ANNALS OF TRANSPLANTATION

ORIGINAL PAPER

e-ISSN 2329-0358
© Ann Transplant, 2018; 23: 360-363
DOI: 10.12659/AOT.909654

Received: 2018.02.26
Accepted: 2018.02.28
Published: 2018.05.25

Usefulness of Pancreas Donor Risk Index and Pre-Procurement Pancreas Allocation Suitability Score: Results of the Polish National Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCEF 1 Kaja Śmigielska
ABCEF 1 Paweł Skrzypek
D 2,3 Jarosław Czerwiński
D 2 Grzegorz Michalak
B 4,5 Marek Durlik
AB 6 Tadeusz Grochowiecki
AB 6 Sławomir Nazarewski
B 6 Jacek Szmidt
B 7 Jacek Ziaja
B 7 Robert Król
B 7 Lech Cierpka
ACDFG 1 Wojciech Lisik
ABCDEF 1 Maciej Kosieradzki

1 Department of General and Transplantation Surgery, The Medical University of Warsaw, Warsaw, Poland
2 Department of Emergency Medicine, The Medical University of Warsaw, Warsaw, Poland
3 Organization and Coordination Center for Transplantation – Poltransplant, Warsaw, Poland
4 Department of Gastroenterological and Transplantation Surgery, Central MSW Hospital, Warsaw, Poland
5 Mossakowski Medical Research Center, Polish Academy of Sciences, Warsaw, Poland
6 Department of General, Vascular and Transplantation Surgery, The Medical University of Warsaw, Poland
7 Department of General, Vascular and Transplantation Surgery, Silesian Medical University, Katowice, Poland

Corresponding Author: Wojciech Lisik, e-mail: wojciech.lisik@wum.edu.pl
Source of support: Departmental sources

Background: Pre-procurement pancreas suitability score (P-PASS) and pancreas donor risk (PDRI) index are scoring systems believed to predict suitability of pancreatic grafts. Most European countries and the United States apply PDRI, while Poltransplant keeps using P-PASS: more than 16 points raises a red flag for graft use. Recent data discourage use of PDRI to predict pancreas graft survival. The aim of the present study was to assess PDRI and P-PASS as predictors of transplanted pancreas survival in a Polish population.

Material/Methods: From February 1998 to September 2015, 407 pancreas transplantations were performed in Poland: 370 (90.9%) simultaneous pancreas-kidney transplantation and 37 (9.1%) pancreas transplantation alone or pancreas after kidney. The endpoint was death-uncensored 12-month graft survival with satisfactory glycemic control without insulin.

Results: Average P-PASS was 15.9±2.66 and PDRI was 0.96±0.37. Recipients who survived 12 months with good graft function had an average P-PASS score of 15.7 and PDRI of 0.95. Recipients with death-uncensored graft loss had a mean P-PASS of 16.4 and PDRI of 0.99. Univariate analysis revealed donor age, body mass index (BMI), and P-PASS to be significant risk factors for 1-year pancreas graft survival.

Conclusions: P-PASS, but not PDRI, is a reliable tool to predict pancreas graft survival in the Polish population.

MeSH Keywords: Donor Selection • Pancreas Transplantation • Tissue and Organ Procurement

Full-text PDF: https://www.annalsoftransplantation.com/abstract/index/idArt/909654

Indexed in: [Science Citation Index Expanded] [Index Medicus/MEDLINE] [Chemical Abstracts] [Scopus]

Background

Transplantation of suboptimal pancreatic grafts often result in severe transplant pancreatitis and thrombosis, which are life-threatening complications that affect both graft and recipient survival. Hence, reliable assessment of a donor and quality of the harvested pancreas is of utmost importance. Histopathology of the graft seems an obvious solution, but steatosis and fibrosis do not correlate with donor age or BMI. Fibrosis is frequent in donors <40 years old [1]. Measurement of tissue adenosine triphosphate metabolites with magnetic resonance spectroscopy prior to transplantation is reliable but too cumbersome to be applied in clinical practice [2]. Recently, measurement of donor hemoglobin A1c levels has been used as a prognostic factor of pancreatic graft survival, but it was not added to the standard criteria [3].

To minimize the risk of complications, in 2008, Eurotransplant introduced use of the pre-procurement pancreas allocation suitability score (P-PASS) as a reliable indicator of graft quality. The model was constructed from donor age and BMI, length of ICU stay, duration of cardiac arrest, serum sodium and amylase concentrations, and catecholamine requirement. P-PASS scores over 16 are considered high risk [4]. However, subsequent studies showed an increased early complication rate but no difference in graft survival with higher P-PASS [5,6]. To overcome the problem of subjective criteria of pancreas donor assessment, in 2010 UNOS introduced a pancreas donor risk index (PDRI), calculated from a huge database of 9400 transplants [7]. The index was constructed from donor sex, age, BMI, cause of death, serum creatinine, donation after cardiac death status, and cold ischemia time. A Dutch study validated both indices in a population of 350 pancreas transplant recipients. P-PASS had no predictive value, while a PDRI over 1.24 was associated with reduced graft survival both in univariate and multivariate analysis [8]. A large UK retrospective analysis showed PDRI to be a relevant predictor for simultaneous pancreas-kidney transplantation (SPKTx) but not for pancreas transplantation alone (PTA) or pancreas after kidney (PAK) transplantation modality [9]. However, a Brazilian study [10] and a Spanish study [11] failed to confirm the usefulness of PDRI. This raises the question of reliability and repeatability of these results in other populations. To validate both indices for the Polish population, we analyzed available data of pancreata transplanted in all 4 centers across the country since 1998.

Material and Methods

Although the first successful simultaneous pancreas-kidney transplantation (SPKTx) in Poland was performed in 1988, systematic accumulation of deceased donor data allowing calculation of PDRI and P-PASS in a national registry of Poltransplant was started in 1998. By the end of 2015, 407 utilized pancreas donors have been recorded: 370 SPKTx and 37 pancreas transplant alone (PTA) or pancreas after kidney (PAK) transplants. All data from the registry were retrieved and missing data, whenever available, were sought in one of 4 active pancreas transplant centers. Donor data are shown in Table 1.

Table 1. Deceased donor characteristics of utilized pancreas grafts.

	Mean ±SD (or%)	Data completeness
Age (years)	29.2±9.6	100.0%
BMI (kg/m^2)	24.1±3.2	99.3%
Male sex (%)	68.8	100.0%
CVA as cause of death (%)	34.7	100.0%
ICU stay (days)	4.6±3.7	99.3%
Donor cardiac arrest* (%)	15.5	100.0%
Dopamine dose (ug/kg/min)	2.8±3.4	72.0%
Norepinephrine dose (ug/kg/min)	0.02±0.03	72.0%
Serum creatinine (mg/dL)	1.11±0.65	99.5%
Serum sodium (mmol/L)	151.9±13.9	100.0%
Serum amylase (IU/L)	159±156	91.6%
Cold ischemia time (hours)	9.43±0.11	78.6%
P-PASS	15.9±2.6	87.2%
PDRI	0.957±0.376	78.1%

* Cardiac arrest prior to or during intensive care, donation after cardiac definition of death was never a source of pancreas graft.

P-PASS and PDRI were calculated according to original formulas described by Vinkers [4] and Axelrod [7]. Both indices were calculated for 294 donors. Follow-up data were not available for 1 patient. Twelve-month pancreas graft survival was defined as recipient and graft survival with fasting C peptide levels exceeding 0.5 ng/ml and satisfactory glycemia control without regular insulin administration.

Statistical analysis

Patient and graft survival were calculated according to Kaplan-Meier method (Statistica 12). To identify risk factors for pancreas graft loss within 12 months after transplantation, Cox regression analysis was performed and hazard ratios were calculated. Nonlinear regression models were constructed, probability of 12-month survival was calculated, and receiver operating characteristic (ROC) curves were drawn.

Indexed in: [Science Citation Index Expanded] [Index Medicus/MEDLINE] [Chemical Abstracts] [Scopus]

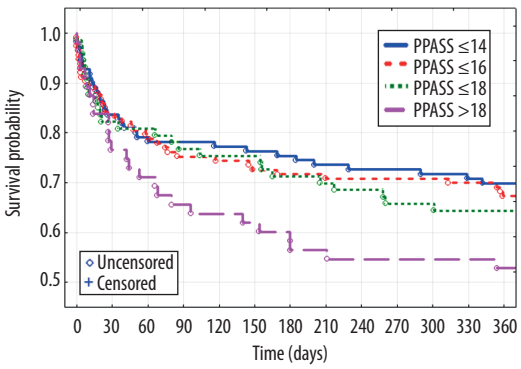

Figure 1. Twelve-month pancreas graft survival according to P-PASS quartile.

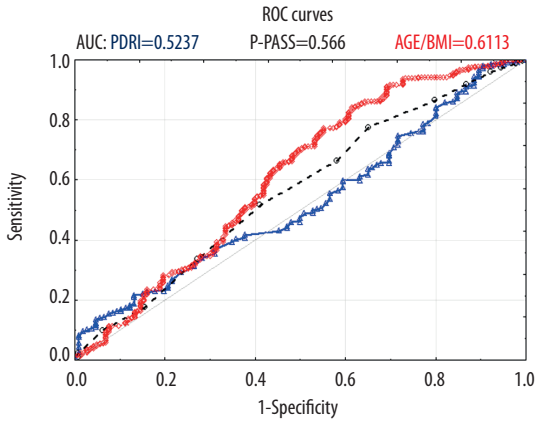

Figure 2. ROC curves and C-statistic of 3 models of prediction of 12-month death-uncensored pancreas graft survival.

Results

Death-uncensored pancreas graft survival was 66%, 55.6% and 44.4%, at 1, 5, and 10 years, respectively. The lowest 12-month graft survival (54%) was observed in the PAK/PTA group. During the first month, 16.9% of pancreatic grafts are lost due to early complications, including early patient mortality (2.5%). Pancreas transplants that survived over 12 months came from younger donors (27.7 *vs.* 32 years, p<0.001), with lower BMI (23.8 *vs.* 24.5 kg/m^2, p<0.04) and with lower P-PASS (15.7 *vs.* 16.4 points, p<0.03). PDRI was also lower in this group (0.944 *vs.* 0.992 points), but the difference was not significant (p=0.3). Cox hazard ratios were 1.039 (CI: 1.022–1.056) for donor age, 1.057 (CI: 1.005–1.111) for donor BMI, and 1.082 (CI: 1.015–1.154) for P-PASS. The confidence interval for PDRI hazard ratio was 0.798–2.158, and thus was not reliable as a prognostic factor of pancreatic graft survival. Pancreas 1-year graft survival according to P-PASS group is shown in Figure 1. Neither of the other donor-dependent factors succeeded in differentiating between surviving and non-surviving grafts.

When logistic regression models were used to calculate survival probability and ROC curves were drawn, the area under the curve (AUC) was 0.566 when P-PASS was used in estimation and 0.524 when PDRI was used. However, a simple model constructed from donor age and BMI resulted in an AUC of 0.611. Probability of death-uncensored 12-month graft survival could be calculated with Z=2.6302–0.0449×[DONOR AGE] – 0.0292×[DONOR BMI]. Graft survival estimation ROC curves of P-PASS, donor age/BMI, and PDRI prediction models are shown in Figure 2.

Discussion

Studies appraising PDRI admit its C-statistic hardly exceeds 0.5, and thus is useless in predicting graft function. It should be noted that donor age and BMI are redundant in the original PDRI equation [7], and BMI coefficient has a negative value while BMI ≥25 kg/m^2 coefficient is positive, which is inconsistent. In our study, the ROC AUC for PDRI was insignificant and almost equal to 0.5. A study by Amaral et al. did not confirm correlation of PDRI with pancreas graft survival, but the quality of the study was questionable because the percentage of incomplete records that were excluded from analysis was 73% [10]. Our data is far more complete, with nearly 100% of 1-year follow-up and 27.8% of missing records. An earlier study from the Amaral group identified independent risk factors for pancreatic graft loss: recipient BMI, induction therapy, donor age, iliac venous drainage, and transplantation of the pancreas as the first graft. A risk stratification model was constructed and ROC curves were calculated, yet the model included few donor-dependent and non-modifiable variables; therefore, its applicability was limited [12]. We did not analyze recipient-dependent factors and tailored our study to allow deciding whether to accept a potential pancreas donor. A study by Blok showed PDRI over 1.24 to be a significant risk factor for graft loss [8]. We had only 74 cases of transplantation with such high PDRIs, but 12-month survival in this group was 67.6% (not significantly different from the low-PDRI group). Although PAK and PTA transplants were not analyzed separately, PDRI index in our study proved unreliable. Instead, we confirmed the usefulness of P-PASS in predicting graft survival; when interquartile differences were analyzed, a P-PASS over 18 points predicted significantly inferior outcomes. This substantially extends the previous limit of 16 points [4]. The most efficient model of prediction we built consisted of only 2 variables – donor age and BMI – and its ROC AUC was superior to P-PASS and PDRI. Although P-PASS and donor age/BMI models proved significant, C-statistics of 0.566 and 0.611 are not impressive and only slightly superior to a 50%/50% chance. Their clinical applicability should be very limited. In our national study, grafts from the worst prognosis quartiles still have

Indexed in: [Science Citation Index Expanded] [Index Medicus/MEDLINE] [Chemical Abstracts] [Scopus]

over 50% chance of surviving beyond 1 year. Hence, the field of pancreases suitable for transplantation is most likely bigger than we use today, although caution and reasonable clinical judgement in accepting grafts at risk is needed.

Conclusions

Recipient- and surgeon-dependent factors were not analyzed in our study. Of course, quality of the recipient contributes to pancreatic graft survival. However, there are no risk prediction systems that specifically address this issue. Some general surgery risk prediction models can be applied with variable effectiveness [13].

References:

1. Kajor M, Ziaja J, Liszka Ł et al: Histopathological examination may be useful for assessment of fibrosis and lipomatosis of pancreas allograft prior to solid organ transplantation. Ann Transplant, 2015; 20: 655–60
2. Carlbom L, Weis J, Johansson L et al: Pre-transplantation 31P-magnetic resonance spectroscopy for quality assessment of human pancreatic grafts – A feasibility study. Magn Reson Imaging, 2017; 39: 98–102
3. Arpali E, Scalea JR, Redfield RR 3rd et al: The importance and utility of hemoglobin A1c levels in the assessment of donor pancreas allografts. Transplantation, 2017; 101(10): 2508–19
4. Vinkers MT, Rahmel AO, Slot MC et al: How to recognize a suitable pancreas donor: A Eurotransplant study of preprocurement factors. Transplant Proc, 2008; 40(5): 1275–78
5. Schenker P, Vonend O, Ertas N et al: Preprocurement pancreas allocation suitability score does not correlate with long-term pancreas graft survival. Transplant Proc, 2010; 42(1): 178–80
6. Woeste G, Moench C, Hauser IA et al: Can the preprocurement pancreas suitability score predict ischemia-reperfusion injury and graft survival after pancreas transplantation? Transplant Proc, 2010; 42(10): 4202–5
7. Axelrod DA, Sung RS, Meyer KH et al: Systematic evaluation of pancreas allograft quality, outcomes and geographic variation in utilization. Am J Transplant, 2010; 10(4): 837–45
8. Blok JJ, Kopp WH, Verhagen MJ et al: The value of PDRI and P-PASS as predictors of outcome after pancreas transplantation in a Large European Pancreas Transplantation Center. Pancreas, 2016; 45(3): 331–36
9. Mittal S, Lee FJ, Bradbury L et al: Validation of the pancreas donor risk index for use in a UK population. Transpl Int, 2015; 28(9): 1028–33
10. Amaral PHF, Genzini T, Perosa M, Massarollo PCB: Donor risk index does not predict graft survival after pancreas transplantation in Brazil. Transplant Proc, 2015; 47(4): 1025–28
11. Salamanca-Bustos JJ, Campos-Hernandez JP, Sánchez-Hidalgo JM et al: Validation of the pancreatic donor risk index in simultaneous pancreas-kidney transplantation performed in Córdoba hospital from 2000 to 2015. Transplant Proc, 2016; 48(9): 3037–39
12. Sousa MG, Linhares MM, Salzedas-Netto AA et al: Risk factors of pancreatic graft loss and death of receptor after simultaneous pancreas/kidney transplantation. Transplant Proc, 2014; 46(6): 1827–35
13. Khambalia HA, Moinuddin Z, Summers AM et al: A prospective cohort study of risk prediction in simultaneous pancreas and kidney transplantation. Ann R Coll Surg Engl, 2015; 97(6): 445–50

Indexed in: [Science Citation Index Expanded] [Index Medicus/MEDLINE] [Chemical Abstracts] [Scopus]