Pancreas transplantation in Singapore

Requisites for Successful Pancreas Transplantation in Singapore

Introduction

While renal transplantation has been performed for over 30 years and liver transplantation for over 15 years in Singapore, there is currently no pancreas transplantation programme in Singapore or the neighbouring region. However, we are exploring the feasibility of a nationwide pancreas transplantation programme.

Pancreas transplants have been performed for over 4 decades and are not experimental anymore. It has been shown to prolong survival in patients with diabetes and renal failure. The results of pancreas transplant have improved mainly over the last 2 decades with significant refinements in surgical technique and improved immunosuppression protocols. Worldwide, about 1,800 pancreas transplants take place annually, according to the International Pancreas Transplant Registry (IPTR) maintained by the University of Minnesota and the University of Arizona. To date, more than 30,000 pancreas transplants have been reported to the IPTR, with more than 22,000 from the USA and more than 8,000 from outside the USA. The 1-year graft survival rates now exceed 80%, and the 1-year patient survival rates are 95%. The 3-year patient survival rates exceed 90%, and the 3-year pancreas graft survival is about 80% for simultaneous pancreas kidney recipients.

Indications

The main objectives of pancreas transplant are to render Type 1 diabetics insulin-independent, to improve quality of life and to reduce long-term diabetic complications.

Pancreas transplant is performed in 3 possible scenarios - simultaneous pancreas-kidney transplantation (SPK), pancreas after kidney (PAK) transplant and pancreas transplant alone (PTA).

The most common scenario will be a SPK transplant which is indicated in Type 1 diabetics who require dialysis within 6 months or are on dialysis. PTA is indicated in Type 1 diabetics who have significant diabetic complications or have life-threatening complications such as frequent and severe episodes of hypoglycemia or have hypoglycemic unawareness. PAK transplant is indicated in patients with stable function of previous renal allograft that meet the criteria of pancreas transplant alone.

For SPK transplants, the rationale for a simultaneous pancreas and kidney transplant is that such patients are obligated to immunosuppression for renal transplant and that the same source donor for pancreas graft minimises tissue incompatibility.

In the last 5 years from 2004 to 2008 in the US, the majority of pancreas transplants were SPKs (73%), followed by PAK (19%) and PTA (8%). The majority of recipients had Type 1 diabetes, while 6 to 7% of pancreas transplants were performed for Type 2 diabetes. Most pancreas recipients were in their 30s and 40s and had diabetes for more than 20 years. The vast majority of pancreatic grafts were from deceased donors, and a small number of living donor pancreas transplants had been performed in specialised pancreas transplant units in the USA.

Is there a need for pancreas transplant in Singapore?

Survival benefits

Pancreas transplantation is justified on the basis of the data for survival, and the single most important factor for long-term patient survival is preservation of the pancreas graft. Recipients of SPK can be expected to live 10 years longer than patients with diabetes given kidney transplant alone from deceased donors (23.4 vs 12.9 years).

Current status of Type 1 diabetics with end-stage renal failure in Singapore

At present, the 5-year patient survival of Type 1 diabetes and end-stage renal failure (ESRF) without transplant is 38% in Singapore compared to 90% 5-year patient survival with transplant in most established pancreas transplant units (data courtesy of the National Registry of Diseases Office, Health Promotion Board, Ministry of Health Singapore). There were 95 patients diagnosed with Type 1 diabetes and ESRF between 1999 and 2006 (about 10-15 patients/year) with a median age of 46 years at diagnosis. As at 31 Dec 2008, of these 95 patients, 64 had died,
The donor pancreas is reconstructed anastomosed to the donor superior mesenteric artery, while venous drainage can be to the recipient’s inferior vena cava, common iliac vein or portal vein. Exocrine secretions can be drained into the bowel or bladder. Surgical technical failures have dramatically decreased from 25% in the 1980s to between 7 to 9% presently. Relaparotomy rates are presently about 33% of cases, and the majority of graft failures occur in the first 90 days. Pancreas graft thrombosis is by far the most frequent serious surgical complication with an incidence ranging from 3 to 10%. It results in graft loss, and the need for relaparotomy and transplant pancreatectomy. The etiology of pancreatic graft loss is multifactorial. Donor risk factors for pancreas graft thrombosis include older donors, cerebrovascular cause of death, significant hemodynamic instability and massive volume resuscitation. Suboptimal pancreas recovery, preservation and back-table preparation techniques are also known risk factors. Due to the delicate organ structure and extensive microvascular bed, the pancreas is particularly susceptible to excessive flush pressures and volumes.

Tissue matching and immunosuppression
Tissue matching for pancreas transplant is performed similar to kidney transplants, mandating blood group match. Matched donor and recipient size is less important for pancreas transplant than it is for liver transplant. Tacrolimus plus mycophenolate mofetil and short-course steroid with antibody induction is the most commonly prescribed regimen. Unlike most solid organ transplants, some form of anti-T cell antibody induction is used for pancreas transplants (80%). The common T cell depleting induction agents include thymoglobulin, an interleukin-2-receptor antagonist (basiliximab or daclizumab) and alemtuzumab.

Islet transplantation
Allogeneic islet transplantation seems a promising alternative to pancreas transplantation; however, patient outcomes remain less than optimal and significant progress is still required in order for this procedure to be considered reliable therapy. Early enthusiasm for islet transplantation was sparked in 2000 when data from Edmonton showed seven patients rendered insulin independent for 1 year using a steroid-free immunosuppressive regimen. Within the next few years, the number of clinical islet centres and patients transplanted increased dramatically. Despite considerable effort and expense, many centres had difficulty in duplicating the Edmonton results. Further, even patients with an initially successful islet transplant had questionable long-term islet survival, with a majority requiring multiple donor islet infusions to achieve normoglycemia. Graft success at 9 years, even among the original Edmonton patients, remained a disappointing 10% or less.

Currently, long-term insulin independence remains elusive in clinical allogeneic islet transplantation patients. Even with patients who receive multiple infusions, few remain normoglycemic over the long run. The Collaborative Islet Transplant Registry (CITR) data, collected across clinical islet programmes, show that 60-70% of patients achieve insulin independence within the first year, but by the third year, the percentage of euglycemic patients is closer to 35%.

Cost of pancreas transplant
The cost of funding of pancreas transplants is not significantly different from kidney transplants, and is estimated to be under $100,000. As such, a simultaneous pancreas kidney transplant will probably cost as much as a liver transplant. At present, the majority of transplants performed in the public institutions in Singapore are heavily subsidized by the Ministry of Health for qualified citizens (often up to 80% of the total bill). No qualified citizen will be denied an opportunity for transplant because of inability to afford the cost of transplant.

National programme setup
At present, we have 3 requisite conditions for a successful pancreas transplant programme in Singapore. Firstly, there is a definite survival benefit compared to no transplant for Type 1 diabetes with end-stage renal failure. Secondly, there is donor availability to meet our transplant wait list demands for pancreas transplants (estimated at 10-15 cases per year). Therefore, 40-50 donor referrals per year with a median donor age of 45 years, resulting in 40-50 deceased donor kidney transplants per year. These same donors are potentially suitable as pancreas donors. Thirdly, the necessary medical and surgical expertise to perform pancreas transplants safely in Singapore is available.

References:

Dr Victor Lee is a consultant in the Department of Surgery at the National University Hospital. His clinical skills and interests are in the areas of transplant surgery, hepatobiliary pancreas and laparoscopic surgery. He was awarded the Human Manpower Development Programme in 2008 for transplant surgery, and was appointed as Clinical Fellow in Transplantation Surgery at the Royal Infirmary of Edinburgh, United Kingdom from 2008 to 2009. In his fellowship year, he is trained in liver transplants, kidney transplants and simultaneous pancreas kidney transplants, in addition to hepatobiliary pancreas and laparoscopic surgery.