TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

INVITED COMMENTARY

A young pancreas or no pancreas?

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Received: 11 July 2013
Accepted: 15 July 2013

doi:10.1111/tri.12162

In this study, Kayler and his colleagues assess the outcome after simultaneous Pancreas and Kidney transplantation (SPKT), focusing on the "elderly" population. They compare the outcome with the patients remaining on the waiting list. In this retrospective study including a considerable number of simultaneous pancreas kidney transplants, recipient age above 40 has no influence on death-censored graft survival, while the use of organs from donors older than 40 years is not beneficial.

The age cut-off of 40 years illustrates that "old" in this group of patients is quite different from the definition of "old" for the general population, and also, for example, a kidney transplant recipient. While the nature and secondary effects of the disease may justify the low age limit for the patient selection, the relativity of "old" in donors should be emphasized. With or without such limitations, the results of the trial are substantial. The study underlines and emphasized the relevance of age in diabetes and pancreas transplantation. Both donor and recipient age play a major role and heavily impact the outcome. The impact of donor age has been previously established. Both early graft loss as a result of technical failures as well as long-term graft survival correlate with donor age. A recent assessment has identified donor age as the only consistent factor differing between organ offers accepted and declined [1]. A correlation between age and technical failure has just recently been shown in a large single-centre analysis [2]. Donor Creatinine, preservation time and donor BMI were the other factors impacting the outcome in this study. This is consistent for long-term graft survival for donor age and preservation time, but not for BMI and Creatinine [3].

It is striking that the patient survival in the group of patients remaining on the waiting list of this study is substantially and significantly less when compared with the group receiving a SPKT. This confirms the selection criteria for this surgery, and also provides further evidence that SPKT is significantly life-prolonging. Considering that SPKT is not uniformly accepted as the treatment of choice for diabetes with kidney failure, this trial provides important and clear evidence that SPKT is the best option for these patients. Withholding the opportunity to undergo SPKT for DM with kidney failure seems ethically questionable.

There seems to be, however, a limit with respect to donor age. Using organs from donors older than 40 years, patient survival is "only" equal to patients remaining on the waiting list. A selection bias for those undergoing transplantation versus those patients remaining on the waiting list may further impact on this as those patients not selected for transplantation may be overall less fit and suitable for (extended criteria) SPKT. This further supports the concept that donors beyond the age of 40 should only considered for selected cases. It is interesting to see that 111 donors were older than 50, indicating that (for the region assessed)

an age limit has not really been established or followed. Despite the increasing demand and discrepancy between organs available and organs needed, such an extension of inclusion criteria for SPKT seems counterproductive. While the simplification for this trial with defining young as <40 and old as >40 might be reasonable for this trial and help set a clinically meaningful age level, a strict allocation to <40 and >40 for donor selection leaves "biologically good" 41-year-old organs unused and "biologically bad" 39-year-old donors falsely transplanted. Hence, the age limit may stay as a strong selection criterion together with, and not instead of, the clinical overall judgment of the physician. The demographics of "older" donors confirms the co-factors possibly contributing to the finding with a higher proportion of African American, female, hypertensive, obese, donation after cardiac death, from a nonlocal organ procurement organization (OPO), highly human leukocyte antigen mismatched, longer cold ischemia time (CIT) and cerebrovascular accident. Hence, donor age, when assessed for a large patient population sub summarized a set of risk factors and may be seen as a surrogate for assessment of larger patient numbers. When assessed in a single centre, donor age alone may not have such strong predictive value and excellent results have been achieved with pancreata from donors aged 50 or older [4]. For the individual decision to accept or decline a pancreas for transplantation, the number and composition of demographic risk factors should be considered. In addition to demographic risk factors, inspection of the pancreas by an experienced surgeon and predicted CIT were suggested as important factors for organ selection [5].

It is notable that, for those wait-listed with OPOs in the middle and lower waiting-time tertiles, no survival benefit from old-donor SPKT could be observed. This underlines the relevance of the deterioration and possibly time on dialysis with continuous glucose dysregulation for these patients. Waiting time, however, is highly dependent on the regional source of donors and regions with less donors might lean towards accepting extended criteria donors as indicated also in this trial.

While the control group chosen for this study is adequate, a selection bias for those undergoing transplantation versus those remaining on the waiting list cannot be ruled out. In the "transplant reality", a preference will often be given to the patient with less medical or surgical risk factors and comorbidities, especially when organs from elderly or extended criteria donors are used. Therefore, the control group might be the best group available, but a selection bias may limit the strength of the comparison.

The study provides further substance and underlines the case for SPKT in patients with insulin dependency and kidney failure. While the information provided in this study may not be entirely new, the impact of both donor and recipient age as a risk factor in pancreas transplantation has been elegantly demonstrated.

It is important to note that old-donor SPKT does not confer a survival benefit relative to waiting. The logic here, however, is disrupted by the overall limited number of organs from younger donors. Excluding all organs of donor beyond 40 years may result in a significant prolongation of the waiting time and overall worse results because of progression of secondary complications of diabetes. The authors point out that an interaction between donor and recipient age cannot be established.

In summary, the fact that organs from older donors are not as good as organs from younger donors is barely news. The strong association of death and graft loss with donor age of below versus above 40 demonstrates the relevance of age and careful donor selection for SPKT. While donor selection bound strictly to one factor may be monodimensional and oversimplifying the selection process, the importance of donor age has been impressively demonstrated in this manuscript. The question if donors of higher age are suitable for pancreas transplantation will be addressed in a Eurotransplant multicentre trial recently initiated. Results from this trial should be awaited prior to systematically excluding higher age donors [6].

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