REVIEW ARTICLE

Pancreas transplantation: review

Trasplante de páncreas: revisión

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Abstract

Pancreas transplant (PTx) is the only treatment that establishes normal glucose levels for patients diagnosed with diabetes types 1 and 2. The paper aims to review and analyze graft survival, patient survival, and the impact on diabetic complications. We describe that the graft survival was 82-98% at 1 year, 90% at 5 years, and 75-54% at 10 years for simultaneous pancreas-kidney recipient; 71% pancreas after kidney (PAK), and 62% PTx alone at 1 year. Patient survival: At 1 year for recipients was 96.9% simultaneous pancreas-kidney transplantation (SPK); for PAK transplantation recipients, 96.3%; and for PTx alone recipients, 98.3%. In general, the pancreas transplantation improves and reverses diabetic complications. Finally, the pancreatic transplant is a morbid procedure and emerges as a significant alternative in diabetes management, directly competing with conventional insulin therapies. Results so far suggest that the most effective transplant model is the SPK. While more patients could benefit from this procedure, surgical complications and the need for immunosuppression pose significant challenges.

Keywords: *Pancreas transplantation. Diabetes mellitus. Pancreas donor selection. Surgical technique. Outcomes.*

Resumen

El trasplante de páncreas es el único tratamiento que estabiliza los niveles normales de glucosa en los pacientes diagnosticados con diabetes tipo 1 o tipo 2. En esta revisión se analizan la supervivencia del injerto, la supervivencia del paciente y el impacto en las complicaciones diabéticas. Se describe la supervivencia del injerto: 82-98% al año para los receptores de trasplante simultáneo de páncreas y riñón, 71% para trasplante páncreas después de riñón y 62% para trasplante de páncreas solitario al año. Supervivencia de los pacientes a 1 año: 96.9% para los receptores de trasplante simultáneo de páncreas y riñón, 96.3% para los receptores de trasplante de páncreas después de riñón y 98.3% para los receptores de páncreas solitario. En general, el trasplante de páncreas mejora y revierte las complicaciones diabéticas. Finalmente, el trasplante de páncreas, un procedimiento mórbido, surge como una alternativa significativa en el manejo de la diabetes, compitiendo directamente con las terapias convencionales de insulina. Hasta ahora, los resultados indican que el modelo de trasplante más efectivo es el simultáneo de páncreas y riñón. Aunque más pacientes podrían beneficiarse de este procedimiento, las complicaciones quirúrgicas y la necesidad de inmunosupresión plantean desafíos significativos.

Palabras clave: *Trasplante de páncreas. Diabetes mellitus. Selección de donante de páncreas. Técnica quirúrgica. Resultados.*

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Introduction

The first report of a human pancreas transplant (PTx) was a simultaneous pancreas-kidney procedure performed in 1966 by Drs Richard Lillehei and William Kelly[1]. In Mexico, the current evidence is limited to a case report of simultaneous pancreas-kidney (SPK) transplantation[2]. The evolution of pancreatic transplant was determined by the advancement of technology as to surgical technique, preservation of organs, and immunosuppression[3]. Transplantation of the pancreas is the only near-cure treatment for type 1 diabetic patients[4]. Diabetes is the leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide[5]. Successful pancreas transplantation provides durable insulin independence, preventing worsening of diabetic complications (microvascular and macrovascular systems, causing multiple complications in the cardiovascular, renal, ophthalmic, and nervous system), and improving quality of life[1,6].

Materials and methods

A bibliographic search was implemented in PubMed/Medline, Clinical Key, ScienceDirect, and Index Medicus with MESH terms, from the year 1967 to 2024. The detailed data retrieval strategies and inclusion procedure of this study are shown in figure 1.

Objectives

Transplantation of a whole pancreas is being offered for the treatment of diabetes, the goals of the pancreas transplantation program should include:

- Surgical procedure with overall low morbidity and mortality
- Progressive elimination of the insulin requirements and close blood glucose monitoring with the creation of a euglycemic state, the HbA1c levels should be comparable to those non-diabetic populations
- Eliminate the occurrence of significant hypoglycemic events
- Improved glucose control reduced the long-term complications of insulin-dependent diabetes[3,7,8].

Epidemiology

According to data from the International Diabetes Federation, there were 536.6 million people between the ages of 20 and 79 with diabetes worldwide in 2021. Mexico ranks seventh in terms of cases, with an approximate estimate of 14.1 million people with diabetes in 2021. However, Encuesta Nacional de Salud y Nutrición (Ensanut) 2021 indicates that 12.4 million people have diabetes. It has been roughly estimated that only about 1% of the reported cases of diabetes correspond to type 1 diabetes (T1D) with greater prevalence among children and young adults; the incidence overall annual increase of approximately 3%[9]. At present, 6.2 million Mexicans with diabetes are experiencing varying stages of renal insufficiency[10].

Diabetes is the second leading cause of death in Mexico, following cardiovascular diseases. According to the most recent numbers released by the Instituto Nacional de Estadísticas y Geografía, the deaths due to this disease in the previous year were 140,729 which represents 13% of the total in 2021; of those who died from Diabetes 105,395 (74.9%), or three out of every four, were not insulin-dependent, meaning they did not require insulin administration; while 3,109 (2.2%) were[11].

Pancreas transplantation for type 2 diabetes (T2D) accounts for 18.4-20.6% of all PTxs performed annually[12].

Most recipients with T2D require an SPK transplant due to the additional ESRD. Between 2016 and 2020, 19% of SPKs, 12% of pancreas after kidney (PAK), and only 2% of pancreas transplant alone (PTA) were performed in patients with T2D, the rest (77%) were due to T1D[13].

Types of transplantation[4,8,14-17]

- SPK transplant is the most common type of PTx. SPK is a well-established treatment modality for patients with severe metabolic complications and ESRD. Both organs are procured from a single deceased organ donor[14]. SPK performed before dialysis (i.e., preemptive SPK) is associated with improved results[18,19].
- PAK transplantation is offered to diabetic patients who have had a kidney transplant. PAK sequence in patients who have a viable living kidney donor identified, because the waiting time for a pancreas alone is much shorter than for a kidney-pancreas, transplantation should be performed < 1 year after kidney transplantation[18,19].
- PTA considered for recipients with eGFR > 60 mL/min/1.73 m^2 is offered to candidates with frequent, acute, and potentially life-threatening

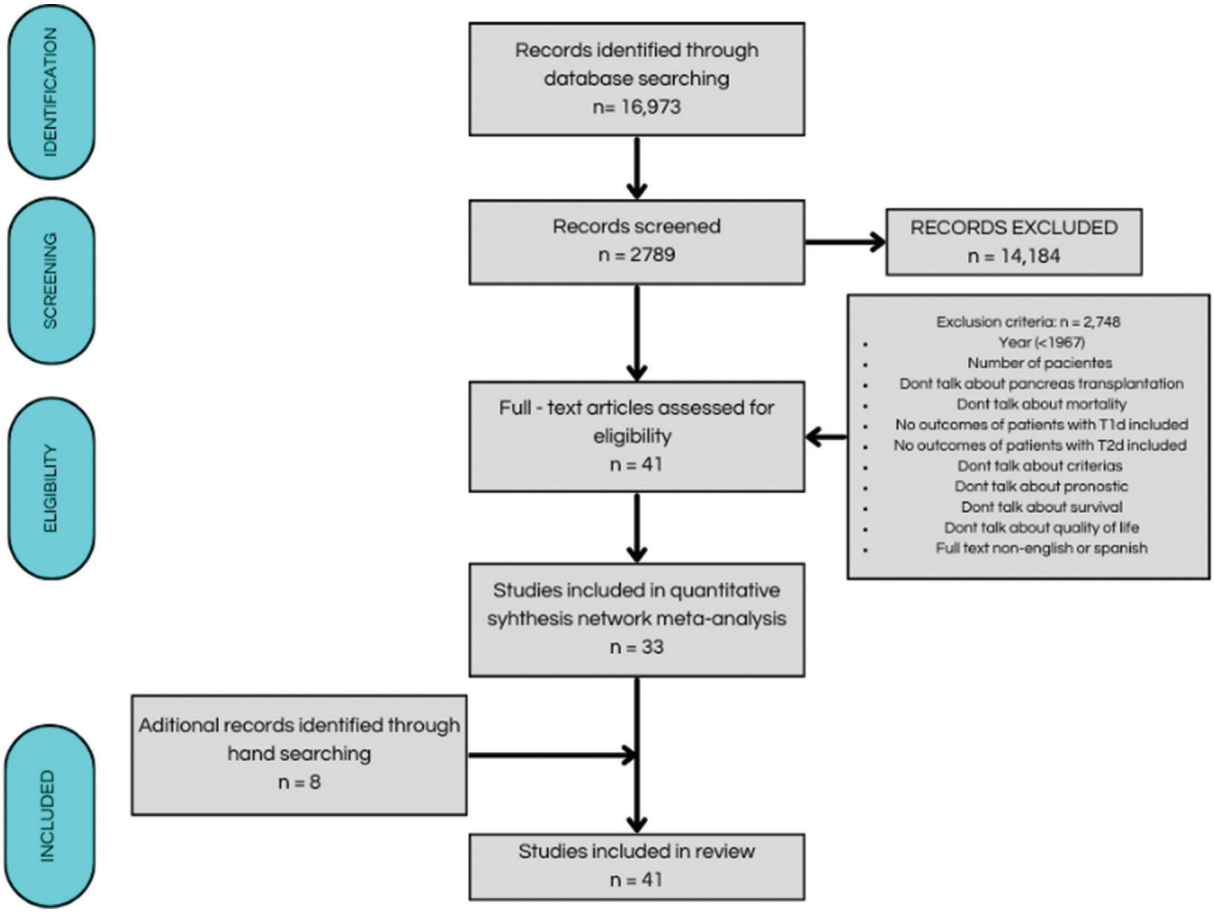

Figure 1. *Data retrieval strategies and inclusion procedure of this study.*

complications of diabetes such as ketoacidosis, hypoglycemia unawareness, and incapacitating problems with insulin therapy is suitable for this type of transplantation. For this patient group, PTx can be lifesaving but must be weighed against the risks of lifelong immunosuppression, and also have stable renal function to tolerate potential calcineurin nephrotoxicity[19,20].

- Living donor segmental pancreas grafts have been described, with or without concurrent living donor kidney transplantation, but are not common[19,20].
- Islet cell transplantation is an appealing alternative to whole pancreas transplantation and it is frequently recommended after total pancreatectomy for benign disease to avoid the insulin-dependent state of these procedure[19,20].

Criteria for waiting list

Patients are listed for PTx after meeting the following United Network for Organ Sharing (UNOS) criteria:

- Insulin therapy and absolute deficiency of endogenous insulin demonstrated by a C-peptide ≤ 2 ng/mL; or
- Insulin with a c-peptide > 2 ng/mL and have a body mass index (BMI) ≤ 28[14].

Other authors establish different criteria, which are listed in table 1.

Contraindications

Absolute contraindications (Table 2) and relative contraindications are shown in table 3.

T2D receptor

Originally considered exclusively for patients with TID, improving outcomes has resulted in an expansion of SPKT to selected patients with T2D as well.

Conceptually, the TID terminology is used to describe patients with diabetes who do not produce sufficient insulin, whereas T2D terminology is reserved

Table 1. Criteria for waiting list

Diabetic patients with imminent or established ESRD who have had or plan to have a kidney transplant[17,35].
A history of frequent, acute, and severe metabolic complications (hypoglycemia, hyperglycemia, ketoacidosis) requiring medical attention[16,36].
Incapacitating problems with exogenous insulin therapy16,36.
Consistent failure of insulin-based management to prevent acute complications[14].
High risk of secondary chronic complications of diabetes (e.g., nephropathy, retinopathy, neuropathy) is judged to be fit enough to survive the operation[7].
A small number of pancreas transplants are also performed for chronic pancreatitis and malignancy requiring pancreatectomy[14,16].

ESRD: end-stage renal disease.

Table 2. Absolute contraindications for PTx[4]

Age over 65
Noninsulin requiring diabetes with the absence of glucose hypermobility or progressive diabetic complications
Significant cardiovascular disease (with severe, non-correctable coronary artery disease, recent myocardial infarction, left ventricular ejection fraction < 50%)
Pulmonary artery systolic pressure over 50 mmHg
Presence of severe peripheral vascular (aortoiliac) disease
Incurable malignancy except localized skin cancer
Active sepsis or peptic ulcer
Inadequate psychosocial support and financial resources
Poor overall functional and performance status (severe deconditioning or malnutrition, frailty, sarcopenia, dementia, wheelchair-bound, need for chronic oxygen therapy)
A major psychiatric history which can result in non-adherence to the treatment
Inability to withstand surgery
Positive crossmatch with a specific donor

Table 3. Relative contraindications for PTx[6]

Excessive need for insulin > 1.5 U/kg/d
Cerebrovascular event with long-standing impairment
Hepatitis B or C viruses (HCV)
Human immunodeficiency viral infection
Peritoneal dialysis with multiple episodes of peritonitis; multiple previous laparotomies; previous intra-abdominal/pelvic irradiation or multiple surgical procedures
BMI > 30 kg/m
Extensive vascular, aortic, and renal artery disease
Presence of an ostomy, feeding tube, or chronic bladder drainage catheter
Limited social support (lives alone, relies, on public transportation) or financial resources
Continuous use of alcohol, smoking, and other drugs.

BMI: body mass index.

Table 4. Pancreas transplantation in patients with T2D[5,15,27,34]

Age < 60 years
BMI < 30 kg/m^2
Fasting a C-peptide level 10 mg/mL or less
Total daily insulin dose < 1.5 U/kg/day and < 100 U/day
Insulin requiring for minimum of 3-5 years
Presence of complicated diabetes including glucose hypermobility
Absence of smoking, major amputation, severe cardiac, or vascular disease
No recent history of dietary and medication non-compliance
Adequate psychosocial and financial support

BMI: body mass index.

for those that are “insulin resistant.” TID continues to produce some insulin but in insufficient quantities. Alternatively, T2D stops producing insulin entirely. For this reason, defining the type of diabetes by C-peptide levels alone is inadequate (Table 4)[16].

PTx was uncommon among recipients aged over 60 years. This practice is changing and in 2016, almost one-fourth of pancreas recipients were aged > 60 years at the time of transplant; reports suggest that these older recipients had similar patient survival compared with younger recipients, although more cardiovascular events occurred in the older recipients[21].

PTx versus insulin

Insulin therapy achieves good glycemic control but does not allow the restoration of damaged β-cells or prevent vascular complications resulting in irreversible organic damage is inevitable in most patients. Sometimes, even in the case of correct administration, episodes of hyperglycemia can occur and if persistent can lead to irreversible complications systemically.

Therefore, the development of pancreas transplantation is not only a research challenge but also a necessity for the entire population[15,18].

Donor selection

The ideal pancreas donor is, as with most other solid organ transplants, a young healthy heart-beating donor aged < 60 y and with a normal BMI. Donors with a BMI (kg/m^2) of > 30 are not routinely used for whole PTx due to concern for fatty infiltration and a higher risk of graft pancreatitis. Donors > 60 years of age have a higher risk of atherosclerosis and islet depletion and are also rarely used[3,14,16].

Since 2009, the Eurotransplant Pancreas Advisory Committee designed the pre-procurement pancreas suitability score (P-PASS) and was introduced to support clinical decision-making and ultimately expand the currently insufficient pancreas donor pool which is a calculated score based on nine donor-specific clinical parameters. Including patient age, BMI, the occurrence of cardiac arrest, serum levels of sodium, amylase, lipase, vasopressor substances (adrenaline or dopamine), and the length of stay in the intensive care unit[22], however, the predictive value remains controversial.

Furthermore, the pancreas donor risk index (pDRI) is a measure of allograft quality that predicts the risk of allograft failure at 1 year. The pDRI consists of the specific donor characteristics that include gender, BMI, serum creatinine, age, race, cause of death, donor after cardiac death, and the parameter of pancreas preservation time[23]. P-PASS and pDRI are used to know whether or not an organ is acceptable for transplantation. The eurotransplant now recommends that pancreas grafts from donors with a P-PASS score of < 17 should be considered for organ transplantation because they have a 3-times higher acceptance rate as compared to grafts with a P-PASS score of $\geq$ 17[22].

Donor contraindications

The donor selection criteria are more strict for pancreas transplantation as compared to other organs, thus limiting potential donors. The donor organ may be rejected due to alcohol intake or a family history of diabetes, pancreatic disease, malignant tumor, prior surgery of the duodenum, pancreas, or splenectomy, positive serology for infectious diseases (human immunodeficiency viral infection, Hepatitis C viruses, Hepatitis B viruses), chronic liver disease, and BMI > 30 kg/m^2.

Macroscopic evaluation of the pancreas considers the presence of signs of acute pancreatitis, glandular edema, hematoma, fatty infiltration (associated with severe reperfusion pancreatitis), and/or hardened consistency since such factors increase the risk of post-transplant complications, and under these conditions, the grafts should be discarded[12].

Surgical technique

The PTx is preferentially done in the right iliac fossa of the recipient as the right iliac vessels are more accessible. The native pancreas and kidneys are left in place[4,6].

Ideally, preservation time should not exceed 12 h, but preservation times up to 24 h can still be accepted[19,20].

- Donor: Procurement of the pancreatic graft is generally part of the removal of multiple intra-abdominal organs[12]. The pancreatic graft is removed *en bloc*, along with the duodenum and spleen, preserving the vascular stumps of the superior mesenteric and splenic arteries, and of the portal vein[3].
- Graft: On back table surgery, the pancreatoduodenal graft is prepared basically by removing the spleen, shortening the duodenal segment, suture, and invagination of the duodenal borders, mobilization of the portal vein, and vascular Y graft reconstruction (iliac arteries from the donor with the pancreatic graft superior mesenteric artery and splenic artery)[3].
- Recipient: The blood vessels of the new pancreas are connected to the external iliac vessels. The pancreas has two arterial supplies, so a “Y” graft from the donor iliac artery sutured onto the donor superior mesenteric and splenic arteries[4,6,7], which allows both to be supplied from a single arterial anastomosis.
- Drainage: The implant of the pancreas can be done by drainage of systemic or portal venous blood. Drainage of pancreatic exocrine secretion of the graft can be enteric (side-to-side duodenojejunal anastomosis) or vesical (side-to-side duodenovesical anastomosis)[3].

With the technique used, there are advantages and disadvantages, as in any procedure. Next, we will discuss the different types of exocrine drainage.

- Exocrine (enteric vs. bladder) drainage:

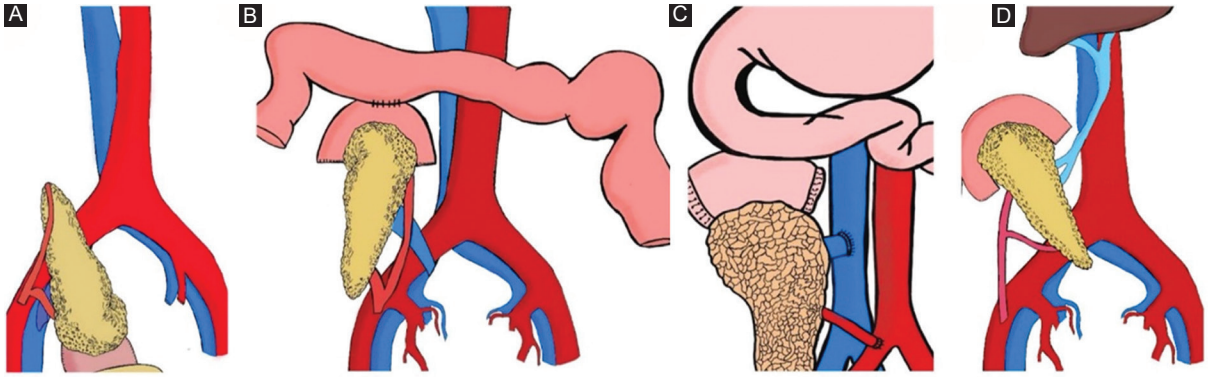

Figure 2. *Types of drainage.* **A:** *bladder exocrine drainage and systemic venous endocrine drainage.* **B:** *enteric exocrine drainage and systemic venous endocrine drainage.* **C:** *duodenal exocrine drainage and systemic venous endocrine drainage.* **D:** *enteric exocrine drainage and portal venous endocrine drainage.*

- Bladder drainage (Fig. 2A). Some advantages include that pancreatic dysfunction can be detected early by changes of urinary amylase, easily accessible for biopsy, and reduced rate of infection due to the relative sterility of the lower urinary tract. It has many technical advantages: bladder vasculature promotes healing anastomosis, bladder mobilization permits tension-free anastomosis, multilayer anastomosis, and control of anastomotic leakage can be achieved by bladder catheter. Some of the disadvantages include fluid and electrolyte imbalance and metabolic acidosis. Local effects include chemical cystitis, hematuria, urethritis and urethral stricture, bladder leak, and reflux pancreatitis; lower urinary tract infection and stone formation; in male effects are epididymitis, prostatitis, and prostatic abscess[8]. Up to 25% of patients with bladder drainage will need a conversion to enteric drainage within 10 years[7].
- Enteric drainage (Fig. 2B)[1]. Lillehei described that enteric drainage is more physiological and avoids urologic complications. Some disadvantages include a higher incidence of pancreatitis, leakage of pancreatic enzymes, and peripancreatic fluid collections, more risk of anastomotic leakage, peritonitis, intra-abdominal collection and sepsis[24], inability to measure exocrine secretions for early detection of graft dysfunction and allograft biopsy is more challenging.
- Duodenal drainage (Fig. 2C). A modification of enteric exocrine drainage with additional benefits in the form of improved accessibility for biopsy through endoscopy, it expands the options for exocrine drainage sites, especially in cases of pancreas retransplantation. Same disadvantages mentioned above with enteric drainage except for relatively easily accessible allograft.

Experts confirmed that enteric drainage should be preferred over bladder drainage with respect to infectious, metabolic, and urinary tract complications[6,20].

- Endocrine (systemic venous vs. portal venous) drainage:
  - Systemic venous drainage (Fig. 2A). Some disadvantages include hyperinsulinemia (predisposes to accelerated atherosclerosis) and hiperlipoproteinemia[25].
  - Portal venous drainage (Fig. 2D). Some advantages include[26] avoiding the risk of postprandial hypoglycemia, better lipoprotein metabolism, and allowing physiological passage of insulin through the liver in which it undergoes 50% first-pass metabolism. Some disadvantages are mentioned above in addition to a higher risk of vascular thrombosis.

Portal venous drainage provides better results than system venous drainage[6,20].

Complications

In general, the primary complication related to pancreatic graft loss is technical failure (loss of the graft in the first 3 months of a transplant), followed by acute or chronic rejection. The risk factors for surgical complications are donor or recipient having a BMI > 30 kg/m^2 for donor or recipient age over 45 years, prolonged preservation time (> 24 h), cerebrovascular disease as a cause of donor death, retransplantation, and prior abdominal surgery. Infectious complications are the

primary causes of morbidity and mortality in pancreas transplantation[4].

Without any risk factors, the risk of technical failure is 7.3%; with one risk factor, it is 12.8%; with two, it rises to 26.7%; and with three or more, it reaches 42.9%. These factors have an impact on graft survival. With just one risk factor, graft survival is 92.5%, but with two, it decreases to 75.9% and with three factors, survival is only 57.1% at 1 year[27].

PTxs are particularly susceptible to graft rejection, with an incidence of 15-21% at 1 year and 27-30% at 5 years. The rejection rate is lower in older than in younger recipients but those > 50 years have an increased rate of post-operative complications that should be taken into account when the benefits and risks are assessed[7].

The complications of PTx can be divided into surgical (early and late), medical, and immunologic (acute and chronic).

Some examples of early surgical complications are infection (incidence 18%), anastomotic leaks (urinary: 5-18% and enteric 4-9%), venous or arterial graft thrombosis (5-15%), hemorrhage intraabdominal, gastrointestinal or bladder (10%), pancreatic-enteric fistula (4-6%), and graft acute pancreatitis (3%).

Some examples of late surgical complications are infection (38%), venous or arterial graft thrombosis (7-20%), peripancreatic collection (20%), pseudoaneurysm (8-16%), wound dehiscence (14%), pancreas retransplant (5.9%), hemorrhage intraabdominal, gastrointestinal or bladder (5%), post-transplant pancreatectomy (4.5%), bowel obstruction (3%), graft pancreatitis (2.5%), incisional hernia (2.5%), and pseudocyst pancreatic (< 1%).

Some examples of medical complications are cytomegalovirus infection (10-42%), acute tubular necrosis (5-30%), and BK virus nephropathy (2.9-7.5%).

Some examples of immunologic complications are acute rejection (15-21%) and chronic rejection (27-30%)[13,27].

Outcomes

Graft survival

Graft survival (defined as total freedom from insulin therapy, normal fasting blood glucose concentrations, and normal or only slightly elevated HbA1c) was 82-98% at 1 year, 90% at 5 years, and 75-54% at 10 years for SPK recipient[6,13,14,28]; 71% PAK, and 62% PTA at 1 year[13].

The best survival of the pancreatic and renal grafts in the first post-transplant year is 86% and 93%, respectively, in the SPK category. Graft loss due to immunological rejection in the first post-transplant year for SPK, PAK, and PTA was, respectively, 1.8%, 3.7%, and 6%[3].

Boggi et al., report 10-y outcomes following PTA in 66 patients with T1D and low BMI (< 30 kg/m^2). At 10-y follow-up, overall mortality was low (7.6%), good or excellent pancreas allograft function (death-censored) was 60% (57% insulin free), and the incidence of progression to stage 4/5 CKD was 10%[24,29].

The longest surviving graft was recorded as SPK transplant 26 years, 24 years pancreas after a kidney, and 23 years for PTx alone[4,19,20].

The most common causes of graft loss after 10 years are death of the recipient (53%) and chronic rejection (33%)[19]. PTx is associated with an all-cause mortality rate of 4% at 1 year and 9% at 5 years. The single most common cause of death is cardiovascular[14].

Patient survival

The patient survival rate after primary deceased donor PTxs at 1 year for SPK recipients was 96.9% in 2016-2020 versus initially 58.3% in 1966-1985; for PAK recipients, 96.3% versus 81.4%; and for PTA recipients, 98.3% versus 75.2%[30].

Fifteen year actuarial patient survival is 56% (pancreas graft success 36%) for SPK, 42% (18%) for PAK, and 59% (16%) for PTA[7].

With the improvement in outcome, long-term survival is dependent on the length of possible follow-up. Long-term patient survival rates have paralleled short-term outcomes: the 5-year patient survival rate has reached over 90% and the 10-year survival rate over 70% in all three recipient categories. At 20 years, after a successful SPK or PTA transplant > 30% of SPK recipients and 25% of PAK recipients were alive.

PTA does not increase the long-term risk of mortality when compared to continued insulin therapy and could be actually associated with a survival advantage, especially in patients who have impaired hypoglycemia awareness[14,19,20].

They found that mortality for PTx and PTA recipients is not higher than for patients on the waiting list and managed by insulin[31].

Therefore, pancreas transplantation is justified on the basis of the data for survival, and the most

important factor for long-term survival is the preservation of the pancreas graft[17].

Effect on diabetic complications

- Nephropathy: diabetic Kidney Disease, often referred to as diabetic nephropathy, is a progressive disorder defined by reduced renal function due to hyperglycemia, often co-occurring with albuminuria. Individuals with diabetes can also present with non-specific kidney disease in which their reduced renal function is a result of risk factors independent of or indirectly related to their diabetes, such as hypertension, obesity, or dyslipidemia
- Neuropathy: diabetes is a leading cause of nerve damage, particularly for the longer peripheral nerves that innervate the lower limbs. In general, diabetic neuropathies can be divided into several subtypes, including the most common form, distal symmetric polyneuropathy (a type of peripheral neuropathy), autonomic neuropathies, atypical neuropathies and also non-diabetic neuropathies common in diabetes. On top of excess pain and decreased quality of life associated with diabetic neuropathy, individuals with diabetes have a 15–25% lifetime risk of foot ulcerations and a 15-fold increased risk of lower-extremity amputation compared with individuals without diabetes[32].
- Retinopathy: hyperglycemia can induce progressive damage to the blood vessels in the retina, which can lead to hemorrhage, retinal detachment, and blindness. Diabetic retinopathy can be classified as an early, more common non-proliferative diabetic retinopathy (PDR) form, characterized by weakened blood vessels, and as the more severe, late-stage PDR form, characterized by the growth of new fragile and leaky blood vessels throughout the retina and into the vitreous. Diabetic retinopathy is the most common diabetes complication and is the most frequent cause of new cases of blindness among adults aged 20-74 years in developed countries.
- Atherosclerotic cardiovascular disease: Defined as coronary heart disease, cerebrovascular disease, or peripheral artery disease presumed to be of atherosclerotic origin[33].

In table 5, chronic complications are listed along with the effect provided by the PTx.

Table 5. Effect on diabetic complications

Complication	Effect
Glycemic control	Lowers Hb1Ac levels; restores glucagon secretion; improves the counter regulatory responses to hypoglycemia[14,13]
Nephropathy	Improvement in glomerular, tubular basement membrane thickening; proteinuria decreased[5,6,13,14,17,19,20,29,37]
Neuropathy	Stabilization and improvement of motor and sensory nerve conduction[5,13,14,17,19,20,37,38.]
Retinopathy	Can deteriorate in 10-35% of patients with unstable eye disease immediately after PTx, however, the benefits become apparent after a few years. Cataracts may worsen due to treatment with calcineurin inhibitors and steroids[7,14].
Cardiovascular disease	Regression of coronary atherosclerosis in 40%, lower incidence of myocardial infarction, left ventricular ejection fraction was higher; control of blood pressure[5,7,13,14,17,19,39,40]
Cerebrovascular disease	Carotid intimal thickness has been seen to improve within 2-y[7,13]

Discussion

Diabetes is a healthcare and social pandemic pathology whose treatment poses several challenges to health professionals and determines a conspicuous health-care expenditure globally[9]. The number of patients with type 1 and T2D is rapidly growing worldwide. Diabetes mellitus is a health care and social pandemic that presents a multitude of a serious challenge for developed as well as for developing countries. Even with improvements in new technologies, for some patients, a successful PTx will remain the best option for an insulin-free life[13].

The complications of chronic diseases also affect health care by increasing the number of hospitalizations, the length of hospital stays, and health management costs[19].

PT recipients are older and the rate of recipients with T2Ds has significantly increased. Over the past years, indications for pancreas transplantation have changed considerably. PTx recipients are older and the rate of recipients with T2Ds has significantly increased. In countries such as China and India, where T2Ds is now endemic and rates are increasing, over 80% of PTx recipients have T2Ds and are primarily patients with ESRD who do require both kidney and pancreas grafts. This trend will continue in the rest of

the world, also in part due to the growing obesity pandemic. In addition, pancreas transplantation is increasingly offered to Black, Hispanic, and Asian recipients, who are no longer considered to be high-risk patients. Initially, pancreas transplantation was developed for young recipients with brittle diabetes and rapidly developing secondary complications[13].

Originally developed as a therapeutic modality to reestablish endogenous insulin secretion responsive to normal feedback controls, vascularized whole organ PTx has evolved into a method of complete β-cell replacement that frees the patient with diabetes from the need to monitor serum glucose concentrations with finger sticks and from dependence on exogenous insulin administration, and hypoglycemic unawareness is no longer a problem. Unfortunately, PTx entails a major surgical procedure, a limited number of donor organs, and the necessity for long-term immunosuppression, which means that despite the high likelihood of rendering patients ex-diabetic, it is considered a treatment rather than a cure. A successful PTx is currently the only definitive long-term treatment that restores normal glucose homeostasis and may prevent, stabilize, or even reverse progressive diabetic complications[16].

Outcome after PTxs significantly improved over the past 50 years in all recipient categories (transplant techniques, immunosuppression therapies, and post-transplant monitoring of graft function and rejection)[8]. As a result of this success, the number of PTxs performed worldwide continues to grow, as does the number of PTx centers around the world. Patient survival during the last decade of the 20th century improved to the point that a PTx, regardless of the recipient category, became not only a viable option but also a desirable option[13].

SPK has been shown to have beneficial outcomes compared to kidney transplant alone with regards to prolonged kidney allograft function, patient survival, quality of life, and delayed progression of diabetic complications.

Clearly, while outcomes of SPK transplantation are equivalent T1DM and T2DM recipients, the recipient profiles are not. Randomized trials will continue to be lacking, and the debate regarding BMI and C-peptide cutoffs remains. Randomized trials are needed to compare different modalities for treating T2DM CKD patients. Despite current UNOS regulations restricting patients with high C-peptide and high BMI from receiving an SPK transplant, the existing medical evidence does not support using BMI or C-peptide for determining SPK candidacy. Insulin-dependent patients with ESRD should be evaluated for pancreas transplantation (SPK or PAK) based on their predicted ability to tolerate the morbidity of the surgical procedure and immunosuppression. PTA transplantation in T2DM will remain reserved for those with severe metabolic disturbances and incapacitating clinical and emotional problems with exogenous insulin therapy, which is generally rare amongst T2DM patients. We currently believe that centers should decide on a case-to-case basis whether to accept a patient for transplantation or not. As national UNOS-mandated BMI thresholds do not exist for other organs such as kidney and liver, we believe they should not exist for pancreas transplantation[34].

Transplantation of a pancreas, unlike the liver, lung, and heart, is not a life-saving operation but it improves quality of life. The long-term advantages of this surgical procedure have to be balanced against the potential morbidity and mortality associated with it, and the side effects from the long-term immunosuppression that is needed to prevent alloimmunity and autoimmune recurrence[7].

Conclusion

The pancreatic transplant, is a morbid procedure, emerges as a significant alternative in diabetes management, directly competing with conventional insulin therapies. Although the latter have been fundamental pillars in diabetes treatment, pancreatic transplantation stands out for its ability to prevent or even reverse late complications associated with this chronic disease. Results so far suggest that the most effective transplant model is the SPK, providing a comprehensive solution to address both pancreatic dysfunction and renal complications. While more patients could benefit from this procedure, surgical complications and the need for immunosuppression pose significant challenges.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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