Mysterious Knowledge – Qualification of Pancreata Suitable For Transplantation: review

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ABSTRACT

Pancreas transplantation and simultaneous transplantation of the pancreas and kidney are a well-known methods of treating patients with diabetes complications. This is regarded as a superior standard of management in patients with end-stage renal failure caused by diabetic nephropathy. The main limitation of this method is a disproportionately low number of organ donors comparing the number of patients awaiting treatment. As the society burdened with an epidemic of obesity ages and the number of optimal organs accessible for transplantation is gradually decreasing. It is necessary to liberalize donor eligibility criteria, which may have an adverse effect on the therapeutic outcomes. This paper attempts to analyze the available literature in order to determine strategies that are used during qualification of potential pancreas donors, criteria used by decision makers to accept a particular organ, and objective effects of donor-related criteria on therapeutic outcomes.

The main limitation of pancreas transplantation and simultaneous transplantation of the pancreas and kidney is a disproportionately low number of organ donors comparing the number of patients awaiting treatment. It is necessary to liberalize donor eligibility criteria, which may have an adverse effect on the therapeutic outcomes.

Diabetes mellitus and its complications are a predominant problem of health care systems (1). Despite more and more advanced strategies to treat diabetes, which significantly prolong expected survival time and reduce the occurrence of complications (2), and that in turn results in a decreasing number of patients awaiting a pancreas transplant, there is still a significant disproportion between a demand and supply of organs considered eligible for transplantation (3). Significant factors with an adverse effect on this disproportion include a gradually increasing number of pancreas transplantations in recipients with type 2 diabetes (4,5) as well as ageing society and an epidemic of obesity that affect a profile of potential donors (6-8). Prolonged dialysis therapy in patients with diabetic kidney
disease, V CKD stage, adversely affects comfort and survival of patients after transplantation. In order to increase the number of transplantations and to shorten the waiting period, there have been attempts to increase the number of pancreata approved for transplantation, using donors with irreversible cardiac arrest (9) and living donors (10) or available through criteria liberalization.

In terms of the number of transplantations and patients on waiting lists for pancreas transplant, the USA has a leading position. The US/non-US division is visible with regard to approaches used to screen for the eligibility of potential pancreas donors and to accept organs, and trends associated with such differences cannot be reviewed together.

Within the last 10 years the number of pancreas transplantations in the USA has been steadily declining. Various interpretations of this phenomenon have been suggested. First of all, it is necessary to pay attention to a declining number of patients added to waiting lists awaiting a pancreas transplant. This tendency is most visible in a group of patients who are eligible for a pancreas transplant alone (PTA). A difference in the number of new patients added to a list awaiting PTA in 2010/2011 got reduced by 73% compared to 2004/2005 period, whereas in a group of patients considered eligible for simultaneous pancreas-kidney (SPK) transplantation and in a pancreas-after-kidney (PAK) group in the same period the difference was lower, namely 37% and 38%, respectively (3). The number of patients considered eligible for pancreas transplantation is reduced due to the fact that conservative treatment for diabetes has improved, therefore the occurrence and frequency of complications is reduced, and it also regards end-stage renal failure due to diabetic kidney disease (4,8,11). Modification of regional rules to qualify potential pancreas recipients may also affect the observed situation (11). Type 2 diabetes, a classic contraindication to pancreas transplantation, is currently more and more common indication to be considered eligible for pancreas transplantation (currently approx. 8% SPK, 5% PTA and 1% PAK are performed in patients with type 2 diabetes); however, it has not had any significant effects on the total number of patients awaiting a pancreas transplant (4). A declining number of patients qualified for pancreas transplantation will not have any significant effect on the waiting period for pancreas transplantation as there has also been a parallel tendency to reduce the number of transplantations. In 2010/2011 period, the number of pancreas transplantations in the US in SPK, PAK and PTA groups was reduced by 10%, 55% and 34%, respectively (3) compared to 2004/2005 period. With regard to a declining number of pancreata that have been approved for transplantation in the US (currently, successful transplantation is performed with the participation of only 15% of potential pancreas donors who are submitted) it has to be assumed that this situation is associated with changes in the characteristics of potential donors (older age, obesity, diabetes mellitus) and with a tendency for a more strict assessment of pancreata qualified for transplantation (11). Due to an extremely large disproportion between the number of potential pancreas donors with regard to the patients awaiting transplantation in the US (especially with regard to patients awaiting SPK) it was necessary to adopt a more liberal approach to donor qualification, as it has been demonstrated that shorter dialysis therapy and a waiting period for transplantation significantly prolongs survival of patients after transplantation(12). A Thomas Starzl Centre in Pittsburgh has promoted a strategy where all potential organ donors with a negative diabetes history were considered to be pancreas donors. Criteria of hyperamylasemia and hyperglycemia were not used as per se exclusion criteria. The basic criterion to assess an organ prior to transplantation was a macroscopic inspection performed by an experienced surgeon, that depended on chronic lesions above all: presence of fibrosis, fat infiltration and calcifications; presence of any of such lesions resulted in organ disqualification. Additionally, the venous return rate during pancreas cold washing was assessed. The most important criterion during organ qualification was a subjective assessment of a surgeon, therefore objective recipient criteria, such as age, weight, cause of death or hospitalization time, were not equally important. Lists of parameters of donors whose pancreata were transplanted are of notice: mean age - mean 29 years (range 6-62 years), mean amylase 136 IU/dl (range 6-1411 IU/dl), lipase 116 IU/dl (range 9-1373 IU/dl), mean glucose 285 mg/dl (range 100-648 mg/dl). Additionally, pancreata from donors with irreversible cardiac arrest were also considered eligible for transplantation. As the results obtained were not significantly different from the ones obtained in cases where organs were transplanted from highly selected donors based on objective features, and the suggested strategy made it possible to significantly increase the number of transplantations, it has been adopted by the majorities of American centres, and it has had a significant effect on the fact that the USA has gained a leading position in the field of pancreas transplantation worldwide (13). Currently, there has also been a tendency to limit donor acceptance criteria, especially with regard to the age and obesity, as these factors are the best-documented risk factors for graft loss (6,14). It has been demonstrated that the donor’s age > 45 years is an independent risk factor increasing the risk of pancreatic allograft loss, cardiovascular complications and recipient’s death. Donor’s BMI above 30 increases the risk of pancreatic steatosis, inflammatory processes, thrombosis, organ infection and rejection. A significant reduction in the number of pancreas transplantations in the US is suppressed by the fact that pancreata from living donors (10) and donors with irreversible cardiac arrest (9) are more and more commonly used. A declining tendency in the number of transplanted pancreata observed for almost ten years, is proportional to improved thera-
Data available from the non-US centres are not homogeneous and they usually come from analyses of studies on small groups of patients. Reports from centres included in Eurotransplant are a relatively large source of information. Based on the analysis of the Eurotransplant 2013 Annual Report, a similar tendency can be seen in the US, because the number of patients awaiting a pancreas transplant, and the number of transplantations has been gradually declining. However, short waiting time for a pancreas transplant is of notice, as in 2013 it was 4 months. Relatively short waiting time for a pancreas transplant, namely a low mortality rate of patients who are active on the list of patients considered eligible for transplantation, is reflected by a strictly formal system to qualify pancreas donors that is based on the P-PASS (Preprocurement Pancreas Suitability Score) introduced by Eurotransplant. Nine parameters are assessed: (age, BMI, time at the ICU, cardiac arrest, blood serum sodium levels, dosage and type of pressor amines, and amylase or lipase levels), but the age and BMI are treated as the most important ones and are scored double points. The number of points gained, depending on various parameters from the table, increases along with poorer organ quality in the range of 9-27. It has been retrospectively determined that pancreata from donors with the score below 17 were collected three times more frequently than others (15). According to the Eurotransplant guidelines (Eurotransplant Manual version 3.0) donors with the P-PASS below 17 should be considered as pancreas donors. Initially, the P-PASS was designed as a tool to increase the reporting rate of potential pancreas donors by Eurotransplant coordinators, but it has become a very convenient tool used by many centres for initial donor qualification (16). Unfortunately, the pancreas assessment based on the P-PASS is only approximate, and no correlation has been demonstrated between the score obtained and transplantation outcomes (17,18). According to parties responsible for qualification of pancreata for transplantation the P-PASS is an important parameter for initial donor qualification, but a macroscopic and microscopic assessment of an organ is decisive (16). A factor that adversely affects the number of pancreas transplantations in non-US centres is associated with the fact that transplant committees are often understaffed, and for organizational reasons sometimes it is not possible to transplant an organ with excellent parameters (16).

There is no unanimous, objective system for qualification of pancreata for transplantation that would be tightly correlated with long-term transplantation outcomes. The basic criterion of the organ assessment is a macroscopic and palpation examination of the pancreas performed by an experienced surgeon. Currently, no methods have been developed to make this assessment more objective, and it significantly makes it more difficult to reference it to long-term transplantation outcomes. Despite the fact that various systems to assess risk factors associated with donor’s parameters have been introduced, a subjective assessment still plays the most important role. It substantially affects how pancreata from reported potential donors are used. Significant factors affecting the decision to accept a given organ include experience of a person assessing this organ, internal policies of a transplantation centre, its transplantation activity and results obtained, as well as pressure associated with a high number of patients awaiting transplantation on waiting lists. It seems that the only method to expand the number of donors and to simultaneously maintain possibly the best outcomes of treatment is to objectivize an assessment of such parameters of an organ that change a decision regarding transplantation into an almost metaphysical activity preventing from treatment optimization.

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