Reappraisal of pancreas transplantation

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Abstract: Pancreas transplantation is currently the most effective and curative treatment for complicated type 1 diabetes mellitus, providing durable and physiological insulin-independent euglycemia, preventing worsening or ameliorating of diabetic complications, and improving quality of life. Currently, more than 31 000 pancreas transplantation procedures have been performed, mainly in the United States. Pancreas transplantation is still an uncommon procedure in Asia, mainly performed in Korea, Taiwan, and Japan. The first pancreas (simultaneous pancreas and kidney transplantation) transplantation was successfully initiated at Taipei Veterans General Hospital on September 19, 2003, and we are the first team to be qualified to perform human pancreas procurement and transplantation by Taiwan Department of Health on August 31, 2007. The technique success rate in our pancreas transplantation is 97%, with 1-year pancreas graft survival rate of 95.8%, 5-year pancreas graft survival rate of 89.9%, and 10-year pancreas graft survival rate of 65.9%.

Keywords: Pancreas transplantation; Simultaneous pancreas and kidney transplantation; Type 1 diabetes mellitus

1. INTRODUCTION

The first human pancreas transplantation was a simultaneous pancreas–kidney (SPK) transplantation performed in 1966 by Kelly et al at the University of Minnesota (Minneapolis, MN, USA).[1] Unfortunately, the patient was complicated by a fatal pulmonary embolism. Currently, >31 000 pancreas transplantation procedures have been performed, mainly in the United States. Pancreas transplantation is still an uncommon procedure in Asia, mainly performed in Korea, Taiwan, and Japan. Pancreas transplantation is currently the most effective and curative treatment for complicated type I diabetic mellitus (T1DM), providing durable and physiological insulin-independent euglycemia, preventing worsening or ameliorating of diabetic complications, and improving quality of life. Outcomes for pancreas transplantation have been improving with a 3-year survival of 94.3% after SPK transplantation performed from 2009 to 2013, compared with 90.9% from 1999 to 2003.[2] The first pancreas (SPK) transplantation was successfully initiated at Taipei Veterans General Hospital on September 19, 2003, and we are the first team to be qualified to perform human pancreas procurement and transplantation by Taiwan Department of Health on August 31, 2007. Until April 17, 2019, there were 151 cases of pancreas transplantation performed at Taipei Veterans General hospital, including 36 SPK, 73 pancreas transplantation alone (PTA), 24 pancreas before kidney (PBK) transplantation, 17 pancreas after kidney (PAK) transplantation, and one pancreas after liver (PAL) transplantation. The technique success rate in our pancreas transplantation is 97%, with 1-year pancreas graft survival rate of 95.8%, 5-year pancreas graft survival rate of 89.9%, and 10-year pancreas graft survival rate of 65.9%.

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2. TYPES OF PANCREAS TRANSPLANTATION

Pancreas transplantation in Taiwan can be categorized mainly into the following:

1. SPK transplantation (Figs. 1–4)
2. PAK transplantation (Figs. 1–3)
3. PTA (Fig. 5)
4. PBK transplantation (Fig. 5)
5. PAL transplantation (Fig. 5)

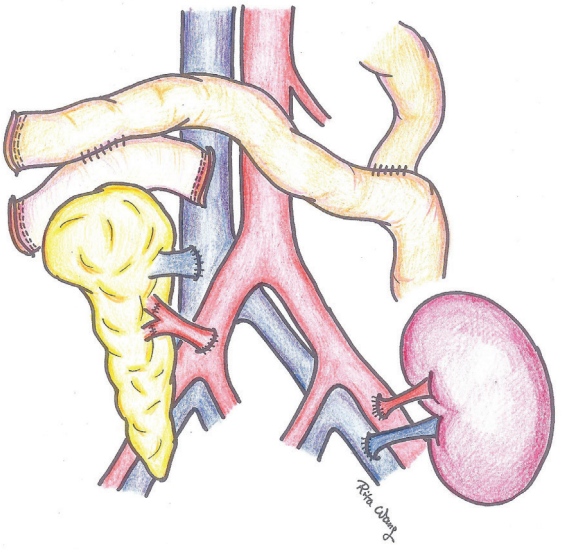

Fig. 1 Pancreas and kidney transplantation for simultaneous pancreas–kidney (SPK) or pancreas after kidney (PAK) transplantation. The pancreas graft portal vein is anastomosed to distal inferior vena cava, a systemic venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, an enteric drainage. Retroperitoneally, the pancreas graft is usually placed in the right side. The kidney is placed in the left, opposite, side.

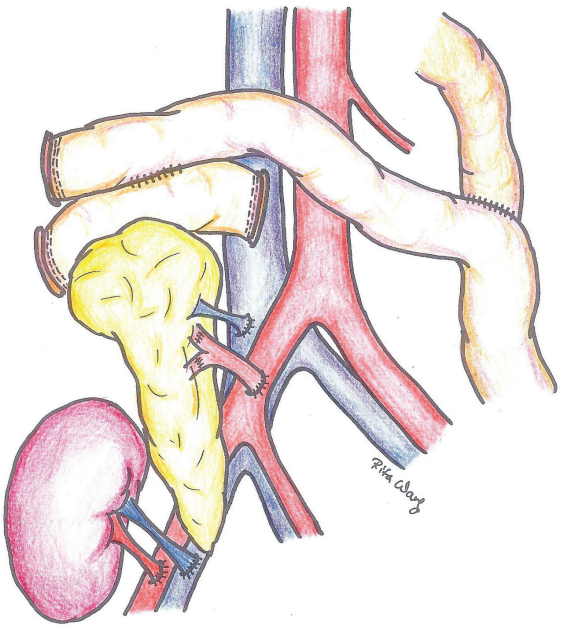

Fig. 2 Ipsilateral placement of pancreas and kidney grafts for simultaneous pancreas–kidney (SPK) or pancreas after kidney (PAK) transplantation. The pancreas graft portal vein is anastomosed to distal inferior vena cava, a systemic venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, an enteric drainage. Retroperitoneally, the pancreas graft is usually placed in the right side. The kidney is also placed in the right side.

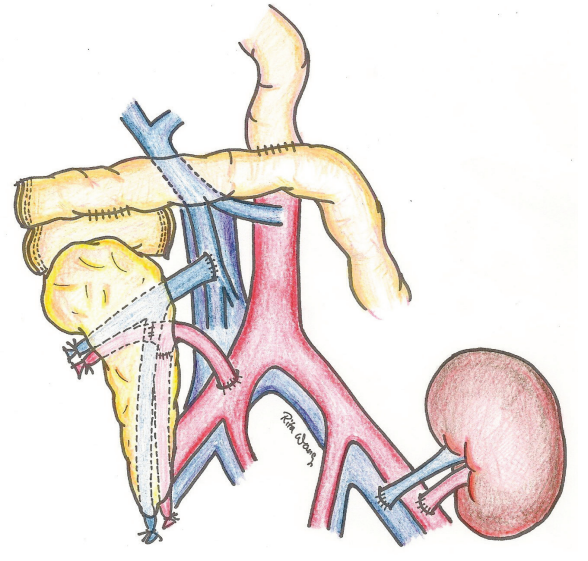

Fig. 3 Pancreas and kidney transplantation for simultaneous pancreas–kidney (SPK) or pancreas after kidney (PAK) transplantation. The pancreas graft portal vein is anastomosed to a big tributary of superior mesenteric vein, a portal venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, an enteric drainage. Retroperitoneally, the pancreas graft is usually placed in the right side. The kidney is placed in the left, contralateral, side.

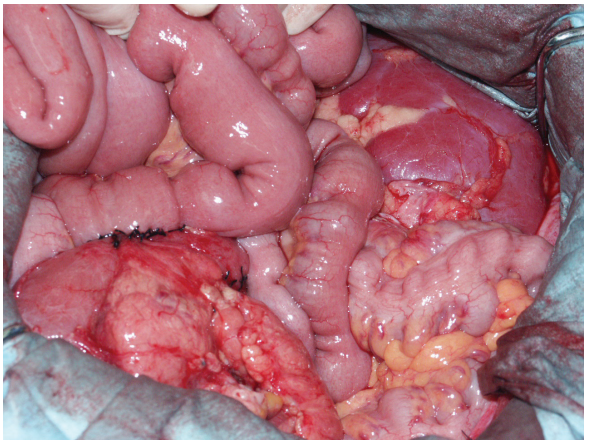

Fig. 4 Solitary pancreas transplantation for pancreas transplant alone (PTA), pancreas before kidney (PBK) or pancreas after liver (PAL). The pancreas graft portal vein is anastomosed to distal inferior vena cava, a systemic venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, an enteric drainage.

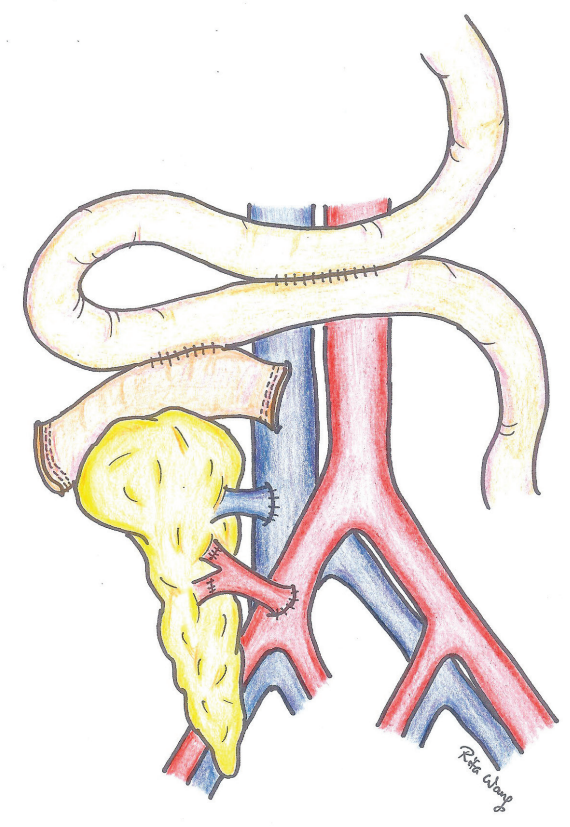

Fig. 5 The first simultaneous pancreas–kidney (SPK) transplantation performed at Taipei Veterans General Hospital on September 19, 2003. The pancreas graft was placed in the right side. The kidney was placed in the left, opposite, side.

Ideally, a combined kidney and pancreas transplantation should be recommended for patients with severe diabetes and end-stage renal disease. Therefore, SPK is the most common type of pancreas transplantation, accounting for 79% of procedures in the United States in 2016.[2] Both organs are usually procured from a single deceased organ donor. PAK transplantation is offered to diabetic patients who have already undergone kidney transplantation. PTA is offered to candidates without end-stage renal disease, but with frequent, acute, and potentially life-threatening complications of diabetes such as ketoacidosis, hypoglycemia unawareness, and incapacitating problems with

Table

Pancreas graft survivals after pancreas transplantation at Taipei Veterans General Hospital

Pancreas transplantation	Mean ± SD, mo	Median, mo	1-year survival	5-year survival	10-year survival
Total, n = 145	63 ± 46	58	95.8%	89.9%	65.9%
SPK, n = 32	100 ± 50	106	96.9%	90.2%	80.1%
PTA, n = 68	58 ± 39	47	93.4%	80.1%	40.8%
PAK, n = 17	56 ± 46	52	85.4%	85.4%	85.4%
PBK, n = 23	36 ± 31	33	95.7%	95.7%	…

PAK = pancreas after kidney; PBK = pancreas before kidney; PTA = pancreas transplant alone; SPK = simultaneous pancreas–kidney.

insulin therapy. For this group, pancreas transplantation would be life-saving, but must be weighed against the untoward risks of life-long immunosuppression.[2]

In Taiwan, it is very competitive for a uremic patient to have a decreased kidney graft because there are always >7000 uremic patients waiting for kidney transplantation.[3] Moreover, the waiting lists of pancreas and kidney transplantation are separate. PTA (48%, 73/151) is the most common type of pancreas transplantation, followed by SPK (24%, 36/151) transplantation, PBK (16%, 24/151), PAK (11%, 17/151), and PAL (1%, 1/151).

3. INDICATIONS FOR PANCREAS TRANSPLANTATION

Traditionally, pancreas transplantation has been reserved for T1DM patients suffering from uremia, and considered as a relative, if not absolute, contraindication for type 2 diabetic mellitus (T2DM) due to its pathophysiology. The reluctance could rely on the pathophysiology of T2DM where insulin resistance on peripheral tissues has been considered as the prevailing disorder, instead of pancreas itself. Therefore, T2DM patients need better peripheral tissue responsiveness to insulin, instead of extra insulin or pancreas graft. However, the distinction between T2DM and T1DM is not always obvious, and many patients may present with overlapping clinical syndromes. Although many criteria, including a family history of diabetes, age of DM onset, body mass index (BMI), human leukocyte antigen association, and detectable connecting peptide, have been proposed to differentiate these two types of DM, several patients are still found to categorically overlap. Moreover, older age, associated cardiovascular risks, and advanced secondary diabetic complications might also be suggested as the listed deterrents.[4–7] The official indications for pancreas transplantation in Taiwan[3] include the following:

1. T1DM patients with diabetic complications such as nephropathy, retinopathy, neuropathy, and cardiocerebral vasculopathy
2. T1DM patients with frequent life-threatening hypoglycemia or hyperglycemia
3. T1DM patients suffering from severe disability in school earning, working, and living
4. T2DM patients with end-stage renal disease waiting for or undergoing kidney transplantation, and requiring insulin injection for blood sugar control with the dosage of insulin requirement <1.5 units/kg/day

According to the Scientific Registry of Transplant Recipients report, the proportion of T2DM candidates waiting for SPK

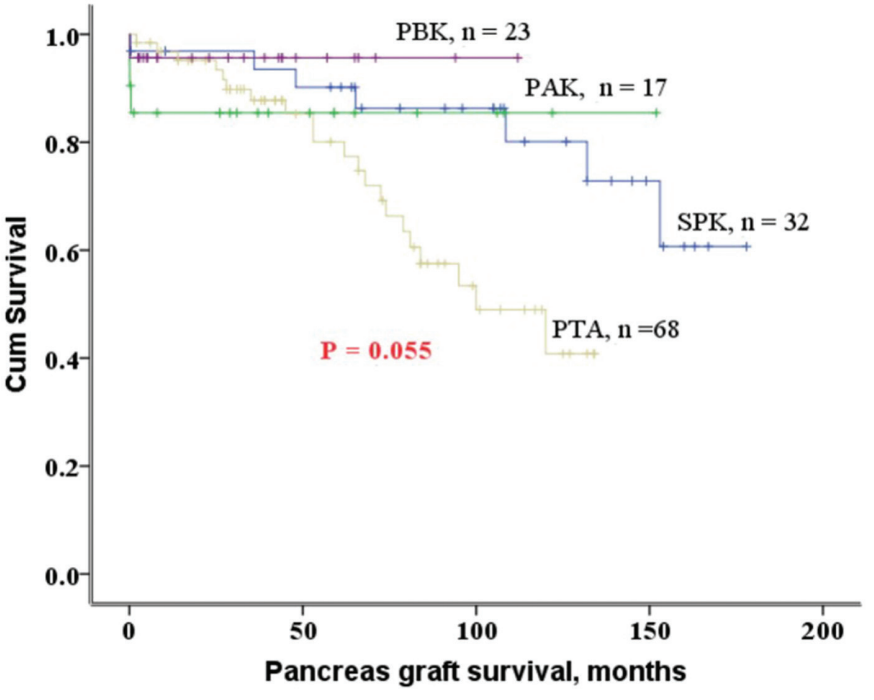

Fig. 6 Pancreas graft survivals after simultaneous pancreas–kidney (SPK) transplantation, pancreas after kidney (PAK) transplantation, pancreas transplant alone (PTA), and pancreas before kidney (PBK) transplantation.

transplantation increased from 10.5% to 11.7% in 2015 and the proportion of T2DM candidates waiting for PAK transplantation increased from 6.8% to 8.3% in 2016, while the rate of T2DM candidates waiting for PTA decreased from 3.9% to 2.9%.[8,9] Although the popularity of pancreas transplantation in T2DM patients remains disproportionately lower than in T1DM, a growing body of evidence has revealed that the endocrine outcome in carefully selected T2DM patients could mirror that of T1DM.[4,7,10–14]

4. OUTCOMES

The most common cause of patient death after pancreas transplantation is cardiovascular event. All-cause mortality rate after pancreas transplantation is 4% at 1 year and 9% at 5 years.[2,15] Pancreas graft survival defined as insulin independence and a normal hemoglobin A1c is 86% at 1 year and 54% at 10 years for SPK recipients.[16] Pancreas graft survival PAK and PTA is lower, probably due to unavailability of serum creatinine as a warning marker of graft rejection. Pancreas graft outcomes are inversely related to recipient age, donor age, BMI, and the burden of cardiovascular disease.[2,17–19] The most common causes of graft loss are thrombosis (31%), chronic rejection (21%), and acute rejection (15%).[2]

At Taipei Veterans General Hospital, the technique success rate in pancreas transplantation is 97% (n = 151). Patient survival rate is 96.5% at 1 year and 89.6% at 5 and 10 years. The overall pancreas rejection rate after pancreas transplantation is 26% (n = 145), with 17% for acute rejection and 9% for chronic rejection. Acute rejection occurs most commonly, 23%, in PTA group, followed by 17% in SPK, 10% in PAK, and 4% in PBK group. Chronic rejection occurs also most commonly, 14%, in PTA group, followed by 11% in SPK, and no chronic rejection in PAK and PBK groups. The overall pancreas survival rate is 95.8% at 1 year, 89.6% at 5 and 10 years, excluding those with technique failure. Table lists the pancreas graft survival outcomes after pancreas transplantation at Taipei Veterans General Hospital. There is no significant difference regarding the pancreas graft survival between the subgroups, $p = 0.055$ (Fig. 6).

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