Predictive and Comparative Study Between Clinic Consensus Document for Pancreas Acceptance and Predictive Value of Preprocurement Pancreas Allocation Suitability Score (P-PASS)

C. Rodríguez-Villar[a,*], D. Paredes[a], R. Roque[a], R. Gelpi[b], A. Ruíz[a], P. Ventura-Aguiar[b], J. Ferrer[c], F. Diekmann[b], and R. Adalia[a]

[a]Donation and Transplant Coordination Section, Hospital Clinic, Barcelona, Spain; [b]Kidney Transplant Unit, Hospital Clinic, Barcelona, Spain; and [c]Hepatobiliopancreatic and Liver Transplant Department, Hospital Clinic, Barcelona, Spain

ABSTRACT

The strict selection of pancreas for transplant has forced the development of different documents to select the suitable organ in order to minimize the risks and complications of the transplant. In 2008, Eurotransplant published the Preprocurement Pancreas Allocation Suitability Score (P-PASS) for pretransplant selection. In 2001 the Hospital Clinic of Barcelona developed a Clinical Consensus Document (CCD).

Objectives. We aimed to analyze the predictive decision of the pancreas acceptance to offers received in the hospital, according to the CCD criteria and compare it with the recommended value of suitability for accepting the pancreas according to the P-PASS value.

Material and Methods. We performed a retrospective comparative study between the criteria of selection of the CCD for pancreas from 2016–2017 in comparison with the values obtained if the P-PASS had been used: ≤ 17, acceptance criteria and P-PASS; > 17, risk criteria. We defined the organ reported as rejected or accepted. The accepted organ could be procured and transplanted or discarded.

Results. With the CCD criteria, 7 more organs were transplanted than if we only applied the potential P-PASS criteria. In contrast, P-PASS would have ruled out an additional 9% of pancreases in relation to CCD criteria.

Conclusions. According our experience, it is difficult to find an adequate prediction model to select pancreas for transplantation. The application of the DCC criteria increases the number of organs valid for transplantation. At present, new criteria should be re-evaluated within multicenter studies.

THE SIMULTANEOUS pancreas-kidney transplant is the most frequent modality of pancreas transplantation, representing 75% to 80% of all transplants, followed by pancreas transplant alone and pancreas after kidney transplant modality [1].

Terminal chronic renal failure is the main indication for simultaneous pancreas-kidney transplantation, especially in patients with long-term type 1 diabetes mellitus (DM) associated with end-stage renal disease (ESRD) [2]. Although the risk of ESRD is higher in type 1 DM, the increased high prevalence of type 2 DM will contribute to a higher percentage of patients with ESRD due to diabetic nephropathy [3].

For most recipients, single kidney transplantation is the best option; however, a selected group can also benefit from the advantages of simultaneous pancreas transplantation.

*Address correspondence to Camino Rodríguez-Villar, Hospital Clinic de Barcelona, Donation and Transplant Coordination Section, Stair 8, 4th Floor, Villarroel 170, 08036, Barcelona, Spain. Tel: +34932275500; Fax: +34932275409. E-mail: crodri@clinic.cat

0041-1345/18
https://doi.org/10.1016/j.transproceed.2018.10.001

The reduction of surgical complications related to improvement of the surgical technique, as well as the reduction in acute rejection episodes with the introduction of new and more powerful immunosuppressive drugs, has allowed reducing high morbid-mortality initially associated with this combined type of transplantation.

Pancreas transplantation is in most cases the best alternative for DM with ESRD, becoming a daily practice with an ever growing number of patients with access to this therapeutic modality, resulting in an increase in the number of patients on the waiting list. This need for organs makes it necessary to consider all possibilities and expand acceptance criteria for pancreas donors [4].

Donor selection has a major impact on pancreas transplantation. The strict selection of pancreas for transplantation has forced development of different donor selection criteria documents to minimize risks and complications of pancreas transplantation.

In 2008, the Eurotransplant International Foundation introduced the Preprocurement Pancreas Allocation Suitability Score (P-PASS). This donor scoring system was based on donor factors (age, body mass index [BMI, calculated as weight in kilograms divided by height in meters squared], duration of intensive care unit (ICU) stay, duration of the cardiac arrest, serum sodium, amylase and lipase values, and type and duration of inotropic therapy. These data suggest that consideration of a combination of preprocurement factors can help identify a suitable pancreas donor. Therefore, they recommend that a pancreas donor score should be calculated for each potential pancreas donor, and donors with a P-PASS < 17 should be considered for pancreas donation [5].

The pancreas transplant program started in February 1983 in the Hospital Clinic of Barcelona, becoming one of the most active teams in Spain. Since 2001, based on many years of clinical experience contrasted with national and international published literature, the Clinic Consensus Document (CCD) for pancreas acceptance was developed by the renal transplant unit, the hepatobiliopancreatic surgical unit, and the donation and transplant coordination unit.

CCD criteria for pancreas acceptance in deceased donors after brain death include donors younger than 45 years independent of cause of death or younger than 50 years when the cause of the death is cranioencephalic trauma, with normal pancreas functionality based in normal fasting serum blood glucose, amylase and lipase levels, and absence or low daily requirements of intravenous insulin; inotropic therapy during donor stay in the ICU; and previous occurrence of cardiac arrest.

The aim of this study was to analyze the predictive capacity of our CCD criteria for pancreas acceptance and compare it with the obtained P-PASS value.

MATERIAL AND METHODS

This is a retrospective study of all pancreases offered to our hospital between January 2016 and December 2017 accepted according to CCD criteria, to evaluate retrieval pancreas acceptance and final pancreas suitability for transplantation. In order to compare with P-PASS, all scores were calculated for all pancreases offered considering P-PASS ≤ 17 as acceptance criteria and P-PASS > 17 as risk criteria.

CCD Selection Criteria

1. Age: <45 years old or >45 and <55 years old if cause of the death is traumatic
2. BMI <27
3. Evaluate previous donor cardiovascular risk factors (smoking, hypertension, alcohol intake)
4. Days in ICU
5. Cold ischemia time <8 hours
6. Normal pancreas functionality
   a. serum glucose level <300 mg/dL
   b. absence or low daily requirements of intravenous insulin
   c. serum amylase and lipase levels <3 times normal value
7. Previous cardiac arrest: duration and abdominal organ functional impact
8. Catecholamine drugs: dosage and time of administration

We considered all pancreas offers received, which could be rejected when not meeting specific CCD criteria or accepted for organ retrieval. Once the surgical team evaluated the organ, it could be considered suitable and be transplanted or discarded in the operating room.

Statistical Methods

Statistical analyses were performed using SPSS version 22 (IBM, Armonk, NY, United States). A Pvalue $<.05$ was considered significant for all analyses.

Parametric, nonparametric, and comparative tests were performed. Predictive CCD models were developed using binary logistic regression. CCD was evaluated as continuous variables for their ability to predict allocation outcome using area under the receiver operating characteristic curve analysis. Sensitive and specific P-PASS values were calculated for offered accepted pancreas according to CCD.

RESULTS

Characteristics of the Study Population

During the study period, 2016–2017, there were 78 potential pancreas donors. A total of 41 of 78 (52.6%) organ offers were rejected and 37 of 78 (47.4%) were accepted. From these, only 24 of 37 (64.8%) were suitable for transplantation and 13 of 37 (35.1%) were discarded. Donor demographic, clinical, and functional data are shown in Table 1.

When we analyze and compare donor variables between offers rejected or accepted and between those accepted, pancreases considered suitable or discarded, only significant differences were found in the group of transplanted pancreases having the higher percentage of female presence ($P = .02$), the lowest BMI ($P = .04$), and the lowest P-PASS values ($P = .03$) compared with the other subgroups. Donor demographic, clinical, and functional data discriminated according to subgroups are shown in Table 2.

Table 1. Study Population Characteristics

Donor Variables	N = 78
Age, mean (SD), y	40.2 (9.62) (range, 19–55)
Gender, No., ♂/♀	40/38
BMI, mean (SD)	25.28 (4.45) (range, 16–40)
ICU stay, mean (SD), d	4.14 (3.80) (range, 1–16)
Na, mean (SD), mEq/L	150.56 (9.39) (range, 128–169)
Amylase, mean (SD), IU/L	93.37 (119.95) (range, 11–823)
Lipase, mean (SD), IU/L	48.06 (37.53) (range, 10–125)
Previous cardiac arrest, No. (%)	15/78 (19.2)
Cardiac arrest time, mean (SD), min	21.57 (11.78) (range, 4–42)
Catecholamine drugs, No. (%)	63/78 (87.5)
P-PASS, mean (SD)	17.75 (2.49) (range, 12–23)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ICU, intensive care unit; P-PASS, Preprocurement Pancreas Allocation Suitability Score.

Results of CCD Predictive Model

When we considered the decision to accept or reject an offer as a dependent variable and age, sex, BMI, days in ICU, serum sodium, amylase or lipase value, existence of previous cardiorespiratory arrest, and the use of catecholamine drugs in the donor as independent variables, the model only explains between 0.267 R^2 of Cox and Snell and 0.366 R^2 of Nagelkerke (OD 0.567; 95% CI; $P = .06$).

Results if P-PASS Has Been Applied for Pancreas Offered and Transplant Suitability Prediction

Table 3 shows the percentage of offers according to CCD and calculated P-PASS. For pancreases offered, we accepted 37 of 78 (47%) offers using CCD criteria; considering a valid P-PASS $\leq$ 17, we would only have accepted 21 of 78 (27%). This translates into 20% less organs valid for evaluation. Even more, for those evaluated during retrieval, 24 pancreases have been transplanted by CCD criteria in comparison with only 17 if we would have used a valid P-PASS $\leq$ 17. On the other hand, when we analyzed the unaccepted offers, 41 of 78 (53%) were rejected using CCD criteria; considering a risk P-PASS $>$ 17 we would have rejected 32 of 78 (41%). This translates into 12% less organs rejected by P-PASS $\leq$ 17: 32 cases vs 41 using CCD criteria.

According to CCD criteria and surgical evaluation during retrieval, 7 of 78 (9%) of the pancreases offered with a P-PASS $>$ 17 were finally considered suitable for transplantation. On the other hand, 9 of 78 (11.5%) of the rejected offers had a valid P-PASS $\leq$ 17. When both subgroups were compared, no significant differences were found in terms of age, BMI, days in the ICU, serum sodium and amylase values, previous cardiorespiratory arrest duration, and use of catecholamine drugs.

Analyzing the causes for rejecting offers within the P-PASS $\leq$ 17 subgroup, 2 cases had elevated serum amylase level, 3 cases had elevated BMI, 2 cases had cardiovascular risk factor, 1 case had an expected long cold ischemia time, and 1 case had a combination of different causes.

Sensitive and specific P-PASS values were calculated for offered accepted pancreases according to the CCD. The CCD was evaluated as continuous variables for its ability to predict allocation outcome using area under the receiver operating characteristic curve analysis. The receiver operating curve showed an area under the curve of 0.307 (95% CI, 188–427; $P = .003$).

Analyzing post-transplant evolution and surgical complications of the transplanted pancreases, 3 cases required early transplantectomy and 12 cases presented surgical minor complications; 2 and 4 cases, respectively, were within the P-PASS $>$ 17 subgroup.

DISCUSSION

In spite of being a single-center and retrospective design that created some study limitations, we showed a clinical

Table 2. Differences Between Accepted Pancreas Offer Considered Valid for Transplantation, Accepted Organ Offer Not Valid for Transplantation, and Rejected Offer Subgroups

Characteristics	Offer Accepted Valid	Offer Accepted Not Valid	Offer Rejected	*P* Value
Cases	24	13	41	>.05
Age, mean (SD), y	38.1 (9.15)	41.8 (6.84)	40.9 (10.59)	>.05
Gender, No., ♂/♀	5/19*	9/4	26/15	.02
BMI, mean (SD)	22.90 (3.07)*	25.60 (3.15)	26.68 (4.97)	.04
ICU Stay, mean (SD), d	3.33 (2.88)	3.46 (2.96)	4.89 (4.52)	>.05
Na, mean (SD), mEq/L	153.87 (7.95)	146.07 (9.09)	149.92 (9.99)	>.05
Amylase, mean (SD), IU/L	62.37 (50.25)	67.27 (40.32)	125.81 (162.88)	>.05
Lipase, mean (SD), IU/L	40.00 (26.22)	32.75 (31.54)	61.42 (45.13)	>.05
Previous cardiac arrest, No. (%)	2/24 (8)	4/13 (31)	9/41 (19)	>.05
Cardiac arrest time, mean (SD), min	30.00 (14.14)	19.25 (10.72)	20.63 (12.47)	>.05
Catecholamine drugs, No. (%)	20/24 (83)	13/13 (100)	30/41 (73)	>.05
P-PASS	17.16 (2.27)* (range, 16–18)	19.18 (2.58) (range, 18–23)	19.48 (2.20) (range, 19–21)	.03

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ICU, intensive care unit; NS, not significant; P-PASS, Preprocurement Pancreas Allocation Suitability Score.
**P* value significant, multiple comparisons, Bonferroni test.

Table 3. CCD in Comparison With Potential P-PASS

	CCD	P-PASS ≤ 17	P-PASS > 17
Cases offered, No.	78	30	48
Offers rejected, No. (%)	41/78 (52.5)	9/78 (11.5)	32/78 (41)
Offers accepted, No. (%)	37/78 (47)	21/78 (27)	16/78 (20.5)
Transplanted, No. (%)	24/78 (31)	17/78 (22)	7/78 (9)

Abbreviations: CCD, Clinical Consensus Document; P-PASS, Preprocurement Pancreas Allocation Suitability Score.

model to increase pancreas allocation offer acceptance, consequently increasing possibilities for organ suitability and transplantation when compared with P-PASS acceptance criteria.

In our center, pancreas donation comes exclusively from deceased donors after brain death, with half the allocation offers accepted and two-thirds considered suitable for transplantation. Similar results are reported in the Spanish National Pancreas Donation Activity Report [6].

The CCD model is based on medical expertise and not on a scoring validated system such as P-PASS. Our model includes different associated medical risk variables described for valid pancreas suitability and transplantation results reported by our center, the literature, and the Spanish National Consensus Document for Pancreas Transplantation, published in 2015 by the National Transplant Organization [7]. However, none of the medical variables included in the CCD have been proved as predictive criteria for accepting a valid pancreas offers. Different studies have not demonstrated predictive donor characteristics for accepted pancreas transplantation [8,9].

In contrast, the P-PASS suggests some evidence that consideration of a combination of preprocurement factors can help identify a suitable pancreas donor. They recommend that a pancreas donor score should be calculated for each potential pancreas offer and donors with a P-PASS < 17 should be considered for pancreas donation [5]. In 2010 in the United States, the United Network of Organ Sharing developed a pancreas donor risk index to predict 1-year graft survival based on donor medical criteria, cold ischemic time, and type of pancreas graft, which has demonstrated good correlations with pancreas acceptance and graft function [10].

Our data suggested that using CCD criteria could expand the organ donor pool with the consequent increase in the use of pancreas grafts from donors with a P-PASS ≥ 17. However, pancreatic resections after transplant were more frequent among those recipients from donors with higher P-PASS. Similar results were published by Schenker et al, who also described that higher P-PASS values were associated with graft loss predicted by the pancreas donor risk index [11,12]. Nevertheless, when we apply CCD criteria we also reject a number of pancreas allocation offers for different medical reasons, despite the low P-PASS value. CCD analysis likely underestimates the number of organs accepted in comparison with the P-PASS. In order to maximize pancreas use, CCD criteria are more likely to be applied in aggressive centers with high transplant volume (>20 transplants/y) [13].

Finally, considering the loss of some pancreas offers based on CCD decision-making and the poor sensitive and specific P-PASS calculated for our offered accepted pancreas according to CCD, the simultaneous use of P-PASS introduced to support clinical analysis could expand the currently insufficient pancreas donor pool. In our opinion, we need more robust methods for identifying objective criteria to assess the quality of donor pancreases.

REFERENCES

[1] Dean PG, Kukla A, Stegall MD, Kudva YC. Pancreas transplantation. BMJ 2017;357:j1321. https://doi.org/10.1136/bmj.j1321.

[2] Gruessner RWG, Sutherland DER, Gruessner AC. Mortality assessment for pancreas transplants. Am J Transplant 2004;4:2018–26.

[3] Ricart MJ. Trasplante de páncreas-riñón. Nefrologia 2001;21(Suppl. 3):108–11.

[4] Mittal S, Johnson P, Friend P. Pancreas transplantation: solid organ and islet. Cold Spring Harb Perspect Med 2014;4:a015610. https://doi.org/10.1101/cshperspect.a015610.

[5] Vinkers MT, Rahmel AO, Slot MC, Smits JM, Schareck WD. How to recognize a suitable pancreas donor: a Eurotransplant study of preprocurement factors. Transpl Proc 2008;40:1275–8.

[6] Organización Nacional de Trasplantes. Spanish National Pancreas Donation Activity Report. www.ONT.es [accessed 18.08.01].

[7] Spanish National Consensus Document for Pancreas and Islets Transplantation. Edición Grupo Aula Médica. 1st ed. Madrid; 2005.

[8] Fischer-Frohlich CL, Lauchart W, Steurer W, Viebahn R. Donor detection for pancreas transplantation. Is an automated prediction of suitable donor by donor characteristics known before procurement possible. Cells Tissues Organs 2009;12:171–86.

[9] Sanchez-Hidalgo JM, Rodríguez-Ortiz l, Arjona-Sanchez A, Ruíz-Rabelo J, Salamanca-Bustos JJ, Rodríguez-Benot A, et al. Pancreas donor hypernatremia: is it really a risk factor for simultaneous pancreas-kidney transplantation? Transplant Proc 2018;50:676–8.

[10] Axelrod DA, Sung RS, Meyer KH, Wolfe RA, Kaufman DB. Systematic evaluation of pancreas allograft quality, outcomes and geographic variation in utilization. Am J Transplant 2010;10:837–45. https://doi.org/10.1111/j.1600-6143.2009.02996.x.

[11] Schenker P, Vonend O, Ertas N, Wunsch A, Viebahn R. Preprocurement pancreas allocation suitability does not correlate with long-term pancreas graft survival. Transplant Proc 2010;42:178–80.

[12] Ayami MS, Grzella S, Kykalos S, Viebahn R, Schenker P. Pancreas donor risk index but not pre-procurement pancreas allocation suitability score predicts pancreas graft survival: a cohort study from a large German pancreas transplantation center. Ann Transplant 2018;23:434–41.

[13] Serrano OK, Vock DM, Dunn TB, Kandaswamy R, Finger EB. Maximizing utilization in pancreas transplantation: phenotypic characteristics differentiating aggressive from nonaggressive transplant centers. Transplantation 2018;102:2108–19. https://doi.org/10.1097/TP.0000000000002334.