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Abstract
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Are Criteria for Islet and Pancreas Donors Sufficiently Different to Minimize Competition?

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Islet and pancreas transplantation may compete for a limited number of organs. We analyzed records from the national Swiss transplant registry during a 4-year period to investigate the proportion of donors that are suitable for islet and pancreas transplantation. Suitability for pancreas transplantation was mainly defined as: age 10–45 years; weight $\leq$ 80 kg; BMI $\leq$ 25 kg/m$^2$; amylasemia $\leq$ 150 U/l; ICU stay $\leq$ 3 days and absence of severe hypotension (MAP $\leq$ 60 mmHG). Between 1.1.1997 and 31.12.2000, data of 407 donors were collected, from which 321 donors were included in the study. Thirty-three (10%), 143 (45%), and 23 (7%) donors fulfilled the criteria for pancreas, islet transplantation, and both procedures, respectively. Giving priority to pancreas transplantation and accepting the absence of one selection criterion, 90 (28%) pancreas and 100 (31%) islet donors were identified. We conclude that with current allocation policies prioritizing pancreas transplantation, pancreas and islet transplantation may coexist with little competition.

Key words: Donor selection criteria, islet transplantation, organ donation, pancreas transplantation

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Introduction

Thanks to improved surgical techniques, refined peroperative management and new immunosuppression protocols, the results of pancreas transplantation have steadily improved over the last two decades (1). One-year pancreas graft survival is now close to 80% for pancreas-after kidney and pancreas alone transplantation and greater than 80% in the setting of simultaneous pancreas and kidney transplantation (2). The number of pancreas transplantations performed each year and reported to the International Pancreas Transplant Registry (http://www.iptr.umn.edu/annualreports.htm) is increasing. During the year 2002, 6186 cadaveric organ donors were identified in the USA; during the same period 1485 pancreas transplants were performed (based on the organ procurement and transplantation network data since February 28, 2003; www.optn.org). The number of islet transplants performed during this period is not available yet, but was probably less than 100 for the year 2002. Different figures are reported from Europe, where pancreas transplantation is performed less frequently (3). For instance, the French organ procurement agency (Etablissement Français des Greffes) reported an average of 1000 cadaveric donors and only 50 combined kidney-pancreas transplants and less than 10 islet transplants per year (4).

The results of islet transplantation have recently improved, reaching 80% 1-year insulin-independence, as reported by the Edmonton group (5,6). Although still requiring multiple donors, these cellular grafts are in the process of entering clinical reality.

New islet transplant programs are starting worldwide, and the question of whether islet and pancreas transplantation compete for cadaveric donor pancreases arises accordingly. The present study investigates which proportion of donors could be considered for islet or pancreas transplantation according to current selection criteria, and to what extent these donor populations overlap.

Methods

We analyzed the records of 407 consecutive donors registered in the Swiss national organ sharing organization (Swiss Transplant) in the 4-year period from 1.1.1997 to 31.12.2000. Swiss Transplant coordinates all organ donations in Switzerland, a country of 7.5 million inhabitants. Twenty-eight nonheart beating donors and 58 donors for whom only incomplete data were available because the pancreas was not procured, e.g. owing to family restricting the donation to kidneys or liver, were excluded. The remaining 321 donors constituted the study population.

We considered that a pancreas was suitable for whole organ transplantation or for an islet isolation/transplantation when the criteria of Table 1 were met. These criteria were defined according to our current practice and to the international literature (1,5,7–9).

We applied the criteria to the study population and we calculated the number of potential pancreas transplantation and islets isolations. We then loosened the criteria for pancreas procurement by accepting donors with one criterion missing (excluding diabetes and/or alcohol abuse), or by extending the limits...
A less restrictive policy to pancreas harvesting, including donors with one of the above-mentioned criteria missing, of some criteria. We finally investigated the overlap of donors being suitable for both pancreas and islet transplantation.

### Results

From 1.1.1997 to 31.12.2000, 407 organ donors were registered in the Swiss Transplant files (13.6 donors per million inhabitants per year). The characteristics of the donors are summarized in Table 2, and were described in greater detail elsewhere (10). Donors were located in 30 different hospitals, with the longest distance between them being 300 km. Thirty percent (122/407) of the donors were registered in the two University Hospitals performing pancreas transplantation in Switzerland (Geneva and Zurich). Pancreata were harvested and grafted as whole organ in 4% of the donors (17/407). Islets were isolated in 25% of the donors (101/407). In the remaining cases, the organs were not harvested because of nonheart beating donor procedure (27 cases), specific family refusal to harvest the pancreas (25 cases), various pancreas abnormalities in 55 cases (including diabetes and alcoholic disease), lack of appropriate recipient, logistical reasons or medical contraindications for pancreas donation (182 cases).

### Potential number of pancreas donors available

Of the 321 donors studied, 33 fulfilled all the criteria for pancreas transplantation (10%, 1.4 donors/million inhabitants/year) and 143 donors fulfilled all the criteria for islet transplantation (45%, 6 donors/million inhabitants/year). Twenty-three donors fulfilled all criteria for both whole pancreas and islet transplantation (7%, 0.95 donors/million inhabitants/year) and were included in these numbers; allocating these donors to pancreas transplantation (prioritized in most programs) would still have left 38% of donors available for islet transplantation. The mean age of whole pancreas donors was 28.1 ± 10 years and of islet donors was 43.3 ± 13 years.

### Potential number of pancreas available with extended criteria

A less restrictive policy to pancreas harvesting, including donors with one of the above-mentioned criteria missing, would have increased the percentage of potential pancreas transplantations from 10% to 28% (3.9 donors/million inhabitants/year). Giving priority to pancreas transplantation, 31% of all donors (four donors/million inhabitants year) would be available for islet procedures (Figure 1). Altogether, loosening the selection by one criterion would allow for procuring the pancreas as a whole organ or islets in 59% of the donor population.

Age, BMI, glycemia, amylasemia and mean arterial pressure were the criteria that excluded the highest proportion of donors (Table 2).

The consequences of omitting or extending the selection criteria for age, glycemia, amylasemia, ICU stay and BMI on the numbers of pancreas and islet donors are illustrated in Figure 1.

### Impact of selection criteria on the competition for donors between pancreas and islet transplantation

According to whether the policy of accepting whole pancreas is restrictive (all criteria fulfilled) or liberal (up to one criterion missing), respectively, 10% or 28% of the donors qualified for pancreas transplantation and 45% for islet transplantation in Figure 1.
transplantation. Loosening the donor acceptability criteria increased the overlap between both procedures from 7% to 14%, and giving priority to pancreas transplantation, the number of pancreas donors increased, and the number of islet donors diminished.

**Discussion**

This study shows that with stringent selection criteria only 10% of cadaveric multiorgan donors qualify for pancreas donation. Our analysis further showed that an additional 38% of the donors were suitable for islet isolation/transplantation. By omitting one selection criterion, the pancreas donor rate could be increased from 10% to 28%, and 31% of donors remained available for islet transplantation.

Selection of donors for pancreas transplantation aims at reducing the risk of graft related postoperative morbidity and mortality in recipients often suffering from advanced chronic diabetic complications. Selection of donors for islet isolation is more of economical value, to reduce the number of islet isolation failing to deliver sufficient islets for clinical use.

Limiting the donor age to less than 45 years may be considered as too a restrictive age limit, but is current practice in many centers. Some experienced teams have extended the upper age limit and still obtained good results with donors between 55 and 60 years, and even beyond 60 years as reported by the Pittsburgh group (11). However, the series reported by the University of Wisconsin indicates that grafts from donors 45 years of age or older have significantly lower 1- and 5-year graft survival rates (12).

We explored the impact of extending the age limit to 50 and 60 years. This increased the proportion of donors potentially suitable for whole pancreas transplantation from 10 to 13% when accepting donor up to 50 years of age and to 15% when the upper age limit was extended to 60 years. This finding indicates that even a marginal age extension can increase the pancreas donor pool.

The importance of normoglycemia in the donor is still controversial. While some groups do not consider high donor blood glucose as a contraindication for pancreas transplantation (13,14) other groups have reported that hyperglycemia is a risk factor for poor pancreas graft outcome (15,16). Accepting peak blood glucose level up to 11 mmol/L would have increased the percentage of pancreas donors from 10 to 14%. When evaluating glucose levels as donor selection criterion, other parameters, which may influence glycemia or insulin-sensitivity in the donor, e.g. glucose infusion or doses of catecholamines have to be considered.

Relaxing other criteria such as amylase levels, extending intensive care stay from 3 to 5 days or accepting donors with a BMI up to 27 kg/m increased the pancreas donor pool only marginally.

Hemodynamic stability has been considered a prerequisite for good organ function when using cadaveric organs for transplantation. In our population, one in four donor was excluded because of episodes of marked hypotension. This high proportion identifies hemodynamic instability as a relevant exclusion criterion, which may be questioned if the pancreas donor pool is to be increased. In a recent report, delayed graft function was more common in pancreas transplants originating from hemodynamically unstable donors, but long-term graft outcome was not different from organs coming from stable donors (11). The use of pancreata from unstable donors for islet isolation has been addressed (17), but needs further analysis.

Although this study is based on the donor population of a whole country, and as such it is freer from selection biases owing to different attitudes towards pancreas and islet donations in specific centers, it presents some limitations. First, we could not analyze the intraoperative findings during the procurement and the evaluation by the surgeon as a selection criterion. Second, the above-presented donor population may differ from the population in countries with different donation rates. Countries with a higher donation rate may have more marginal donors and countries with a higher incidence of traumatic brain deaths may have a younger donor population. However, our registry data match the figures reported by most European and North-American countries (18). With a donation rate of 13.6 donors per million inhabitants per year, our results are likely to apply to most organ-sharing regions. It is remarkable that the calculated 28% rate of donors suitable for pancreas transplantation using the liberal criteria was very close to
the 24% pancreas utilization rate in the USA for the year 2002 (1485 pancreata were transplanted from 6168 cadaveric donors, www.optn.org).

In our analysis, we gave priority to pancreas transplantation, considering that at the present time islet transplantation is still an experimental procedure and clearly less efficacious in terms of pancreas utilization. The process for islet isolation is still somewhat unreliable, depending on the quality of the pancreas, degree of cold storage, and digestion characteristics of the lot of enzyme used (19). Currently, to achieve insulin-independence, islet preparations from often two, and occasionally three, donors are required. Once islet transplantation is more reliable and consistently achieves insulin-independence with a single donor at the same rate as pancreas transplantation, current allocation policies may be revised. Then a single donor at the same rate as pancreas transplantation can be used for islet transplantation: continued insulin reserve provides long-term glycemic control. Diabetes 2002; 51: 2148–2157.


References


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