Pancreas transplantation

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Abstract

Pancreas transplantation is now the standard of care for selected patients with diabetes and end-stage renal failure or life-threatening diabetic complications. The morbidity and mortality of pancreas transplantation is higher than other transplant types, and for this reason selection criteria for both donors and recipients are more stringent. Meticulous organ retrieval technique and back-table preparation, and a standard implantation technique using enteric drainage are central to good outcomes. Modern immunosuppression has reduced acute rejection rates and lowered the need for long-term corticosteroids. Results have improved over time and recipients of a simultaneous kidney−pancreas transplant can now expect 5-year transplant survival of around 80%. The addition of a pancreas to a kidney transplant for suitable recipients has clear benefits in both length and quality of life, and there is increasing evidence that pancreatic transplantation can reduce or halt the progression of diabetic nephropathy, neuropathy, retinopathy and cardiovascular disease. In patients with normal renal function, pancreatic islet transplantation offers an alternative with reduced peri-procedural morbidity and mortality, at the expense of lower rates of long-term insulin independence.

Keywords Diabetes; islet transplantation; pancreas transplantation

Introduction

Clinical transplantation of the pancreas was first performed in December 1966 at the University of Minnesota Hospital. Since then, over 63,000 pancreases have been transplanted worldwide with an annual rate of approximately 2,500.[1] In the UK, where there has been central NHS funding of pancreas transplantation since 2004, there were 334 pancreas donors (i.e. donors that fulfilled nationally agreed criteria) in the financial year 2021−2022, resulting in 131 solid-organ pancreas transplants (92% of which were transplanted simultaneously with a kidney) and 22 islet transplants. Pancreas transplantation has evolved from being an experimental to a routine procedure, but these relatively small numbers also reflect that, despite the high prevalence of

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diabetes, transplantation of the pancreas does not yet have the impact of kidney or liver transplantation. Indeed, annual numbers of pancreas transplants worldwide declined during the period between 2005 and 2015, mainly resulting from a decrease in pancreas-alone transplants in the US, before stabilizing over the past few years.[2]

Indications

Pancreas transplantation is the only curative treatment for patients with diabetes mellitus. Traditionally, only patients with type 1 diabetes were candidates for pancreas transplantation. This disease is characterized by immune-mediated destruction of the insulin-producing beta cells of the islets of Langerhans in the pancreas leading to complete insulin deficiency. However, this accounts for only about 10% of all cases of diabetes mellitus in a Caucasian population. In such patients pancreas transplantation can restore the physiologic hormone balance and, if performed at early stage, pancreas transplantation probably has the potential to stabilize or improve the complications of long-term diabetes (e.g. retinopathy, nephropathy and neuropathy).

In contrast, type 2 diabetes is often characterized by obesity and peripheral insulin resistance and, until recently, it was generally accepted that pancreatic transplantation would not be of benefit. However, it is increasingly clear that there is a wide spectrum of conditions with the label of type 2 diabetes and several recent reports have demonstrated improved glycaemic control after pancreas transplantation in subsets of type 2 diabetic patients. Thus, the old paradigm is no longer generally applicable, and 18% of pancreas transplants are performed in type 2 diabetic patients.[1,3] Suggested criteria for suitable type 2 diabetic patients include longstanding insulin dependence with requirements less than 1 unit/kg/24 h, BMI less than 32 kg/m^2 and absence of cardiovascular disease.[4]

Solid organ pancreas transplantation

Three main types of solid organ pancreas transplant are commonly performed.

Simultaneous transplantation of pancreas and kidney
SPK is the most common type of pancreas transplant, accounting for around 90% of all procedures. Combined kidney and pancreas transplantation is generally recommended for patients with type 1 diabetes and chronic renal failure. These patients receive both a kidney and pancreas from a single deceased organ donor.

Pancreas transplantation after kidney transplantation
PAK is performed in diabetic patients who have had a successful kidney transplant. This type of transplant is particularly relevant to the growing number of diabetic patients who initially undergo kidney transplantation from a living donor. Today 8%−15% of pancreas transplants are performed as PAK.

Pancreas transplantation alone (PTA)
Patients with type 1 diabetes with (yet) normal kidney function but life-threatening diabetic complications (e.g. hypoglycaemic unawareness) or rapidly progressing and severe side effects of type 1 diabetes (neuropathy, retinopathy, etc.) may be suitable to

receive a pancreas transplant alone. The decision is based on a risk—benefit analysis, comparing the risks of on-going diabetes with those of transplantation (particularly long-term immunosuppression). Historically, this type of pancreas transplantation has been associated with inferior outcomes when compared to SPK, and most of the recent decline in transplant numbers is in this group.

Islet transplantation

Islet transplantation is the transplantation of a purified preparation of isolated pancreatic islets. In order to achieve insulin independence, transplantation of two or more donor organs may be needed sequentially. In most, if not all, clinical programmes, the islets are infused via the portal vein, which is accessed by a radiological, trans-hepatic approach, into the liver. The strategy of transplanting only the endocrine component of the pancreas is highly attractive as this comprises only about 2% of the gland and excludes the exocrine component that is responsible for much of the morbidity of the whole organ transplant. At present, however, the medium-term results of islet transplantation are inferior to those of the whole organ, with many transplanted patients reverting to insulin by 5 years. Nevertheless, even in patients who continue to require insulin therapy, islet transplantation often reduces the necessary dose, improves blood glucose control, and greatly reduces the risk of episodes of severe hypoglycaemia (hypoglycaemic unawareness) in this selected group of patients with very hard-to-manage diabetes. Simultaneous transplantation of the islet and kidney is also increasing in popularity for those patients with contraindications to solid pancreas transplant (e.g. cardiovascular disease).

Recipient selection

While pancreatic transplantation may potentially benefit any diabetic patients in the categories defined above, the risks of transplantation must be weighed against the potential benefits for each recipient. An assessment must be made of the potential additional benefit of a pancreas transplant over that of a kidney transplant alone. Transplantation of the pancreas is associated with greater perioperative morbidity and mortality than renal transplantation, and this patient population has a high incidence of cardiovascular and peripheral vascular disease. The importance of adequate pre-transplant assessment cannot be overemphasized, which may include 12- lead ECG, echocardiogram, myocardial perfusion studies and cardiac stress testing depending on local protocol. Any cardiac disease that is detected should be treated prior to addition to the waiting list; untreatable cardiac disease is a contraindication.

The usual contraindications to transplantation apply to this population, including recent history of malignancy and active infection. Most units have an upper age limit of around 60 years of age, and would exclude patients with a body mass index (BMI) of greater than 30, although there is a tendency to widen recipient selection criteria over time.[1]

Donor selection

While selection criteria for recipients have relaxed over time, the criteria for selection of potential donors have tended to become more restrictive in recent years. This trend has occurred on the realization that the penalties of transplanting a substandard organ are severe, and pancreas transplantation is not an immediately life-saving operation. This represents a significant challenge in light of an increasingly marginal donor population, with more donors after cardiac death (DCD) and older, obese donors. Absolute contraindications include donor diabetes, acute or chronic pancreatitis, transmissible infection and malignancy. The ideal donor is a donor after brain-stem death (DBD), less than 45 years of age, haemodynamically stable, BMI less than 30 and with only a short period of intensive care treatment. However, most pancreas centres transplant organs from donors with a broader limit of inclusion criteria. The upper age limit varies, with differences between transplant centres, between 50 and 60 years. Grafts from older donors and a cerebrovascular cause of death have poorer outcomes, as do organs with signs of fatty infiltration or fibrosis. Fatty infiltration, in particular, increases the risk of reperfusion pancreatitis and for this reason most units have an upper limit for donor BMI of 30 kg/m^2. However, recent evidence suggests that carefully selected donors with BMIs between 30 and 35 kg/m^2 may have equivalent outcomes.[5] The risk factors for poor outcome are likely to be additive, which has led to the development of tools to assess donor risk and guide organ use.[6] Organs which qualify for islet separation share many of the requirements with whole organ grafts; however, some differences exist: isolation of the islets of young donors (<18 years) is technically challenging, whereas these are often excellent whole pancreas donors. Conversely, and in contrast to solid organ transplantation, older donors often make good islet donors. Pancreases from obese donors have a higher beta-cell mass and may be good islet donors. However, there is substantial overlap between the solid organ and islet groups with respect to suitable donor organs and the system of allocation to patients awaiting these two procedures may be controversial.[7]

Surgical technique

The donor operation

Technique: almost every pancreas retrieval is part of a multi-organ retrieval procedure. After an initial period of dissection in the warm phase, the abdominal organs are perfused *in situ* with ice-cold preservation solution. The pancreas is usually retrieved together with the spleen after removal of the liver; alternatively, the pancreas can be retrieved *en bloc* with the liver and the organs then separated during back-table preparation. The advantage of the latter is a faster organ removal and shorter warm ischaemic time; however, this procedure might be technically more challenging. The pancreas is very easily injured and any parenchymal damage can render the organ unusable.

The nature of the *in situ* perfusion is important. If the liver is perfused via the portal vein as well as the aorta, it is important to avoid obstruction to the portal venous outflow of the pancreas as this leads to venous distension. This situation is most likely to apply when a portal cannula is inserted via the superior or inferior mesenteric veins. Pancreas outflow can be secured by insertion of the portal vein cannula above the pancreas after the initial aortic cold flush and complete transection of the portal vein after insertion of the cannula to allow free outflow of preservation solution from the pancreas.

Commonly occurring pathology, particularly fatty infiltration or fibrosis, cannot be detected before retrieval surgery; this highlights the importance of an experienced surgical team for evaluation of the organ during surgery. The lack of clarity in quantifying 'donor quality' significantly contributes to the high number of pancreases being discarded for transplantation.[8]

Organ preservation: cold storage is the universally used method for pancreas preservation: the majority of units use University of Wisconsin solution (UW), whereas others use HTK solution. Several studies have addressed the question of the best preservation solution; although many show no difference, others demonstrate a higher incidence of acute rejection, graft pancreatitis and decreased rates of insulin independence when HTK is used.[9] The advantages of UW solution were also reported from an analysis of the UNOS database, especially in cases of longer cold ischaemic times (>12 hours).[10] Machine preservation, either normothermic or hypothermic, has not yet been introduced to the clinical practice of pancreas transplantation.

The recipient operation

When donor organs become available, time is paramount — the shorter the cold ischaemic time (time from cold flush in the donor until reperfusion in the recipient), the better the outcome. Ideally the whole process of organ procurement and transplantation takes place in less than 12 hours. The ischaemic tolerance of a pancreas is intermediate — it is not as highly sensitive to ischaemic damage as the heart or lung, nor is it as resistant as the kidney (see Nicholson/Hosgood in this issue).

The final confirmation of compatibility of donor and recipient is based on laboratory testing (e.g. a lymphocyte cross-match), which confirms the absence of donor-specific anti-HLA antibodies in the serum of the recipient. Serum of the recipient and a tissue preparation of the donor (from blood, lymph nodes or spleen) are analysed for this assay.

Back-table preparation (Figure 1a): in pancreas transplantation preparation of the organ before implantation is a major component of the procedure. The back-table preparation of the pancreas is paramount to success: technical failure, still the most common reason for graft failure in the early postoperative period, is reduced by meticulous care during this part of the operation.

Reconstruction of the arterial supply — on arrival at the transplant centre, the donor pancreas comprises the whole organ, the duodenum and proximal jejunum and the spleen. There are two arterial inflow vessels, the splenic artery and the superior mesenteric artery (SMA). The coeliac artery usually remains with the liver graft which leaves a short splenic artery stump with the pancreas. For reconstruction of the splenic artery and SMA, a Y-shaped artery graft is normally used; most commonly the donor iliac artery bifurcation provides an adequate graft (alternative potential bifurcated vascular segments include the brachiocephalic trunk or carotid artery). The gastroduodenal artery is only occasionally important for perfusion of the head of the pancreas; in most cases it can be ligated without consequence.

Preparation of the duodenum — the duodenum is stapled and transected at both ends during the retrieval procedure. In order to secure sufficient blood supply to the transplanted duodenum, the segment is shortened and the new staple line inverted by an interrupted or running suture line.

Clearance of peri-pancreatic tissue — the pancreas is embedded in retro-peritoneal connective tissue and fat. This tissue is mostly removed during back-table preparation of the organ. Larger vessels (including the inferior mesenteric vein) are ligated. Use of the harmonic scalpel may help to seal the small blood vessels in this well-vascularized tissue. The spleen is removed from the tail of the pancreas with careful ligation of all vessels.

Root of the mesentery — the root of the mesentery including the infra-pancreatic SMA and superior mesenteric vein (SMV) are normally dissected using a linear stapler device during the donor operation. This staple line can be secured with a running suture during back-table preparation. It is important that this staple/suture line is not applied so close to the lower border of the pancreas as to cause occlusion of the inferior pancreatico-duodenal artery (the first branch of the superior mesenteric artery and a vital blood supply to the head of the pancreas, especially if the gastro-duodenal artery is ligated).

Implantation (Figure 1b): in simultaneous pancreas kidney transplantation, the pancreas graft is usually implanted first in order to minimize cold ischaemia time. Pancreas transplantation is 'heterotopic' and the native pancreas is not removed. In most centres a midline incision is preferred over an iliac fossa incision or transverse abdominal incision for reasons of better access and greater flexibility in choice of anastomosis sites. There are considerable technical variants practised in pancreas transplantation; some, but not all, of these are described below.

The pancreas is placed on the right side of the pelvis with the duodenum/head of the pancreas placed cranially. Access to the inferior vena cava (IVC) and right common iliac artery is achieved by mobilization of the caecum, the ascending colon and the root of the small bowel mesentery. The short donor portal vein stump is anastomosed end-to-side to the recipient IVC. The portal vein should ideally not be extended with a vascular graft as this increases the risk of venous thrombosis post-transplant. The single pedicle of the arterial Y-graft is then anastomosed to the right common iliac artery. Once reperfusion is performed the graft is inspected for bleeding. The duodenum is then anastomosed to a convenient location on the proximal jejunum. This may necessitate a window in the right mesocolon. If kidney transplantation is also being performed, this is typically placed in the left iliac fossa and renal vessels anastomosed to the common or external iliac vessels.

Variations: although first performed in the 1960s, pancreas transplantation was widely adopted as a therapeutic procedure much more recently than kidney, liver and heart transplantation. Pancreas transplantation was associated with a high rate of severe complications, many of which related to technical issues in general and the management of exocrine drainage in particular. Pancreatic exocrine secretions contain highly potent proteolytic enzymes and, while not required for the successful reversal of diabetes, may cause serious complications. The fact that so many surgical variants have been tried over many years is an illustration that a satisfactory solution was not easily achieved. The most important variants of surgical technique will be briefly discussed:
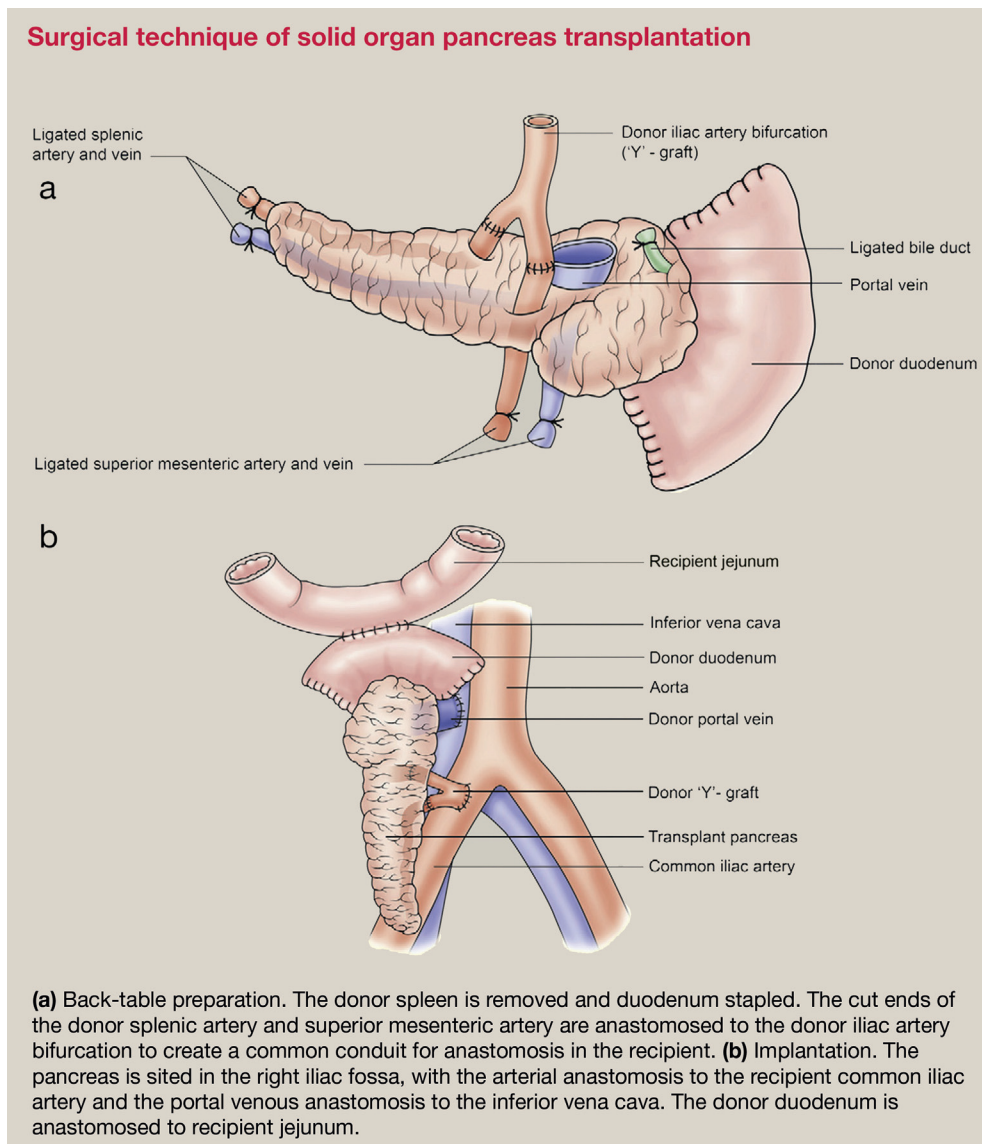
Surgical technique of solid organ pancreas transplantation

(a) Back-table preparation. The donor spleen is removed and duodenum stapled. The cut ends of the donor splenic artery and superior mesenteric artery are anastomosed to the donor iliac artery bifurcation to create a common conduit for anastomosis in the recipient. **(b)** Implantation. The pancreas is sited in the right iliac fossa, with the arterial anastomosis to the recipient common iliac artery and the portal venous anastomosis to the inferior vena cava. The donor duodenum is anastomosed to recipient jejunum.

Figure 1

Exocrine pancreas drainage − the pancreas produces about 1.5 litres of alkaloid, digestive, enzyme-rich fluid per day. As an alternative to the anastomosis of the duodenal segment with the proximal jejunum, anastomosis of the donor duodenum to the bladder was favoured for many years. In recent years, however, the more physiological approach with enteric drainage has regained popularity and with atraumatic surgical technique complication rates are now comparable with those of bladder drainage.

- The major advantage of bladder drainage is the readily available option to measure exocrine pancreas secretion in the urine. Urinary amylase correlates well with pancreas function and changes in concentration can be used as a surrogate marker for graft rejection. This is particularly useful in pancreas-alone transplantation, where there is no renal transplant to act as a rejection 'sentinel'. However, bladder drainage of exocrine secretions causes significant complications (cystitis, urethritis, infection) which often

necessitate later conversion to enteric drainage. Also, constant loss of bicarbonate sometimes leads to metabolic acidosis. For these reasons, conversion to enteric drainage is quoted in some series to be as high as 30%. Since the widespread use of enteric drainage these complications are rarely seen today.

- Duodeno-duodenostomy has been described more recently as an alternative to the duodeno-jejunostomy. The primary benefit is the ease of endoscopic surveillance; however, in case of complications and the need for graft pancreatectomy this technique could result in difficult handling of the residual native duodenum.

Portal or systemic drainage − a frequently debated technical aspect of pancreas transplantation is the site of venous outflow. Most commonly the portal vein is drained into systemic circulation via the IVC. Advocates of the more physiologic drainage into the portal venous system argue that systemic drainage leads to unphysiologically high systemic insulin levels, potentially

giving rise to complications, including pro-atherosclerotic effects. There has also been a suggestion that portal venous drainage may decrease the incidence of acute rejection.[11] However, available data do not show significant differences in metabolic or functional parameters between systemic and portal venous drainage.[12] The majority of units drain the pancreas into the systemic circulation, and the debate remains unresolved.

Live donation − in response to the shortage of suitable organs from deceased organ donors (and in line with transplantation of other abdominal organs) pancreas transplantation has been performed with grafts retrieved from living donors (using the body and tail of the gland). However, since the first attempts in 1979, numbers have remained low and this has been practised in only a very few centres. The potential benefits include decreased immunologic risks and higher rates of initial graft function based on shorter preservation times. However, the risks for the donor have to be balanced against these benefits; surgical complications (pancreatitis, pancreatic leak or fistula, etc.) and the potential for long-term endocrine insufficiency in the donor. These risks are a serious cause of concern and have prevented the more widespread adoption of this technique.[13]

Postoperative management

Immunosuppressive therapy
The pancreas is an immunogenic organ and immunosuppressive treatment after pancreas transplantation is of comparable intensity to that used in kidney transplantation. Most centres use combination therapy based on antibody induction, calcineurin inhibition and mycophenolate mofetil with or without corticosteroids. Induction treatment consists of single or multiple doses of polyclonal or monoclonal antibodies. Anti-IL-2 receptor antibody induction has demonstrated excellent graft survival rates, but the incidence of acute rejection might be increased when compared with induction therapy with lymphocyte depleting alemtuzumab or anti-thymocyte globulin (ATG).[14] It would seem rational to avoid corticosteroid use following pancreatic transplantation, and indeed this has proven possible and safe in many protocols. Despite this, there is little published evidence for a benefit of steroid avoidance.

Specific complications
Surgical technique has substantially advanced in recent years and pancreas transplantation has become a standard procedure. While transplant-related complications common to all transplants (e.g. infection, malignancy) occur at similar rates, several factors contribute to an increased overall complication rate of pancreas transplantation when compared with other organ transplantations. Up to 25% of recipients of pancreas transplants need further surgery to deal with complications. Pancreas-specific risks are often related to the exocrine secretion of this gland.

Graft rejection: acute rejection of the pancreas is often difficult to diagnose but probably occurs in up to 25% of pancreas grafts (according to the International Pancreas Transplant Registry). Newer induction protocols using alemtuzumab or anti-thymocyte globulin may reduce the rejection rate to 10%−15%, but acute rejection remains an important cause of graft loss. In patients with a simultaneous kidney and pancreas transplant, the kidney may act as an 'immunological barometer' and enable an earlier diagnosis of rejection (dysfunction of the pancreas causing hyperglycaemia is a late manifestation of rejection); this may explain the better survival of simultaneous pancreas and kidney transplants.

Most clinical signs and symptoms of pancreas graft rejection are non-specific and might even relate to infectious complications which are favoured by over-immunosuppression (e.g. fever or leucocytosis). Changes in fasting and post-prandial blood glucose levels and biochemical serum markers (lipase, amylase) may well be useful but are often late symptoms and might also have their origin in factors other than rejection (e.g. pancreatitis). Non-invasive biomarkers such as donor-derived cell-free DNA may be more sensitive and specific for the diagnosis of acute rejection than biochemical measurements.[15] Pancreas graft rejection in the early postoperative phase has also to be balanced against delayed graft function and diagnosis is sometimes empirical. It is this lack of sensitive markers for pancreas rejection that promoted the technique of bladder drainage as described above.

Pancreas biopsies are the most specific method for diagnosing acute rejection of the pancreas allograft. Core biopsies can be obtained either percutaneously under ultrasound or CT guidance depending on the implant site of the pancreas graft and adjacent anatomy. As in kidney and liver transplantation, an international standardized nomenclature for the grading of graft biopsies specific is available (the Banff Schema for Grading Pancreas Allograft Rejection).[16] Many units do not routinely perform biopsies of the transplanted pancreas for fear of complications. In those units routinely employing US- or CT-guided biopsies, major complication rates are around 2%−3%.

Treatment of rejection (proven or presumed) is performed with either prednisone bolus therapy (500−1000 mg) over a period of at least 3 days or, in cases of steroid resistant rejection, polyclonal or monoclonal T cell depleting antibody treatment.

Transplant pancreatitis: acute inflammation of the pancreas graft is one of the most frequent complications following pancreas transplantation. In its minor appearance it is a normal reaction of any pancreas following transplantation. Although essentially a manifestation of ischaemia-reperfusion injury, the reasons for post-transplant pancreatitis are multi-factorial and dependent on donor factors (e.g. age, fat content of the graft, etc.), organ procurement and preservation factors (iatrogenic injuries in the first instance) and factors during transplant surgery (anatomy of the recipient, time of anastomosis etc). Any inflammation of a (transplanted) pancreas causes digestive enzymes to be released to the peri-pancreatic tissue. This can cause severe local and systemic inflammatory responses. Mild forms of transplant graft pancreatitis are often self-limiting, but attention should be paid to fluid collections, which can pose a serious risk to the immune-compromised patient. Encapsulated small fluid collections can often be left untouched under close surveillance, but larger collections and necrotic tissue require surgical debridement, drainage, or even graft pancreatectomy if there is evidence that the inflammatory cascade is not resolving with repeated interventions. The purported benefits of parenteral nutrition or administration of somatostatin analogues during

episodes of graft pancreatitis are controversial. The major complications of a severely inflamed pancreas graft are bleeding and abdominal infections/sepsis.

Graft thrombosis is a serious complication following pancreas transplantation and a frequent cause of early graft loss. The cause is multifactorial in most cases, although several independent risk factors have been identified: transplantation of marginal organs (increased donor age, cerebrovascular cause of death, haemodynamic instability), organ procurement and preservation parameters (iatrogenic lesions, prolonged ischemic times) and technical faults during transplantation. Thrombus formation is favoured by local factors; the low flow rates in the vessels (after separation from the spleen and intestinal circulation) may combine with ischaemia-reperfusion damage to the endothelium and impaired microcirculation and local factors of hyper-coagulability to create a very thrombogenic environment. Venous thrombosis of a pancreas graft is more frequent than arterial thrombosis. In order to minimize the risk of venous thrombus formation, the portal vein is kept short and the use of vascular graft extension generally avoided. Thrombosis on the arterial side may be related to complications relating to the arterial Y-graft.

Clinical signs which might suggest thrombus formation include unexplained sudden hyperglycaemia, unexpected need of higher insulin doses, graft tenderness or anomalies in Doppler ultrasound flow patterns. If there is suspicion of thrombosis, an MR or CT angiogram is performed. Partial venous thrombosis of the splenic vein can be managed successfully by therapeutic anticoagulation. More extensive thrombosis can occasionally be managed successfully by thrombectomy but is more likely to result in graft removal. Because of the high risk of thrombosis, postoperative thrombosis prophylaxis is essential, with most centres using a combination of early heparin, intravenous dextran and longer-term anti-platelet agents.

Outcomes

Graft and patient survival after pancreas transplantation have substantially improved in recent decades, mainly due to: (1) improved immunosuppressive regimes; (2) better donor and recipient selection; (3) improved surgical technique; and (4) advances in postoperative care. The 1-year patient survival rates for UK patients transplanted between 2011 and 2015 are similar for SPK (97%) and pancreas-alone transplants (98%). The 1-year pancreas graft survival for SPK recipients is 94%, and for pancreas-alone recipients 87%. Five years after transplantation, about 82% of SPK and 66% of PTA pancreases continue to function. The first year following transplant is critical to long-term outcome; patients with a functioning pancreas transplant at 1 year have significantly better survival than those who lose their transplant during the first year.[17]

In patients with end-stage renal failure secondary to diabetic nephropathy, a number of studies have demonstrated a clear survival advantage with the addition of a pancreas transplant to deceased donor renal transplantation.[18,19] There is also good evidence of improved quality of life following successful pancreas transplantation.[20] Finally, there is evidence that a successful transplant has benefit in terms of secondary complications of diabetes, with a reasonable expectation of stabilization or even some

improvement in the retinal changes, reduction in the risk of cardiovascular events and also of improvements in the manifestations of peripheral and autonomic neuropathy. In recipients of pancreas-alone transplants, as well as avoidance of hypoglycaemia-unawareness (the primary indication for transplantation) there is a potential halting of progression or even reversal of diabetic nephropathy, although this must be balanced against the nephrotoxic nature of many immunosuppressive drugs.

Summary

Patients with type 1 diabetes and kidney failure are best served by simultaneous pancreas and kidney transplantation or kidney transplantation from a living donor, followed by a pancreas transplant. The benefits include: (1) independence from exogenous insulin; (2) stabilization of diabetes-related complications; and (3) improvement in quality of life and life expectancy. In selected patients, transplantation of pancreatic islets may be highly effective in improving glucose control in patients with life-threatening hypoglycaemic unawareness.

After over 63,000 pancreas transplantations performed to date, the surgical technique has been largely standardized to provide high rates of success and safety. Outcome after transplantation is dependent on several factors, including the quality of the donor organ, recipient comorbidity, surgical technique in both donor and recipient surgery and the postoperative immunosuppressive management. The long-term implications of transplantation and the need for follow-up and compliance are similar to that after kidney transplantation. However, in the short term, the surgical morbidity and mortality are greater.

The 1-year function rates of above 85% after combined pancreas and kidney transplantation can be achieved in the best units, but with consistently inferior results for pancreas-alone transplantation. ◆

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Practice points

- Pancreas transplantation is standard of care for selected patients with diabetes and end-stage renal failure or life-threatening diabetic complications. It improves both life expectancy and quality of life
- For patients with end-stage renal failure and type 1 diabetes, simultaneous pancreas−kidney transplantation should be considered if fit to undergo the surgical procedure
- For patients without renal failure, pancreas-alone transplantation should be considered in the presence of life-threatening complications such as hypoglycaemic unawareness
- Careful recipient assessment is required due to the high prevalence of cardiovascular and peripheral vascular disease in this patient population
- The ideal donor is a donor after brain-stem death, less than 45 years of age, requiring minimal inotropic support and with a BMI less than 30 kg/m^2
- Most centres now undertake venous drainage to the systemic circulation and exocrine drainage to the recipient bowel. Bladder drainage is an alternative means of draining the exocrine secretions, but has a higher incidence of dehydration, acidosis and cystitis
- Potential early complications include bleeding, graft pancreatitis, enteric leaks and graft thrombosis. Up to 25% patients require re-operation for complications during the index admission
- Monitoring for rejection is challenging due to the risks of pancreas biopsy. Imaging, biochemical monitoring (amylase, lipase) and novel biomarkers such as donor-derived cell-free DNA may be useful