after transplantation was associated with recipient age, as well as center volume. Higher recipient age was a risk factor for patient death, whereas high center volume was a protective factor. The better patient survival might be explained by a more rigorous pretransplant screening, especially regarding cardiovascular status of the intended recipients, and more optimal posttransplant management of cardiovascular complications in higher volume centers. A recent study from Scalea et al[15] demonstrated comparable

patient survival in older recipients in a high volume center with very strict pretransplant cardiovascular workup.

In univariate analysis, we could not find a significant difference in graft survival and center volume. However, when correcting for relevant donor and recipient characteristics in multivariate analysis, the association with graft failure and center volume became clear. High volume centers have better results compared with low volume centers, even though they are more aggressive in their acceptance policy, indicated by higher PDRI. Furthermore, from our available recipient data, we did not establish a significant difference in transplant recipient demographics (age, BMI, waiting time, retransplantation) that could have explained these results.

Even though it is not the aim of our study, next to the volume-outcome relationship, several other factors that were significantly associated with pancreas graft survival were identified. The first is the pancreas donor risk index (PDRI), which was found to be associated with graft failure. This is in line with results from previous studies.[16,17] Next to donor risk, 2 recipient factors were also found to be risk factors for inferior graft survival. Higher recipient BMI is considered a risk factor in many types of surgery, being associated with higher complication rate, and this relationship has recently been confirmed in 2 studies on pancreas transplantation.[18,19] The results of our study confirm this increased risk for recipients with higher BMI. Also, retransplantation was a risk factor for graft failure (in fact, the strongest). The authors believe that this is independent of the transplant type, because we corrected for transplant type using the PDRI. Our results are in line with previously published results from a large registry analysis from the United States.[20] For the subgroup of SPK transplantations, retransplantation was not a significant risk factor. This may be because of small numbers, because most retransplantations are performed in a PAK/PTA setting.

The protective effect of UW as perfusion solution in univariate analysis disappeared after multivariate analysis of all transplantations. Possible explanations could be that HTK was used in higher risk donors, retransplantations or that HTK was used more frequently in low volume centers. On the other hand, HTK was identified as an independent risk factor for graft failure in the subgroup analysis of SPK transplantations. The authors think that this study provides more evidence regarding the optimal cold storage solution for pancreata.[21] To identify an association was not within the scope of this study and to adequately investigate the relationship between outcome and perfusion solution a randomized controlled trial would be preferred. No association with transplant year and graft survival was found in this study, indicating that in this cohort, the era effect was of minor importance. The relatively modern cohort (without major changes in surgical techniques, preservation methods and immunosuppression) may be the reason for this absent association.

This study had some limitations. Most important one is the definition of graft failure. Because there appears to be no consensus on the definition of pancreas graft failure, graft

failure was left up to the discretion of the centers. There may be significant differences in reported survival rates, depending on the definitions. Furthermore, data on reported survival and exact numbers lost to follow-up may not be complete; this may have influenced the results. Also, Eurotransplant depends on data filled in by the donor and transplant centers. Some data were missing, however, multiple imputation has been shown to provide valid results and is an accepted technique to handle missing data.[22,23] We believe that using this technique did not influence the results in any way and has provided valid estimations of the missing data. The authors realize that the volume cutoffs that were chosen are debatable, however, still feasible, when looking at centers privacy and current group sizes. It could be that, next to recipient age, patient survival was associated with factors, such as preexistent peripheral artery disease, coronary or cerebrovascular disease; however, these data were not available in this study.

In conclusion, it is a remarkable finding that almost one third of all pancreas transplantations in the Eurotransplant region are being performed in centers that had performed less than on average 5 transplantations each year in the 5 preceding years. Given the fact that the highest risk organs are transplanted in the high volume centers with good outcome, it is an interesting thought that improving experience in the pancreas transplant centers may facilitate acceptance and allow transplantation of higher risk organs and increase transplant numbers.

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