Evidence-Based Practices in GASTROINTESTINAL, COLORECTAL AND HEPATOBILIARY SURGERY

Evidence-based Practices in Gastrointestinal, Colorectal and Hepatobiliary Surgery is meant to be a practical guide for the young gastrointestinal surgeon or trainee. The book has a global authorship and is focused on evidence-based care and multidisciplinary care of the complex gastrointestinal or liver patient. The chapters are succinct yet comprehensive making it an efficient read. The practical approach of the book will make it a good adjunct to textbooks that address the pathophysiology and basic science of disease processes.

Govind Nandakumar MD FACS FASCRS completed his medical school at Mount Sinai School of Medicine, and completed his basic surgical training at Weill Cornell Medical College, and Memorial Sloan Kettering Cancer Center, New York, USA. He completed his advanced Colorectal Fellowship at Washington University in St. Louis and his upper gastrointestinal and hepatobiliary training at Weill Cornell Medical College, New York, USA. Subsequently, he was recruited to the division of Gastrointestinal Surgery at Weill Cornell Medical College and continues to maintain his faculty appointment at Weill Cornell Medical College. In 2015, he was recruited to Columbia Asia Referral Hospital, Bengaluru, Karnataka, India to build a state-of-the-art integrated gastrointestinal and liver center.

He has an interest in developing innovative and endoluminal approaches to gastrointestinal surgery. He also has a special interest in evidence-based, multidisciplinary and integrated care for gastrointestinal and liver diseases. He has written several articles and book chapters in leading surgical textbooks on topics within gastrointestinal surgery. He is a reputed teacher and has received several teaching and training awards from students, residents and fellows. He is an active member of the SSAT, ASCRS, ACS, SAGES, IHPCA, SSO, IASG and the ASI.

Reviews
"Dr. Govind Nandakumar used his experience at the Center for Advanced Digestive Care (CADC) at the New York Presbyterian Hospital and is in the process of developing a similar center called the Integrated Digestive Liver and Cancer Centre (IDLCC) at Columbia Asia Hospitals, Bengaluru".

"Dr. Govind Nandakumar, an experienced gastrointestinal surgeon, has edited a very comprehensive book on the topic with contributions from an outstanding group of authors. The evidence based approach and the section on "Landmark Trials" gives the necessary background information and yet encourage the reader to constantly review and update the ever changing literature".

"Dr. Govind Nandakumar has chosen a topic and author list to disseminate knowledge in the field of surgical gastroenterology in an evidence-based, comprehensive and yet concise manner. Global authorship, well-defined chapters that address topics of relevance and importance are delivered with clarity."

—Nandakumar Jairam MBBS MS

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Govind Nandakumar

Forewords
Jeffrey W Milsom
Fabrizio Michelassi
Nandakumar Jairam
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Dedication

This book is dedicated to my family, teachers and mentors
To my mother and first teacher, Rameshwari Nandakumar who instilled in me the passion to do better every day.
To my father, Dr Nandakumar Jairam who has been a close friend and a mentor throughout my life and career.
To my brother and best friend, Krishna Nandakumar who has helped me through several difficult situations.
To my soul mate and the love of my life, Dr Pallavi Patri who has stood by me and been an immense support.
She has helped me excel in my career and has given meaning to everything I do.
To my children, Dhruv and Maya who have given up family time for the sake of my career.
Thanks to the mentorship and guidance of Dr Fabrizio Michelassi and Dr Jeffrey Milsom.
They were instrumental in training me and guiding me in my career.
A special mention to Dr TS Jairam, my grandfather and the person who has inspired me.
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The field of gastrointestinal surgery is changing dramatically. Laparoscopy and minimally invasive surgery began this “revolution” in the 1990’s. What next? Working within the lumen of the bowel (endoluminal surgery) combined with better, cheaper endoscopes and tools will lead the way. Biomaterials and advanced imaging methods are the other essential elements for revolutionizing digestive disease care. Dr Govind Nandakumar has been my student since 2000 and over the years, he has learned, developed and improved many of the thoughts and concepts I have believed in. This book brings together all the relevant specialties in gastrointestinal surgery. Chapters on innovative approaches will hopefully stimulate new approaches to the care of patients with digestive disorders. Dr Nandakumar used his experience at the Center for Advanced Digestive Care (CADC) at the New York Presbyterian Hospital, New York, USA and is in the process of developing a similar center called the Integrated Digestive Liver and Cancer Centre (IDLCC) at Columbia Asia Hospitals, Bengaluru, Karnataka, India. This book talks about many of the concepts that address integrated care and will be a valuable tool for any gastrointestinal surgeon.

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The field of gastrointestinal surgery has seen impressive innovations in recent years. Dr Govind Nandakumar, an experienced gastrointestinal surgeon, has edited a very comprehensive book on the topic with contributions from an outstanding group of authors. The book will be valuable to the aspiring gastrointestinal surgeon or a junior consultant as it provides an easy read on several complex gastrointestinal topics. The chapters are comprehensive and yet concise to read efficiently prior to a difficult case. The evidence-based approach and the section on "Landmark Trials" gives the necessary background information and yet encourage the reader to constantly review and update the ever changing literature. The inclusion of nonsurgical topics and techniques helps in guiding and formulating a multidisciplinary care of the patient. The step-by-step procedural review is a nice tool to prepare for an operation quickly. This book is a valuable adjunct to well-established textbooks as it provides a practical, concise and evidence-based approach to the surgical care of the complex gastrointestinal and hepatobiliary patient.

**Fabrizio Michelassi** MD  
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I have witnessed the evolution of surgery over the last four decades. Health care is changing rapidly and faster than ever before. Better and more efficient patient care and clinical outcomes are an automatic sequel. Analysis of why this occurred indicates changing trends in communication and advancing technology, which amongst other things, makes it easier for global merger of clinical practice. Also available are newer and efficient surgical tools which drive procedures and practices much more than in the past. Subspecialties such as surgical gastroenterology are creating an identity for themselves. Focused care of disorders of the gastrointestinal tract is more possible today than ever before. All this has created an abundance of knowledge and information that needs to be dissipated. Dispersal of knowledge, now needs to be very different—accurate, focused, concise and yet comprehensive. Dr Govind Nandakumar has chosen a topic and authors list to dissipate knowledge in the field of surgical gastroenterology in an evidence-based, comprehensive and yet concise manner. Global authorship, well-defined chapters that address topics of relevance and importance are delivered with clarity.

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The field of Gastrointestinal Surgery has grown tremendously and is rarely practiced as one field with superspeciality services like Hepatobiliary, Colorectal and Bariatric Surgery blossoming. The goal of this book was to provide a high quality, state-of-the-art, evidence-based book that is efficient to read and could be a quick reference for a busy trainee or a junior surgeon. There are several good textbooks that address the pathophysiology and basic science of surgical gastroenterology, so our book is focused on a practical approach to these diseases. The value of multidisciplinary care of Complex Gastrointestinal (GI) diseases is understated. This book includes chapters on several allied specialties that are required to take care of the complex GI patient.

The book addresses the basics and fundamentals of each disease process while reviewing new and innovative approaches. We have listed key randomized trials for each section to facilitate rapid access to relevant content. Progress in the field of gastrointestinal and liver diseases has created a wealth of knowledge. Imparting and absorbing the knowledge efficiently has become increasingly difficult. We have made an effort to present important and relevant content in a manner that is easy to read.

Dr Subroto Paul has done fantastic job with gathering an elite panel of surgeons to cover the section on esophageal diseases. This section would not have been possible without his help.

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Pancreas Transplantation
Samuel Sultan, Anthony Watkins

BACKGROUND

Type 1 diabetes mellitus affects ~30 million people worldwide and the incidence has been increasing recently, by about 3% per year.\(^1\) Prior to the discovery of insulin, the average life expectancy was only 2 years after being diagnosed with diabetes. The advent of purified insulin improved the prognosis significantly; however, it consequently led to the recognition of a number of long-term sequelae of hyperglycemia including neuropathy, retinopathy, and nephropathy. In 1966, Kelly and Lillehei described the first simultaneous pancreas-kidney transplants (SPK), performed at the University of Minnesota for a uremic diabetic patient.\(^2\) The goal was to simultaneously restore functioning \(\beta\) cells allowing adequate insulin production, thus preventing recurrent diabetic nephropathy in the renal allograft. Although initial results were dismal, outcomes significantly improved with the advent of improved immunosuppression and modifications in surgical technique.

The Diabetes Control and Complications Trial established that tight glycemic control is imperative to avoid the development of secondary complications.\(^3\) Unfortunately, these complications are not reversed by intense insulin therapy and there are risks of iatrogenic hypoglycemia. Currently, no form of exogenous insulin administration is able to achieve the euglycemic, insulin-independent state that is possible with pancreas transplantation (PTx). The American Diabetes Association (ADA) recommends that SPK transplantation should be considered for type 1 diabetes who require kidney transplantation (KTx), and pancreas transplantation alone (PTA) for patients with brittle diabetes or episodes of hypoglycemic unawareness. Recent studies have also documented a benefit of PTx in a select group of patients with type 2 diabetes.\(^4\)

Almost a half-century later, SPK transplantation remains the definitive and optimal treatment for patients with both type 1 diabetes mellitus and end-stage renal disease (ESRD). During this time, there have been numerous developments and modifications to PTx, and several innovations still remain on the horizon.

EVIDENCE-BASED REVIEW

The immediate goal and benefit of PTx are to achieve a euglycemic state without the need for exogenous insulin. In addition, PTx adds the potential to not only halt the progression of some secondary diabetes-associated complications, but also lead to resolution of some of these processes.\(^5\) Lastly, several studies have demonstrated a survival benefit associated with SPK in comparison to uremic patients who remain on hemodialysis and recipients of KTx alone.\(^6\)\(^,\)\(^8\)

While the kidney remains the most commonly transplanted organ, the number of PTx has been limited for several reasons. First, as is the case with organ transplantation in general, a significant discrepancy exists between organ supply and demand. In addition to the limited supply, pancreas allograft acceptance is more highly selective than other organs. In this case, the possibility of underutilization has been examined. Finally, optimal selection of recipients is equally important to ensure successful outcomes, particularly since the surgery is more extensive.

While deceased donation experienced a significant increase from 2002 to 2007, coinciding with the inception of the Organ Donation Breakthrough Collaborative sponsored by Health Resources and Services Administration, PTx rates decreased during the same time period.\(^9\)\(^,\)\(^11\) Several groups have attempted to define the challenges with pancreata utilization. Based on the data from the United Network for Organ Sharing, Stratta and Bennett noted that only 60% of the pancreas grafts recovered were transplanted. The reasons cited for discard were often labeled as unknown, indicating the need for improved data tracking.\(^12\) Wiseman et al. examined Organ Procurement and Transplantation Network data from 2005 to 2007 and
identified a subgroup of 1,763 potential pancreas donors (PPDs) defined by age (19–40 years), body mass index (BMI; <30 kg/m²), successful liver donation, and negative viral serology testing, which were not used. They discovered that 85% of the 1,763 donors declined for pancreas procurement were reported as relating to donor age/quality. They were neither able to define specific medical or social or behavioral characteristics of PPD that precluded successful donation nor able to identify a correlation with donor service area (DSA), making it difficult to clearly ascertain the reason for such high discard rates.

Geographic variability in utilization of potential transplantable pancreata led to the development of the pancreas donor risk index (PDRI). This tool was established to assess the differential impact of organ quality on PTx outcomes, specifically as a function of the type of transplant [SPK, pancreas after kidney transplants (PAK), and PTA] and recipient severity of illness to help guide the clinician to optimize pancreas utilization. Retrospective analysis of all PTx from the Scientific Registry of Transplant Recipients from 2000 to 2006 was performed using a Cox regression analysis controlling for the donor and recipient characteristics. Ten donor variables including age, BMI, race, and serum creatinine, and one transplant factor (cold ischemia time) were used to develop the PDRI. The median risk donor was defined as a 28-year-old non-black, non-Asian man, with a BMI of 24 kg/m², a height of 173 cm, non-cerebrovascular accident (CVA) as the cause of death, pancreas preservation time of 12 hours, non-donation after cardiac death (DCD) and serum creatinine <2.5 mg/dL. Increasing PDRI was associated with a significant, graded reduction in 1-year pancreas graft survival. Importantly, recipients of PTAs or PAKs whose organs came from donors with an elevated PDRI (1.57–2.11) experienced a lower rate of 1 year graft survival (77%) compared with SPK recipients (88%). Further investigations have supported these findings with negative prognostic donor factors including donor BMI ≥30 [hazard ratio (HR) 1.87, p=0.005], donor Cr ≥2.5 (HR 3.16, p=0.007), donor age >50 (HR 1.73, p=0.082), and preservation time >20 hours (HR 2.17, p<0.001).

In addition to the importance of a carefully selected donor, a comprehensive pretransplant recipient workup is essential. A multidisciplinary approach that consists of a thorough medical, surgical, and psychosocial evaluation common to the evaluation of a potential KTx recipient is necessary. A major focus of the recipient evaluation is the cardiac assessment because cardiovascular disease is responsible for the largest fraction of recipient deaths and the majority of waitlist deaths. While there is no absolute age cutoff for PTx, many institutions have placed age limitations on potential pancreas transplant recipients due to some data suggesting that age is a risk factor for inferior outcomes. For example, in one study, recipients ≥50 years of age had higher incidence of graft thrombosis and bleeding requiring re-exploration, as well as a higher incidence of pulmonary infections. Other studies have also shown a lower patient survival for older patients (≥45 years) undergoing PTx. However, it is important to point out that there are data showing good outcomes in carefully selected older patients. Afaneh et al. found comparable outcomes between patients of ≥50 years of age versus younger patients in relationship to surgical morbidity, incidence of infections, and acute rejection (AR) rates. A group from Indiana University similarly found that recipient age had no statistically significant effect on PTx outcomes, in which 18 of the 405 patients were >60 years of age, suggesting that older patients should not necessarily be excluded from PTx solely on the basis of age, as long as they are otherwise carefully screened.

Additional factors that affect outcomes include the type of pancreas transplant performed and technical aspects of the procedure. SPK transplantation has been shown to have superior outcomes in comparison to PAK and PTA. The most recent report from the International Pancreas Transplant Registry (IPTR), a database that has been collecting allograft and patient survival outcomes since 1980, demonstrated 1-year allograft survival rates of 86% and 93% for the pancreas and kidney, respectively, after SPK. Following PAK and PTA, 1 year allograft survival reached 80% and 78%, respectively. These differences in outcomes are partly related to the benefit of earlier recognition of rejection in the SPK due to the concordant nature of rejection in 60–70% of cases. Since renal function abnormalities (i.e. creatinine rise) are detectable earlier than pancreas dysfunction (amylase, lipase, or hyperglycemia), rejection is often detected and treated more promptly in these cases. Early outcomes were marred with graft loss due to technical complications. In all three categories, early technical graft loss rates have decreased significantly over time, now affecting ~8–9% of patients; however, they remain a challenge. The 1-year and 5-year PTx allograft survivals when performed SPK are 86.4% and 72%, respectively. In addition,
the 1-year KTx allograft survival is 93% in the SPK group. The 1-year and 5-year allograft survivals for PTAs were lower at 75.4% and 48.3%, respectively. The 1-year and 5-year allograft outcomes for the PAK allografts are modestly superior to the PTA group with survivals approaching 80% and 58%, respectively.

The options for venous drainage include portal via the superior mesenteric vein (SMV) or systemic via the iliac or inferior vena cava (IVC). Portal venous drainage has the potential advantage of replicating the natural physiology by allowing first-pass degradation of insulin in the liver. Systemic drainage leads to hyperinsulinemia, which is thought to be an independent risk factor for increased ischemic cardiovascular disease, although in clinical practice no cardiovascular adverse effects have been demonstrated. Most importantly, studies have demonstrated similar outcomes with both types of venous drainage.\(^23,24\)

In recent series, the prevailing mode is systemic drainage.

Drainage of exocrine secretions can be performed by either bladder or enteric anastomoses. Bladder drainage provides the advantage of having the ability to monitor the rejection by measuring urinary amylase, less severe complications, and the ability to perform a cystoscopic biopsy. The disadvantages of bladder drainage include electrolyte abnormalities, chronic acidosis, dehydration, and urinary tract infections. Urologic complications such as hematuria, cystitis, urethritis, and bladder stones may also occur. The solution for poorly tolerated complications of bladder drainage is re-exploration with conversion to enteric drainage.\(^25,26\)

Enteric drainage can be accomplished by anastomosing the allograft duodenum to the recipient intestine. This is commonly performed with a hand-sewn anastomosis, although techniques for stapled anastomosis using an end-to-end anastomotic (EEA) stapler device are also described.\(^27\) The main advantage of the enteric drainage technique is that it is more physiologic and avoids the metabolic and urologic complications associated with bladder drainage. The disadvantages include a loss of the ability to monitor the exocrine pancreatic secretions and higher, more severe complication rate. Recent IPTR data show that >80% of transplants are done with enteric drainage.

As opposed to whole PTx, an alternative and developing option is islet cell transplantation. First performed in 1977 at the University of Minnesota, islet transplants emerged in the setting of the early discouraging results for whole PTx.\(^29\) Islet cell transplantation involves the extraction of islets of Langerhans from multiple pancreata through the use of a complex purification process. These cells are then typically injected into the portal vein where they engraft in the parenchyma of the liver and secrete insulin. The Edmonton protocol established the safety and effectiveness of islet transplantation, given a sufficient number of islets.\(^30\) Refinement of isolation and digestion of the pancreas to obtain islets has allowed ∼3,000 islets/kg of recipient weight, a key element in the Edmonton protocol. The major challenges with islet transplants include obtaining optimal engraftment and poor long-term results in relationship to insulin independence. As further improvements in islet cell transplantation are attained, this approach could supplant PTx as a more attractive option due to its less invasive nature.

**LANDMARK TRIALS**

Pancreas transplantation began with poor graft and patient survival rates; therefore, very few procedures were initially performed. The major improvements in outcomes were derived from better immunosuppression and refinements in surgical technique. As such, these landmark trials provided insight into these new discoveries and innovations that led to successful PTx and widespread recognition of its benefits.

- Sutherland DER, Gruessner RW, Dunn DL, et al. Lessons


**DONOR PROCUREMENT**

**Preoperative Planning**

Careful evaluation and recovery of the pancreas is critical to the success of the subsequent transplant regardless of the approach. While the use of living donors has been described, our focus will be limited to the deceased donor. Although donor selection criteria may vary among surgeons and transplant centers, the primary criteria, as mentioned before, include age, BMI, cause of death, and, most importantly, the gross appearance of the organ (evidence of inflammation, fibrosis or fatty infiltration) at the time of recovery. Again, factors such as older age (>40–50), obesity and stroke as the cause of death have been shown to negatively affect graft survival.

**Surgical Anatomy**

The pancreas serves as both an endocrine and an exocrine gland, and lies in the retroperitoneum at the level of the second lumbar vertebrae. The exocrine function includes the secretion of digestive enzymes, water, electrolytes, and bicarbonate, which are delivered to the duodenum via the pancreatic duct of Wirsung. The endocrine function is comprised of the secretion of insulin, glucagon, and somatostatin by the islets of Langerhans, A cells and D cells, respectively. The pancreas is divided into five parts including the head, uncinate process, neck, body, and tail. The head of the pancreas lies to the right of the superior mesenteric artery (SMA). The uncinate process is a variable posterolateral extension of the head that passes behind the retropancreatic vessels and lies anterior to the IVC and aorta. The neck is defined as the portion of the gland overlying the superior mesenteric vessels. The body and tail lie to the left of the mesenteric vessels; there is no meaningful anatomic division between the body and tail. The arterial supply to the duodenum and pancreas is derived from the celiac axis and the SMA. The head of the pancreas receives blood supply from the gastroduodenal artery (anterior and posterior superior pancreaticoduodenal arteries) and SMA (providing the anterior/posterior inferior pancreaticoduodenal arteries). The splenic artery supplies the neck, body and tail of the pancreas. The venous drainage follows the arteries to provide tributaries to the splenic vein and SMV, which drain into the portal vein.
Step-by-Step Illustration of Procedure

1. Dissection begins with mobilizing the spleen so that it can be used as a handle allowing a “no touch” approach to the pancreas dissection (Fig. 1).
2. The duodenum is kept long by dividing distal to the pylorus and distal to the ligament of Treitz with a gastrointestinal (GI) stapler (Fig. 2).
3. The portal vein is divided about halfway between the pancreas and the liver, leaving at least 1.5 cm of portal vein length above the superior pancreatic border (Fig. 3).
4. The common bile duct and gastroduodenal and splenic arteries are ligated and divided (Fig. 4).
5. The SMA is divided at the aorta (Fig. 5).
6. The root of the small bowel mesentery is stapled (Fig. 6).
7. Remove a segment of the donor common; internal and external iliac arteries are removed for Y graft creation.

Operative Tips

It is important to coordinate the pancreas procurement with other surgical teams when present. While pancreas
Pancreas dissection can be performed either prior to or after cross-clamp, we prefer to perform this dissection in the warm (prior to crossclamp) to assist with better hemostasis upon reperfusion in the recipient operation. Although isolated procurement of the pancreas is described above, an alternative option includes the en-bloc recovery technique that involves removal of the pancreas with the liver followed by separation on the backtable. At some point prior to crossclamp it is important to advance a nasogastric tube into the duodenum to instill 500 mL of amphotericin solution (50 mg/L) into the second portion of the duodenum. This helps decontaminate this portion of the GI tract and combat future infectious issues.

Avoid dissection of splenic artery into the pancreas parenchyma where the dorsal pancreatic artery can be injured. While either University of Wisconsin or histidine-tryptophan-ketoglutarate (HTK) solutions can be used, there are several reports of higher rates of AR, graft pancreatitis and worse graft survival with HTK. Some surgeons limit pancreatic flush to 1–2 L by occluding the SMA with a vessel loop.

**Pancreas Transplantation**

**Preoperative Planning**

The selection of a candidate for transplant is a complex process that ensures that a detailed medical and surgical history is obtained, including a focused review of diabetes history. Typically, type 1 diabetes begins before the age of 30, causes ketoacidosis, frequently requires insulin administration, and is not associated with excessive weight. However, patients do not always present as the prototypes of either type 1 or type 2, and such a distinction may be an oversimplification. Nonetheless, patients who have had multiple episodes of diabetic ketoacidosis or hypoglycemic unawareness are typically considered to be absolute indications for PTx. In order to identify other patients who would benefit from PTx, a careful risk–benefit analysis should be performed, accounting for the type of pancreas transplant, depending on the renal function, and the patient’s overall risk profile. The recommended indications for transplant according to the ADA are shown in Table 1. Conversely, there are a number of important contraindications, both absolute and relative. The main absolute contraindications relate to a significant cardiac impairment—namely, significant and untreatable coronary artery disease, a recent myocardial infarction, or an ejection fraction <30%—or an active infection. Other contraindications include a history of untreated or recent malignancy, human immunodeficiency virus, hepatitis B (surface-antigen positive), substance abuse, major psychiatric illness, noncompliance, a life-limiting systemic illness, or significant hepatic or pulmonary dysfunction. Specific surgical aspects of the preoperative evaluation should include a detailed history of prior abdominal surgery, and focus on issues that would increase the risk of complications, including obesity and peripheral vascular disease (PVD).
Diagnostic testing for a preoperative evaluation should include standard testing for major abdominal surgery, as well as testing relevant to transplantation, including viral serologic panels and tissue typing, and finally laboratories pertinent to both the pancreatic function—a C-peptide and hemoglobin A1c level—and renal function, possibly including a kidney biopsy, and a 24-hour urine collection for protein and creatinine clearance. Standard screening for cancer should be performed, for breast, cervical, colorectal, and prostate cancer, as applicable, given the increased risk of cancer post-transplantation. For patients with a history of cancer, a variable waiting time is required depending on the type of cancer. Radiologic evaluation should include either an abdominal ultrasound, or more typically a computed tomography (CT) scan; such testing should look for any abnormal masses, gallstone disease, any kidney pathology, and/or significant vascular disease. Given the high prevalence of cardiovascular disease in this population, typical evaluation includes a stress test, whether exercise or pharmacologic, and an electrocardiogram and echocardiogram. Other general measures include smoking cessation, blood pressure control, correction of hyperlipidemia, increased exercise tolerance, and weight reduction. Ultimately, a thorough preoperative evaluation is best performed via a multidisciplinary collaboration, synthesizing input from surgery, medicine, and psychosocial.

**Surgical Anatomy**

Regardless of the type of PTx performed, the approach is similar where the colon is mobilized or is to expose the retroperitoneal vessels including the IVC and iliac vessels.

**Step-by-Step Illustration of Procedure**

There are four key components to the recipient operation: (1) bench preparation, (2) incision and exposure, (3) revascularization, and (4) duct management.

**Bench Preparation**

1. The initial step involves a thorough inspection of the gland’s color, consistency, and fat content, looking for any injuries to the parenchyma or to the duodenum, and ensuring that the vasculature is adequate for reconstruction (Fig. 7).
2. The splenectomy is typically performed first utilizing either stapler device or individually ligating vessels with silk ties ligation (Fig. 8).
3. Excess fat and surrounding tissues are removed from the body and tail of the pancreas (Fig. 9).
4. The portal vein and splenic and superior mesenteric arteries are then dissected free by removing excessive tissue (Fig. 10).
5. Excessive duodenum is then removed with a gastrointestinal anastomosis stapler and the staple line is oversewn (Fig. 11).

**Table 1: Indications for pancreas transplantation.**

<table>
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<th>Type of transplant</th>
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| Simultaneous kidney and pancreas transplant | CKD stages 4 or 5 (creatinine clearance <30 mL/min) with type 1 diabetes and with other diabetic complications  
• Prior renal transplant which is failing in a type 1 diabetic |
| Pancreas after kidney transplant | Prior functioning kidney transplant in type 1 diabetic with other diabetic complications |
| Pancreas transplant alone | Hyperlabile diabetes defined by frequent acute severe metabolic complications (hypoglycemia, marked hyperglycemia, and ketoacidosis) requiring medical attention  
• Clinical and emotional problems with insulin therapy that are incapacitating  
• Consistent failure of insulin-based management to prevent complications  
• Presence of (two or more) diabetic complications that are progressive and unresponsive to intensive insulin therapy  
• Early diabetic nephropathy  
• Proliferative retinopathy  
• Symptomatic peripheral or autonomic neuropathy  
• Vasculopathy with accelerated atherosclerosis |
6. The root of the small bowel mesentery should be reinforced for hemostasis with a running 4-0 polypropylene suture (Fig. 12).
7. The arterial reconstruction begins by preparing the donor iliac artery by removing excessive tissue (Fig. 13).
8. The Y graft is then used to create an end-to-end anastomosis between the hypogastric and the splenic artery and between the external iliac and SMA using 6-0 Prolene (Fig. 14).

**Incision and Exposure**

1. There are two main options for the choice of incision: a lower quadrant extraperitoneal incision or a midline intraperitoneal approach (Figs. 15 and 16).
2. Upon opening the peritoneal cavity, a Bookwalter self-retaining retractor or similar retractor should be used (Fig. 17).
3. The right colon is mobilized to expose the retroperitoneal vessels (Fig. 18).
Revascularization

1. For systemic drainage, the right common iliac artery and IVC and/or right common iliac veins should be dissected free (Fig. 19).
2. Portal venous drainage is performed via an end-to-side anastomosis from the allograft portal vein to the recipient SMV (Fig. 20).

Duct Management

Bladder drainage

1. The bladder anastomosis is performed between the antimesenteric border of the duodenum and the dome of the bladder in a two-layered hand-sewn fashion (Fig. 21).
Alternatively, an EEA stapler can be used to perform this anastomosis (Fig. 22).

**Enteric drainage**

2. Alternatively, an EEA stapler can be used to perform this anastomosis (Fig. 22).

**OPERATIVE TIPS**

The backbench preparation of the pancreas requires substantial work, even more so than other solid organ transplants, and is considered paramount to successful transplantation. The allograft should remain immersed in...
a cold preservation solution-surronded by slushed ice, in a large sterile basin during this preparation. While the length of the duodenal segment does not need to be precise, care should be taken to avoid an excessively lengthy segment, which may be at risk for ischemia, bearing in mind that the entire perfusion is dependent on retrograde flow through the inferior pancreaticoduodenal artery. The limbs of the Y graft should be kept short, typically <1 cm, to minimize the risk of twisting or kinking.

Various approaches exist in regard to the recipient portion such as the initial incision, the position of the graft, the artery and vein used for anastomosis, the type of exocrine drainage, the use of staplers, and the use and location of abdominal drains. The key is to adhere to surgical principles so that regardless of the approach, good outcomes will be achieved. For example, with the extraperitoneal approach, it is advisable to open the peritoneum to allow for drainage of peripancreatic fluid.
The more common, systemic drainage was described. For portal venous drainage, the SMV is isolated and utilized. When the common or external iliac vein is used for systemic drainage, it should be completely mobilized in order to facilitate tension free anastomosis. Since it is a larger vessel, when anastomosing to the IVC only enough of the vein needs to be dissected to allow for vascular control, thereby saving time and enabling a less difficult anastomosis.

The head of the pancreas can either be oriented superiorly or inferiorly, and the type of exocrine drainage or surgeon’s preference determines positioning. Of note, an
intrapерitoneal approach is preferred when bladder drainage is utilized. Also, since the head of the pancreas is oriented downward, the vessel anastomoses are approached slightly differently. The iliac vein is often used for venous drainage and requires complete mobilization with division and suture ligation of all branches to allow correct orientation of the portal vein and Y graft. In addition, the arteriotomy and venotomy are placed in a fashion that allows medial placement of pancreas allograft. Since the iliac vessels tend to be more superficial in the right lower quadrant, right-sided implantation is typically pursued. This allows a technically easier anastomosis and left-sided implantation has been correlated with increased risk for graft thrombosis.40

After the allograft is reperfused, bleeding is controlled with the help of suture ligatures and clips. Inspection and palpation over the entire length of the graft should be performed to ensure adequate perfusion.

**COMPLICATIONS**

In the earlier stages of PTx, in the 1980s, nearly 25% of pancreas transplants failed due to surgical complications.41 More contemporary series demonstrate that there has been significant improvement over the last few decades, with technical failure rates now typically <10%.42 Nevertheless, complications after PTx are not uncommon and typically cause significant morbidity. The most notable complications include thrombosis, pancreatitis, anastomotic leak, infection, rejection, and bowel obstruction. As previously mentioned, additional complications that are unique to the use of bladder drainage include cystitis, metabolic acidosis, bleeding at the duodenal cuff, and fluid losses causing dehydration. Overall, the most common serious surgical complication is vascular thrombosis, which affects approximately up to 12% of transplants, and is the main cause of nonimmunologic graft failure.43

Thrombosis usually presents as hyperglycemia, tenderness over the graft, graft enlargement, and in bladder drainage with hematuria and decreased urinary amylase levels. The diagnosis is made based on ultrasound, CT angiography, magnetic resonance angiography, or conventional angiography. A key piece in preventing complications involves identifying the relevant risk factors. An analysis of vascular thrombosis revealed several risk factors: donor age, death from vascular disease (cardiac or cerebral), the use of an aortic Carrel patch, reconstructions other than the Y-graft, left-sided implantation, and graft pancreatitis.40 In addition to mitigating or avoiding such risk factors, there are various protocols for treating the patient with a form of anticoagulation, whether a heparin infusion, acetylsalicylic acid, or even warfarin.44

The management of vascular thrombosis typically entails exploration and removal of the graft, in order to prevent a leak and sepsis—doing so promptly reduces the risk of morbidity and mortality.45 Rarely, a thrombosis may be safely managed nonoperatively, or with endovascular interventions.45,46 As an alternative to complete removal of the graft, partial removal has been described in the setting of a partially thrombosed graft with a viable remainder.47 Another consolation in the management of thrombosis involves the possibility of simultaneous retransplantation at the time of pancreatectomy of the thrombosed graft, provided the patient is stable.48

Aside from thrombosis, another possible complication is pancreatitis, which can occur either early (typically defined as within 3 months) or late after transplant. In the earlier period, it can be difficult to diagnose, given that hyperamylasemia is seen in up to 35% of patients posttransplant.49 Late-stage pancreatitis occurs on average 28 months after transplant.50 Similar to native pancreatitis, graft pancreatitis typically presents with tenderness over the graft, and may lead to further complications such as abscess, necrosis, fistula, or pseudocyst. Risk factors for early pancreatitis include donor age and obesity, and cold ischemia time. An analysis of late graft pancreatitis, on the other hand, did not reveal any significant risk factors.50 A CT scan may be useful in determining the pancreatic parenchymal viability and the possible need for debridement of pancreatic necrosis. Patients with bladder drainage may be treated with a urinary catheter to prevent reflux as a possible cause of pancreatitis. And for cases of recurrent reflux-induced pancreatitis, it may necessitate a revision to enteric drainage. Otherwise, treatment is similar to that for native pancreatitis, primarily involving bowel rest, along with percutaneous drainage and antibiotics as needed, and outcomes are typically favorable.

Anastomotic leak represents a significant complication, but it has variable significance depending on the method of drainage, whether bladder or enteric. In bladder drainage, duodenal leaks typically occur within the first 3 months postoperatively, are readily diagnosed with a cystogram, and are often not devastating. Such leaks can be managed with prolonged indwelling catheterization to decompress the bladder, which is effective
treatment in the majority of cases. More complex cases may require surgical repair, or conversion to enteric drainage. On the other hand, leakage from an enterically drained graft typically causes sepsis and peritonitis due to enteric spillage. Leaks may occur at any time, although early leaks are technically related, whereas late leaks may be caused by rejection, infection, or ischemia. Leaks are best diagnosed by the CT scan. Once diagnosed, prompt surgical re-exploration is warranted, with a conversion to a Roux en Y drainage, or even graft pancreatectomy if the contamination is severe or the patient is unstable.

Intra-abdominal infection may occur with or without an associated anastomotic leak. Such infections typically occur within the first 30 days postoperatively, and are usually bacterial, but occasionally may be fungal in origin. Risk factors include older donor age, retransplantation, pretransplant peritoneal dialysis, extended preservation time, graft pancreatitis, and immunosuppression with sirolimus. In stable patients, a CT scan is helpful in determining the extent of the infection, and also in diagnosing an associated anastomotic leak. For an isolated infection without a leak, percutaneous drainage and antibiotics are the recommended treatment, and are effective in over 80% of cases.

Like any transplant, PTx can be complicated by immune-mediated rejection. As such, a more complete discussion of rejection can be found elsewhere. However, there are several unique aspects of pancreatic rejection. Monitoring for rejection typically includes measurement of glucose levels, and serum amylase and lipase levels, and in the case of bladder drainage, urinary amylase levels. Yet, such measurements are not highly accurate gauges of rejection, and a tissue biopsy is required to firmly establish a diagnosis of rejection, and its subtype. In a large series, biopsy of the pancreas graft has been shown to have a low rate of clinically significant complications. Alternatively, especially in centers with less experience in pancreas biopsy, a sentinel organ is often biopsied, whether from the kidney graft in the case of a SPK, or from the duodenal patch, though studies have found approximately a 20% rate of discordance between biopsies of a sentinel organ compared to the pancreas graft. Similar to rejection, the long-term infectious complications of PTx are related to the immunosuppression, and are similar to that of other solid organ transplants.

In comparison to whole-organ transplantation, islet transplantation is associated with significantly fewer and less severe complications. The rate of serious complications is ~10%, including the possibilities of portal vein thrombosis and intra-abdominal hemorrhage. Longer-term complications are similar to that of whole-organ transplantation, and relate mostly to infectious complications due to the immunosuppression. Additionally, there is a potential for sensitization and the formation of antibodies.

OUTCOMES

Cardiac function improves within 6 months of PTx, and other peripheral vascular disease PVD may stabilize, although the data are mixed. Most studies show some improvement in neuropathy and gastroenteropathy after transplant. Early nephropathy improves after pancreas transplant, but not retinopathy. Respondents report better quality of life after transplant.

Graft and Patient Survival

Now 3-year patient survival rates after PTx are 89%, with 3-year graft survival rates of 65%. A higher risk of graft failure is associated with solitary pancreas transplants, which leads some centers to have more stringent selection criteria for PTA and PAK.

CONCLUSION AND FUTURE DIRECTIONS

Since its inception nearly 50 years ago, there have been numerous advancements in the field of PTx. As such it has taken root as the definitive treatment for patients with type 1 diabetes and ESRD, and is useful in various other circumstances. As outcomes continue to improve, and complications reduced, the indications for transplant may expand further, particularly for the large pool of patients with type 2 diabetes.

There are several developments on the horizon spanning the entirety of the transplant process, ranging from refining the surgical technique to exploring new immunosuppressive agents. In 2012, Boggi et al. reported their experience with the world’s first robotic-assisted pancreas transplant. The future role of robotics in PTx is yet to be determined, although it may offer a solution for reducing the persistently high rate of surgical complications. Immune therapy has evolved significantly both in efficacy and minimization of toxicity, and there are numerous new drugs being developed and tested, such as the protein kinase C inhibitor—sotrastaurin, the JAK 3 inhibitor—tolfacitinib, the proteasome inhibitor—bortezomib, the
the future of PTx is unpredictable, but the overall outlook is encouraging, and the long-term prospects are open to the imagination, to be filled with the possibilities of surgical innovation, pharmacogenetics, personalized medicine, stem cells, and cellular reprogramming.59

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