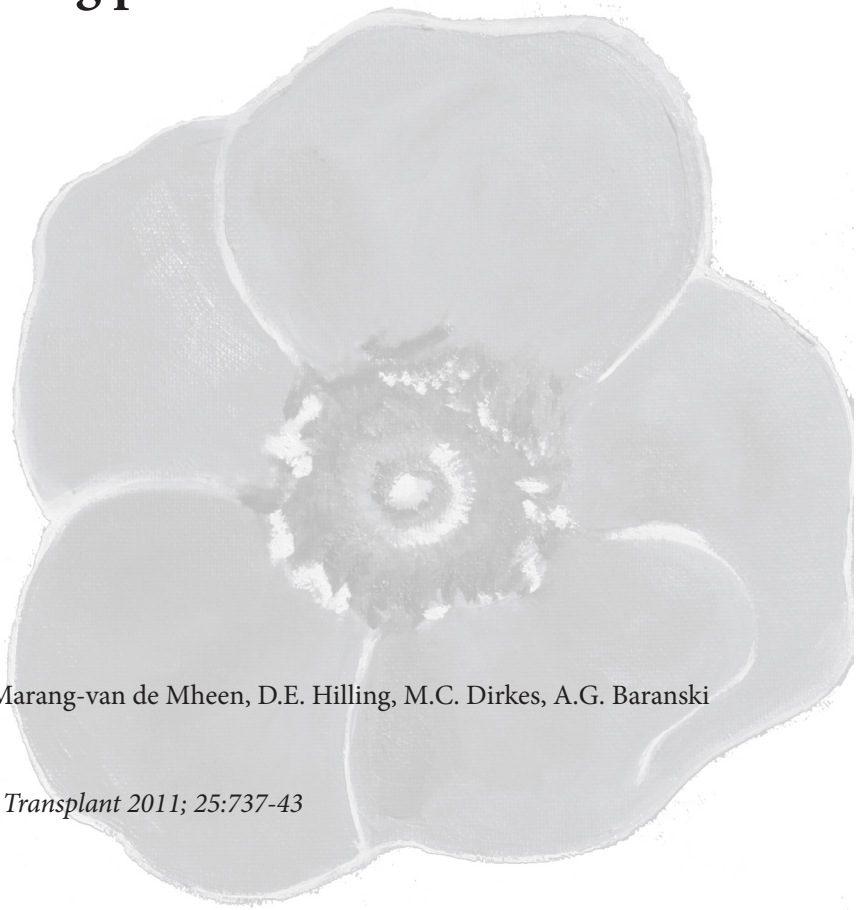
# Chapter 3

## Surgical injuries of pancreatic allografts during procurement



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## ABSTRACT

### Background

Quality of most procured pancreata is considered acceptable or good by surgeons, but remains difficult to ascertain. Little is known on how often pancreata are refused for transplantation during back-table inspection. Purpose of this study was to determine the frequency and type of problems responsible for refusal during back-table inspection, and to identify possible risk factors.

### Methods and Materials

All 134 pancreata accepted and procured for whole-organ transplantation and transported to the Leiden University Medical Center in the period February 2002 until May 2008 were included. These were retrospectively analyzed on: donor characteristics, procurement characteristics and (non-)critical problems.

### Results

A total of 111 (82.8%) pancreata were transplanted while 23 (17.2%) were refused for transplantation during back-table inspection, regardless of procurement region ($\chi^2$ = 0.16 p = 0.93). Fourteen pancreata (13.4%) were refused solely due to surgical injuries. In refused pancreata, on average 2.7 critical problems per pancreas were found and 0.6 non-critical problems (versus 0.3 in transplanted pancreata, $t$ = 1.83 p = 0.08). Chances of refusal increased in pancreata from older donors (Odds Ratio 1.08 [1.02 – 1.14]) procured in centers not performing pancreas transplantations (Odds Ratio 7.95 [2.43 – 25.97]).

### Conclusions

We conclude that pancreatic allografts are frequently refused during back-table inspection, partly due to surgical injuries suggesting that quality of procurement may be improved.

# INTRODUCTION

Since the first pancreas transplantation in 1966 (1), this procedure has developed into an acceptable treatment for diabetes type I. In the period 2002-2008, on average 21 pancreas transplantations are performed annually in the Netherlands of which 18 Simultaneous Pancreas Kidney (SPK) transplantations (2). Most (85%) of the pancreas transplantations in this period are carried out in the Leiden University Medical Center. The surgical procurement technique of this fragile organ is essential for good graft outcomes, but may be challenging for local procurement teams.

Pancreas procurement may be cancelled for reasons such as abnormal arterial vascularization between the liver and the pancreas making it impossible to successfully split and transplant both organs, problems relating to the organ itself (e.g. fibrosis) or neoplasms in the donor discovered during the organ donation procedure (3). Surgical injuries that occur during pancreas procurement may lead to complications after transplantation, impaired function of the allograft, graft loss or even death of the patient. These injuries may be so severe that the pancreas is not transplanted in order to protect the recipient. Proper procurement and constant training of surgeons are therefore very important to maintain high quality of abdominal organ procurement.

In the Netherlands, a pancreas is offered to the first patient on the national waiting list. If the pancreas is refused by the first center, then it is refused for all patients in that center (so regardless of any recipient risk factors) and is consequently offered to the next patient on the waiting list. Once accepted and transported to a center, a pancreas is only refused during back-table inspection if it is considered too dangerous for the patient to transplant the pancreas given for instance severe injuries that are encountered. Other recipient factors do not play a role anymore at this stage.

Little is known on how often pancreata are refused during back-table inspection. A recent report from Germany shows that vascular lesions were observed in three of the 18 (16.7%) pancreatic grafts, which could be transplanted after back-table repair procedures, but also suggests that procurement may be improved by better surgical training and standardization in procurement techniques (4). Schultz et al. (5) showed that 8% of the pancreatic grafts procured by teams that were not part of the pancreas transplant team, were discarded for transplantation during back-table preparation. Liposis of the graft and critical vessel situations (e.g. severe atherosclerosis) were reported as the main reasons for pancreas refusal. In the Netherlands, information on the type of problems encountered during back-table inspection is always returned to the procurement center on the standard Pancreas Quality Form for each pancreas procurement as feedback to the procurement team. However, this does not give procurement teams information on whether this was just a problem for this particular case, or that this type of problems occur more in their center than in others, because data on the most frequently encountered problems on a national level are not available.

Purpose of the present study therefore was to retrospectively evaluate all accepted pancreata transported to our center for transplantation in the period February 2002 until May 2008, to determine how often pancreata were refused for transplantation during back-table inspection and which type of problems were responsible for the decision not to transplant the pancreas. Furthermore, we aimed to determine whether donor characteristics, injuries or other factors in the procurement process may increase or decrease the probability of pancreas refusal. These findings may be used in training programs of organ procurement surgeons to avoid injuries and thereby improve the quality of procured pancreata.

## MATERIALS AND METHODS

### Technical aspects

All pancreata accepted, procured and transported for transplantation to the Leiden University Medical Center in the period February 2002 until May 2008 were included. Allografts primarily destined for islet transplantation were excluded. All allografts were procured in one of the contributing centers within the Eurotransplant zone and procured using standard procurement techniques (3, 6). According to the Dutch pancreas procurement protocol in that period, all abdominal organs are first mobilized, the common bile duct is ligated close to the pancreas head and transected. After organ perfusion, the duodenum is sterilized before it is closed with 50-80 ml povidone-iodine water solution together with Amphotericin B given through the nasogastric tube with the aim to decontaminate the duodenum content (3). After closure of the duodenum, the stomach, small bowel and colon are completely dissected and placed outside the abdomen. Then, liver and pancreas are separated starting with further dissection of the hepatoduodenal ligament. The gastroduodenal artery is transected and the pancreatic distal stump is tagged with a suture. The length of the portal vein and level of transection must be agreed upon by the procurement team, but is usually 2-3 cm above the pancreas head. Next, the celiac axis with the common hepatic artery is dissected along the superior edge of the pancreas head until the celiac trunk. The splenic artery is transected close to its origin and tagged with a suture to facilitate later identification. The spleen is always procured with the pancreas. To finish the pancreas procurement, the superior mesenteric artery (SMA) is transected carefully with a small aorta patch (3). As viability of the pancreatic allograft depends on restoration of the blood flow through the superior mesenteric and splenic artery, the procured vessels (mostly iliac arteries and veins) must have sufficient length to allow this mandatory reconstruction. In case of abnormal anatomical arterial vascularization of the pancreas (occurring in about 17% of the cases) when the dorsal pancreatic artery arises from the celiac trunk or common hepatic artery, the celiac trunk and the SMA on the aorta

patch were procured with the pancreas to ensure its best arterial vascularization (3). In all other cases, the dorsal pancreatic artery is not seen during organ procurement, so that the celiac trunk is procured with the liver. In our series, a simultaneous intestine-pancreas procurement did not occur. A right aberrant hepatic artery was never considered a contraindication for pancreas procurement.

In the Leiden University Medical Center, all organs are inspected by the transplant surgeon prior to taken the recipient to the operating room. All problems (or none if no problems were encountered) are reported on the Pancreas Quality Form, which is routinely used in the Netherlands and always faxed to the procurement center as feedback on the procurement. This form distinguishes between arterial problems, venous problems, duodenal problems, quality of parenchyma and other problems.

**Data and definitions**

For all pancreata, donor characteristics (age, gender, Body Mass Index (BMI)), preservation solution, pancreas anatomy and quality of procured organ, as assessed by the surgeon performing organ procurement, were obtained from the Eurotransplant Pancreas report. Furthermore, data were collected on type of problems reported by the pancreas transplant surgeon on the Pancreas Quality Form. Procurement centers were categorized into 3 regions: Netherlands West (Leiden, Rotterdam, Amsterdam, Utrecht), Netherlands East (Maastricht, Nijmegen, Groningen), and International (all pancreata procured outside the Netherlands). Furthermore, procurement centers were grouped based on whether or not they also performed pancreas transplantations (yes/no). Centers were categorized as not performing pancreas transplantations if they had not performed any pancreas transplantation in the entire period 2002-2008. Data on the number of pancreas transplantations per year per procurement center were obtained from Eurotransplant.

Problems reported on the Pancreas Quality Form were retrospectively categorized into critical and non-critical problems. Problems were considered critical if they were so severe that even when encountered alone, this was sufficient reason to refuse the pancreas for transplantation. Non-critical problems in itself are not responsible for pancreas refusal, but added to other problems may lead to refusal of the pancreas for transplantation. With respect to the type of problems, we distinguished between arterial injuries (head, neck, body or pancreas tail), venous injuries (portal, mesenteric superior or splenic vein), pancreas parenchyma injuries, duodenal and other problems, consistent with the categories on the Pancreas Quality Form. Atherosclerosis was considered severe if vascular reconstruction between the "tool-kit" and the pancreas was impossible, thereby increasing the risk on thrombosis.

### Statistical analysis

We first estimated the frequency of pancreas refusal by the type of problem. Consequently, the frequency of refusal for transplantation was compared between procurement regions using chi-square tests, to assess whether some regions could improve more than others. Transplanted and refused pancreata were then compared on donor characteristics (age, gender, BMI), preservation solution, procurement region, procurement center performing pancreas transplantations (yes/no), average number of pancreas transplantations per year in procurement center, pancreas quality as assessed by the procurement surgeon, as well as on the number and type of critical and non-critical problems. Chi-square tests were used for categorical variables and *t*-tests for continuous variables. Variables that significantly differed between transplanted and refused pancreata were consequently entered in multivariate logistic regression analyses to assess whether these had an independent effect on the probability of refusal when adjusted for the other variables.

## RESULTS

Of the 134 pancreata transported to our center, 111 (82.8%) were transplanted while 23 (17.2%) were refused during back-table inspection, regardless of procurement region ($\chi^2 = 0.16$ p = 0.93) (Table 1). The probability of refusal did not depend on whether the pancreas was procured in our own region (West of the Netherlands) or in another region (respectively 19% versus 16.3%, $\chi^2 = 0.15$ p = 0.70). In the 23 pancreata refused for transplantation, 63 critical problems occurred, ranging between one and five per pancreas. Fourteen pancreata (13.4%) were refused solely due to critical surgical injuries without any other critical problems. An example of a pancreas with one critical injury was a pancreas in which the parenchyma of the pancreas tail was completely destroyed. Within all regions, pancreata refused for transplantation more often were procured in centers not performing pancreas transplantations, or showed a trend towards significance (data not shown).

Nearly one-third of the pancreata refused for transplantation had severe atherosclerosis as a critical problem thereby increasing the risk on pancreas thrombosis,

**Table 1.** Pancreatic allografts by region of organ recovery: number of organs transplanted and refused for transplantation at back-table inspection (Leiden University Medical Center, February 2002 – May 2008)

| Region of organ recovery | Transplanted Number (%) | Refused Number (%) | Total Number |
|---|---|---|---|
| Netherlands East | 56 (83.6%) | 11 (16.4%) | 67 |
| Netherlands West | 34 (81.0%) | 8 (19.0%) | 42 |
| International | 21 (84.0%) | 4 (16.0%) | 25 |
| Total | 111 (82.8%) | 23 (17.2%) | 134 |

such that reconstruction became impossible (Table 2). Most critical injuries in the pancreata refused for transplantation concerned severe injuries of the pancreas parenchyma, superior mesenteric or splenic vein, and splenic or dorsal pancreatic artery such that reconstruction and transplantation became impossible (Table 2). In addition, 14 non-critical problems occurred in these pancreata, ranging from 0 to 3 per pancreas. In comparison, 33 non-critical problems occurred in transplanted pancreata, which did not differ from the pancreata refused for transplantation (on average 0.3 versus 0.6 in rejected pancreata, $t = 1.83$ $p = 0.08$). Most frequently occurring non-critical problems were portal vein injuries (or too short but with possibilities for reconstruction) or other problems like an open choledochal duct because of not ligating the common bile duct or severe atherosclerosis (which increases the risk on pancreas thrombosis) but with possibilities for reconstruction (Table 2).

The procurement surgeon also makes an assessment of the quality of the pancreas after procurement, reported in the Eurotransplant Pancreas report, which can be rated as poor, acceptable or good. Of the 23 pancreas allografts refused for transplantation,

**Table 2.** Frequency of critical and non-critical problems encountered in pancreatic allografts during back-table inspection (Leiden University Medical Center, February 2002 – May 2008)

| | | **Pancreas transplanted** (n=111) | **Pancreas refused** (n=23) |
|---|---|---|---|
| **Critical problems** | | | |
| Average number per pancreas (SD) | | - | 2.7 ± 1.6 |
| *Injuries* | | | |
| Severe injuries pancreas parenchyma | | - | 17 (73.9%) |
| Arterial | – head, neck, body pancreas | - | 1 (4.3%) |
| | – tail pancreas | - | 8 (34.8%) |
| Venous | – Portal vein | - | 7 (30.4%) |
| | – Splenic vein | - | 9 (39.1%) |
| | – Mesenteric superior vein | - | 7 (30.4%) |
| *Other problems* | | | |
| Duodenal problems (e.g. open duodenum) | | - | 6 (26.1%) |
| Severe artherosclerosis, reconstruction impossible | | - | 7 (30.4%) |
| **Non-critical problems** | | | |
| Average number per pancreas (SD) | | 0.3 ± 0.5 | 0.6 ± 0.8 |
| *Injuries* | | | |
| Minor injuries pancreas parenchyma | | 6 (5.4%) | 1 (4.3%) |
| Arterial | – head, neck, body pancreas | 2 (1.8%) | 1 (4.3%) |
| | – tail pancreas | 4 (3.6%) | 1 (4.3%) |
| Venous | – Portal vein (e.g. too short) | 9 (8.1%) | 0 (0%) |
| | – Splenic vein | 0 (0%) | 1 (4.3%) |
| | – Mesenteric superior vein | 0 (0%) | 1 (4.3%) |
| *Other problems* | | | |
| Duodenal problems (e.g. no povidone iodine) | | 8 (7.2%) | 2 (8.7%) |
| Other (artherosclerosis but reconstruction possible, open ductus choledochus) | | 9 (8.1%) | 9 (39.1%) |

Values are mean ± SD

20 (87.0%) were assessed as a good-quality organ by the procurement surgeon (Table 3). Quality was not reported for the other three pancreas allografts. Part of the reason for the missing quality assessment may be that the procurement surgeon was not sure about the quality but thought that the pancreas may be potentially usable and needed to be examined on the back-table by someone more experienced. Of the 111 pancreas allografts that were transplanted, 31 (27.9%) had missing quality assessment, 2 (1.8%) were assessed as acceptable quality and 78 (70.3%) as good quality pancreas by the procurement surgeon.

All pancreas allografts were procured from deceased heart-beating donors. Pancreata refused for transplantation during back-table inspection on average were procured from older donors, with higher BMI, more often procured during office hours and by centers with significantly less experience in pancreas transplantation, compared with transplanted pancreata (Table 3). However, when looking at donor BMI $\geq$ 25, a risk factor for surgical complications and technical failure in pancreas recipients (7), the difference between refused and transplanted pancreas allografts was no longer statistically significant (Table 3). A higher percentage of male donors and on average more non-critical problems in refused pancreata showed a trend towards significance (Table 3). Because part of these differences may be caused by differences in some of the other variables, these variables were entered in a multivariate regression analysis. Only pancreata from older donors and procurement by centers not performing pancreas transplantation, were independent risk factors for pancreas refusal (Table 4). The probability of refusal increased by 8% per year increase in age of the donor, and was increased 8-fold for procurement teams from centers not performing pancreas transplantations.

## DISCUSSION

This study has shown that pancreatic allografts are frequently refused during back-table inspection, partly because of surgical injuries. Most critical problems concerned severe injuries of pancreas parenchyma, superior mesenteric or splenic vein, and splenic or dorsal pancreatic artery such that reconstruction and transplantation became impossible, or severe atherosclerosis. Donor age and procurement by centers not performing pancreas transplantations were both found to significantly increase the probability of pancreas refusal. Quality of procurement may thus be improved by constant (compulsory) training of procurement surgeons by surgeons who perform pancreas transplantations, showing which type of injuries occur frequently, how to prevent these, and how to procure organs with severe atherosclerosis.

The frequency of refusal (17.2%) is higher than the 8% reported by Schultz et al. (5). They reported liposis of the graft and critical vessel situations as the main reasons for pancreas refusal, whereas parenchyma injuries and severe atherosclerosis were the

**Table 3.** Differences between pancreatic allografts transplanted and refused for transplantation at back-table inspection (Leiden University Medical Center, February 2002 – May 2008)

| | **Pancreas transplanted** (n=111) | **Pancreas refused** (n=23) | **Test of difference** |
|---|---|---|---|
| **Donor characteristics** | | | |
| Age (years) | 31.7 ± 12.6 | 39.5 ± 8.7 | t=3.56 p<0.01 |
| Age ≥ 35 years | 48.6% | 73.9% | $X^2$=4.88 p=0.03 |
| Male gender | 49.5% | 69.6% | $X^2$=3.06 p=0.08 |
| Body Mass Index (kg/m²) | 23.0 ± 3.0 | 24.3 ± 2.0 | t=2.72 p<0.01 |
| BMI ≥ 25 | 24.3% | 30.4% | $X^2$=0.38 p=0.54 |
| Cause of death | | | |
| Brain bleeding | 50.5% | 65.2% | $X^2$=1.67 p=0.20 |
| Trauma | 36.0% | 26.1% | $X^2$=0.84 p=0.36 |
| **Procurement** | | | |
| UW preservation fluid | 94.6% | 91.3% | $X^2$=1.54 p=0.67 |
| Good organ quality, assessed by procurement surgeon | 70.3% | 87.0% | $X^2$=2.80 p=0.25 |
| Procurement time during the day[a] | 27.0% | 47.8% | $X^2$=3.88 p<0.05 |
| Procurement center performing PTx | 66.7% | 21.7% | $X^2$=15.89 p<0.01 |
| Average number of PTx per year in procurement center | 4.7 ± 5.9 | 0.5 ± 1.0 | t=-7.06 p<0.01 |
| Number of non-critical problems | 0.3 ± 0.5 | 0.6 ± 0.8 | t=1.83 p=0.08 |

Values are mean ± SD

[a] Procurement between 8.00 and 18.00

**Table 4.** Determinants of pancreatic allografts being refused for transplantation (Leiden University Medical Center, February 2002 – May 2008)

| | **Odds Ratio [95% Confidence Interval]** |
|---|---|
| Donor age (years) | **1.08 [1.02 – 1.14]** |
| Male donor | 2.67 [0.85 – 8.43] |
| Donor Body Mass Index (kg/m²) | 1.07 [0.86 – 1.33] |
| Procurement time (day[a] versus night) | 2.45 [0.81 – 7.47] |
| Procurement center performing PTx (no versus yes) | 7.95 [2.43 – 25.97] |
| Number of non-critical problems | 2.18 [0.96 – 4.93] |
| Model fit: Nagelkerke R-square=0.391 | |

Odds Ratio's in bold indicate significant differences

[a] Procurement between 8.00 and 18.00

most frequent critical problems in our study, besides severe injuries of (pancreatic) vessels. One of the explanations may be a more strict selection of pancreatic grafts in our center. If this were true, transplanted pancreata from our center may be expected to have better graft survival rates. Schultz et al. (5) reported a 83% one-yr graft survival rate which is comparable to the rates reported by the International Pancreas Transplant Registry (IPTR) over the period 2000-2004 (8, 9). We have shown previously that pancreata transplanted in our center seem to have better graft survival

rates than the IPTR, in particular with primary bladder-drainage followed by elective enteric conversion 6-12 months later, used in most of the patients (10). All pancreas recipients in this study were insulin-dependent diabetes mellitus type I with end-stage diabetic nephropathy, and the rate of post-operative complications was comparable to that in other studies. Complications like enteric or bladder leaks, possibly related to procurement techniques, occurred as frequently as reported in other studies (10). Selection may thus explain part of the difference with the study by Schultz et al. However, given the large number of 63 critical problems found in 23 refused pancreata (on average 2.7 per pancreas), this does not seem to be the entire explanation. Another explanation may be that the study by Schultz et al concerned an earlier period (1994-2003) when it may have been customary that pancreata were procured by teams with experience in pancreas transplantation, or that solely by chance they were offered more organs procured in centers experienced in pancreas transplantation. Another option relating to this difference in time period is that the population of donors has become more marginal over time (11). Since we did not have more detailed data, this could not be further explored.

Donor age was found to increase the chances of pancreas refusal. One of the explanations is that it is a true age effect, e.g. reflecting increased atherosclerosis at older ages. Another option may be that procurement is more difficult in older donors, for because of the fattening of the pancreas. It is known that acceptable outcomes can be achieved with pancreatic grafts from older donors but that graft survival is reduced on average (11). If it is true that procurement is more difficult in older donors, it is likely that experienced procurement surgeons are performing organ procurement in older donors. Selection of experienced procurement surgeons may then interact with donor age, but would underestimate chances of refusal for pancreata procured from older donors rather than that it would increase refusal rates. Another explanation would be that transplant surgeons use more stringent criteria to accept an organ from an older donor, requiring the organ to be more 'perfect' than from a younger donor given that they know that graft survival is reduced on average (11). This hypothesis seems likely, but is difficult to test.

Higher chances of refusal were also found for procurement centers without experience in pancreas transplantation in the entire period. This makes sense because a pancreas transplantation surgeon may be more aware of potential consequences of procurement for pancreas transplantation, given that he has faced these problems and knows what is possible and what is not. On the other hand, it may seem contrary to results from previous studies, which have shown that early outcomes after SPK transplantation are not influenced by the surgical team (from the transplant center versus another center) (12). However, no information was given on the experience of the 'other center', which may have performed pancreas transplantations in recent years, whereas the reference category in our study concerned procurement centers

without any pancreas transplantations in recent years. Furthermore, given that the pancreata were transplanted, it may be assumed that the organs were well procured in the study by Fellmer et al. (12), whereas our study focused on pancreas refusal due to procurement problems. To our knowledge, this is the first study showing that chances of refusal are higher when pancreata are procured in centers without experience in pancreas transplantation.

Experience of the individual performing the procurement would be an important variable in this context, but unfortunately no data were available on the level of training of the procurement surgeon. In the Netherlands, as in other countries, trainees may be sent to procure pancreas allografts, supervised by a more experienced procurement surgeon. However, the latter surgeon may be more experienced but not necessarily in pancreas transplantation. It is therefore not clear whether procurement surgeons are experienced enough to always perform a well-procured pancreas, even in difficult cases. The decision to refuse the pancreas is thus made based on organ quality only. Experience or name of the procurement surgeon is not considered since even the most experienced surgeon may make a mistake or overlook something, and excellent quality procurement may be performed by relatively inexperienced surgeons.

It is important to note in this context that there is a difference between a pancreas with unrecognized damage, which is potentially dangerous if the injury goes unnoticed and expensive, and a pancreas that is considered potentially usable but needs to be examined during back-table inspection by a more experienced pancreas transplant surgeon. It seems more appropriate to let a more experienced pancreas transplant surgeon examine a graft from, e.g., an older donor, than to accept the opinion of a less experienced procurement surgeon that it is not transplantable. A recommendation may therefore be to add the option 'potentially usable, requires further examination' to the Eurotransplant Pancreas report in the assessment of organ quality, along with a specification of which part of the pancreas requires further examination.

Pancreata procured during office hours at first seem to be the best procured organs with the lowest chances for refusal, because these teams should be fresh. However, even though non-significant, our data seem to suggest the contrary. One of the explanations may be that procurement surgeons during the day are more junior, since the senior surgeons have other daytime commitments, suggesting procurement by less-experienced surgeons during the day. No data were available to test this hypothesis of seniority of retrieval teams, but it would give support to the evidence presented above that less experience – both in pancreas transplantation and procurement – results in higher refusal rates. Further research is needed to support or refute this hypothesis.

These results have important implications for current practice in pancreas procurement. Quality of pancreas procurement may be improved by reducing refusal rates, which can be achieved by more extensive and recurrent training of pancreas

procurement surgeons. Surgeons with experience in pancreas transplantation may be excellent teachers in such a training program. Another possibility to reduce pancreas refusal may be to leave pancreas procurement to those centers also performing pancreas transplantations, but this seems hard (if not impossible) to implement in practice. It seems better to complement training with annual feedback to each center on the extent to which procured organs could be transplanted compared to other centers, which may lead to further improvement if rates are lower than expected. Given the crucial importance and lack of organs, it is vital that all procured organs can be used and do not have to be discarded because of injuries inflicted in the procurement.

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