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# Multi-Modality Imaging Evaluation of the Whole-Organ Pancreas Transplant

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Pancreas transplants are an important treatment options for patients with severe diabetes mellitus and other medical conditions. Multiple-imaging modalities, including computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound (US) are available to evaluate the pancreas transplants and their vascular supply, with the graft having a characteristic appearance on each modality. Complications of the graft and its vascular supply present interesting challenges to the clinicians and radiologists caring for this patient population. Being able to identify the imaging appearance of normal and abnormal pancreas transplants, it is necessary to ensure these patients are provided optimal care.



## Introduction

Pancreas transplantation was first performed in 1966, and since that time advances in surgical and post-transplant immunosuppression have allowed this procedure to become a well-established method for treating patients with severe Type 1 diabetes mellitus (DM) complicated by end stage renal disease (ESRD), poorly controlled severe diabetes (Type 1 or Type 2) and cystic fibrosis.[1] In the setting of severe diabetes, pancreas transplantation significantly improves quality of life, and has been shown to extend life in the cystic fibrosis population.[2] Pancreas donors may be living (islet cell or pancreatic segment transplantation) or cadaveric (whole organ) and the transplanted organ may be placed with or without a simultaneous renal transplant.[1] Simultaneous pancreas and kidney transplants are the most common form of transplantation and most often come from the same cadaveric donor.[3] Up to 78% of pancreas transplants are performed as simultaneous pancreas and kidney transplants with the most common surgical approach of having the pancreas placed in the right lower quadrant and the kidney being placed in the left lower quadrant. Approximately 16% of patients will have a pancreas after kidney transplantation, whereby the recipient has a prior history of renal transplant (living or cadaveric) with preserved renal function, and requires a subsequent pancreas transplant.[4,5] These patients are typically diabetic, with ongoing severe secondary complications due to pancreatic dysfunction, including hypoglycemic unawareness.[5] The least commonly performed type of pancreatic transplantation is Pancreas Transplant Alone.[3] Pancreas Transplant Alone cases are typically reserved for younger and pediatric patients, who have no history of renal dysfunction or diabetic nephropathy; this approach may be seen in cystic fibrosis patients with preserved renal function.[3,5]

## Surgical Technique and Normal Anatomy

The donor pancreas is harvested with its native blood supply and a portion of the donor's duodenum.[6] The graft is then transplanted into the recipient's pelvis, typically in the right iliac fossa.

### *Vascular Supply*

The vascular supply is then restored to the graft via connection of the donor arterial and venous circulation to the recipient's common iliac vascular system.[6] The donor pancreatic artery is harvested along with the donor superior mesenteric artery (SMA) in order to supply the pancreatic head, while the donor splenic artery is harvested to supply the pancreatic body and tail. These two arterial supplies are then merged to form the typical "Y-graft," which is then connected to the common iliac artery. The donor portal venous system, including its branches: the superior mesenteric vein (SMV) and splenic vein, are harvested. These two branches provide full venous drainage for the organ and, via the portal vein, were historically connected to the recipient common iliac vein. While connection to the common iliac vein is still very common, a newer approach of connecting the donor portal vein to the recipient portal venous system (usually the recipient SMV) is being increasingly utilized, due to the endocrine function of the pancreas.[7] The endocrine aspect of the pancreas, including regulation of blood sugar via insulin and glucagon, is typically drained by the portal venous system in non-transplanted patients, so connecting the transplant's venous drainage to the recipient's venous drainage does provide similar anatomy and physiology with regards to this process and may prevent hyperinsulinemia. The arterial and venous supply of the pancreatic graft is illustrated in Fig 1, with

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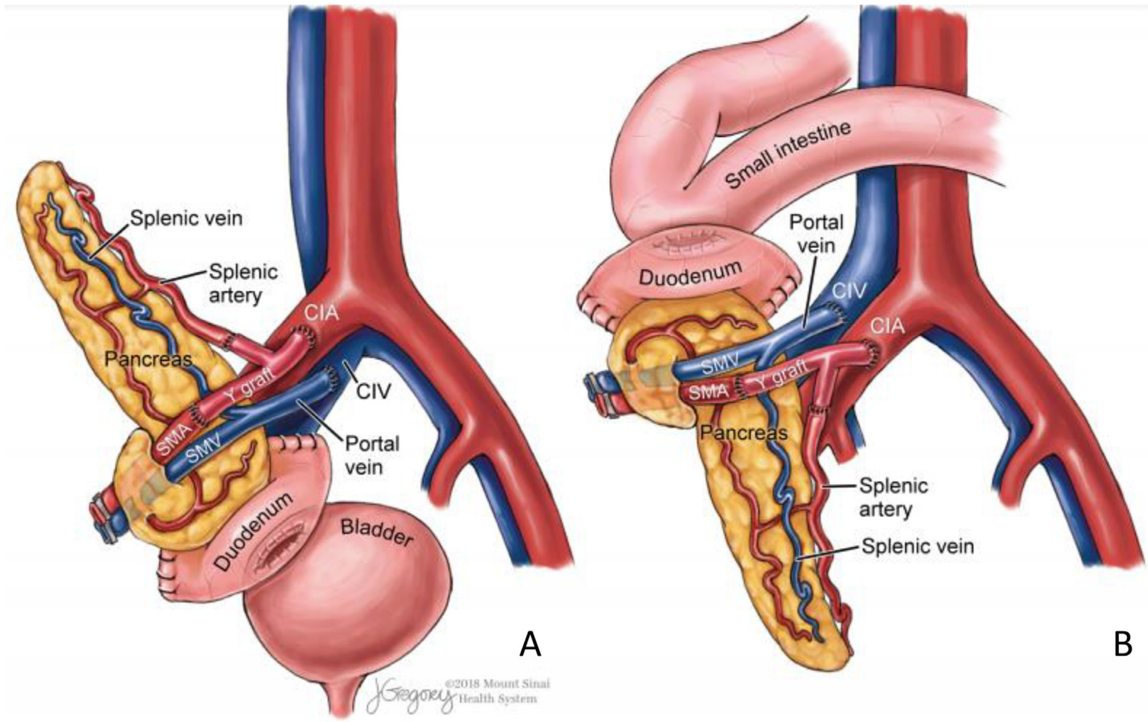


**FIG 1.** This image is a medical illustration of two possible surgical techniques for placement of a pancreas transplant, its vascular supply, and its enteric drainage. Image A demonstrates the harvested pancreas and duodenum with surgical attachment to the bladder for exocrine drainage, with the pancreatic head in caudal position. Image B shows surgical attachment of the harvested duodenum to a loop of the recipient's small intestine, with the pancreatic tail in caudal position. In both techniques, vascular attachments are the same. The recipient common iliac artery (CIA) is attached to graft material (Y-graft), which connects to the donor splenic artery and superior mesenteric artery (SMA) via surgical sutures. Venous drainage is achieved via anastomosis of the donor portal vein with its branches, the superior mesenteric vein (SMV) and splenic vein, to the recipient common iliac vein (CIV).

anastomoses demonstrated between the donor vessels and the recipient common iliac vascular systems.

*Exocrine Drainage*

The exocrine drainage of the transplanted pancreas is the final portion of the procedure.[5] The donor duodenum, harvested at the time of explantation, acts as a reservoir for the exocrine products excreted by the pancreas to support the digestive system.[8,9] This drainage may be achieved in two different ways: connection of the duodenum to the recipient's small intestines or connection of the duodenum to the recipient's urinary bladder. Both the bladder drainage and enteric drainage techniques have been the more common technique at one point and this status has fluctuated over time, the currently preferred method is via enteric drainage.[7-9] Bladder drainage (Fig 1A) is achieved by connecting the donor duodenum to the dome of the recipient's bladder.[5,7-9] When bladder drainage technique is used, the pancreatic head is caudal to the rest of the pancreas in the pelvis.[10] The advantage of bladder drainage over enteric drainage is that it allows the recording of urine amylase and lipase levels, in order to serve as a marker for rejection; however, it is associated with technique specific complications including: hematuria, reflux pancreatitis, urinary tract infections, bladder stone formation, urinary leaks, and metabolic acidosis.[5,11] For enteric drainage (Fig 1B), the donor duodenum is connected to the recipient's small bowel, either a loop of ileum or jejunum, and the pancreatic tail is caudal in the pelvis.[9, 10] This anastomosis can be end-to-end or side-to-side depending on the surgeon's preference. Despite the limitation for not being able to measure the urinary amylase levels to assess for dysfunction, the enteric drainage technique's popularity has increased for multiple reasons.[5] Since pancreas transplants are normally placed with renal transplants, measuring renal graft dysfunction can be used in lieu of assessing pancreatic graft dysfunction for signs of rejection. Additionally, this form of transplantation is associated with lower immunologic graft loss rates, when performed simultaneously with portal venous drainage of the graft venous supply. Enteric drainage is a risk for certain complications, including graft vascular thrombosis, anastomotic leaks, and sepsis.[5,9]

## Diagnostic Imaging Appearance of Normal Pancreas Transplants

Diagnostic imaging plays a significant role in the post-operative management of pancreatic graft recipients.[12] US, CT, and MRI each have a specific role in evaluating the appearance of the graft organ and its vascular supply, as well as assessing for potential complications. Additionally, image guided biopsies either using US or CT, are standard of care for determining possible rejection and direct angiography can be employed to confirm vascular complications or as a part of endovascular treatment procedures.[13]

*Ultrasound*

Ultrasound (US) has an advantage over other diagnostic modalities in that, it is portable; thus allowing for instant evaluation of the pancreatic transplant and the vascular supply in the immediate post-operative period.[12] On US, the transplanted pancreas appears as a homogenous structure, which is grossly hypoechoic to the surrounding mesentery and donor duodenum (Fig 2).[10] Color and Doppler US imaging allows for full evaluation of the graft's vascular anatomy.[14] Arterial waveforms can be assessed to ensure rapid systolic upstroke followed by persistent diastolic flow, while venous waveforms should be monophasic in nature in appropriate direction (Fig 3).[10,12,14] A comprehensive US evaluation of the transplanted pancreas should include location within the lower abdomen (right, mid or left), transplant morphology (size, echogenicity), arterial parameters (wave form, peak

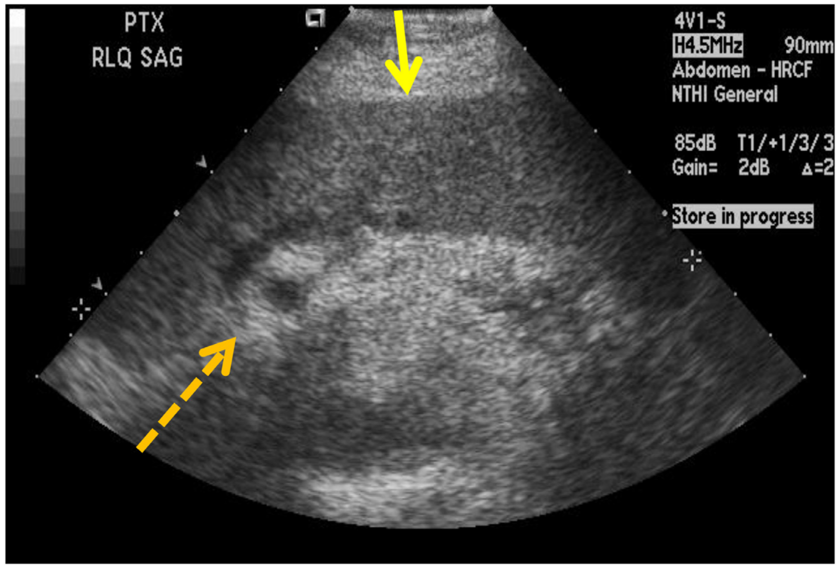


**FIG 2.** Sonographic image of a 29-year-old female reveals a normal appearing graft (solid arrow) in the right iliac fossa, which is homogenous and hypoechoic compared to the surrounding structures including visceral fat. The patient's associated donor duodenum can also be seen adjacent to the pancreas (dashed arrow) and is hyperechoic in appearance. (Color version of figure is available online.)

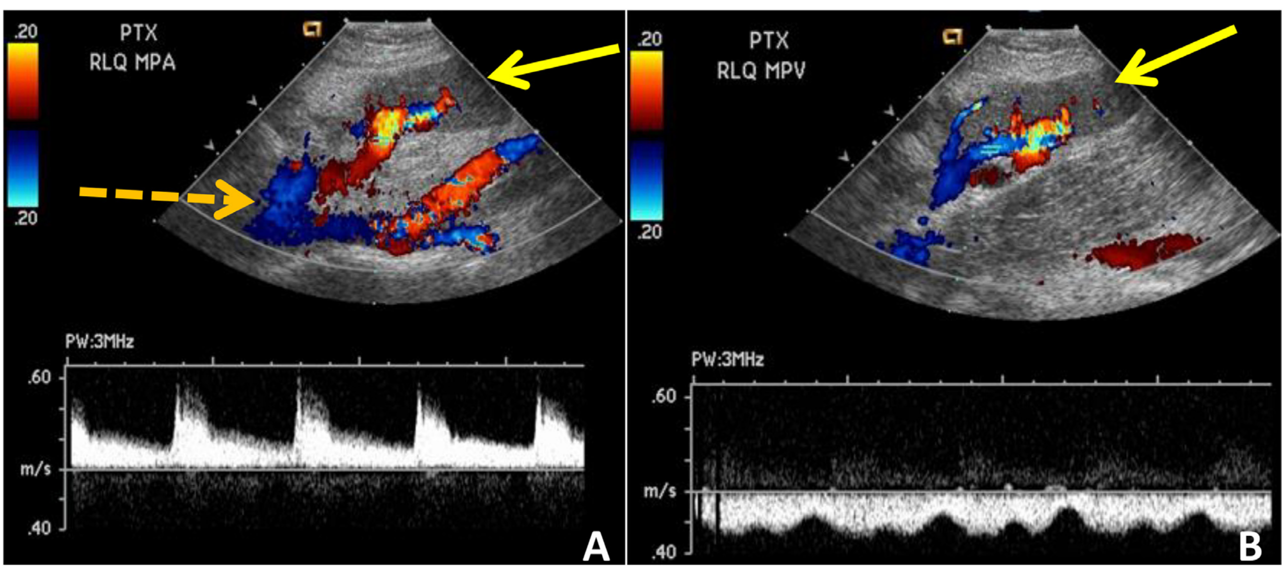


**FIG 3.** Arterial (Image A) and Venous (Image B) color Doppler images of the transplanted pancreas demonstrating normal arterial and venous wave forms in a 29-year-old female. Blood flow is noted to the normal sonographically appearing transplanted pancreas (solid arrow). The typical "Y-Graft" (dashed arrow) configuration is seen on arterial phase imaging.

systolic velocity, resistive indices, and patency), venous parameters (wave form, patency), enteric drainage (enteric vs bladder), pancreatic duct size, and presence or absence of a peri-transplant fluid collection. Contrast-enhanced US can also be utilized to increase visualization of the graft and potential complications.[10]

*Computed Tomography*

Computed Tomography (CT) allows for simultaneous visualization of both pancreas and kidney transplants, and is extremely valuable for delineating axial anatomy in the setting of abdominal complications, such as small bowel obstruction and fluid collections.[15,16] Benefits of CT include: fast image acquisition, excellent spatial resolution and ability to detect gas. Assessment may be performed with or without intravenous contrast depending on the patient's renal function.[15,16] In the absence of intravenous contrast, the transplant appears homogenous soft-tissue density, with high density suture material noted around the graft (Fig 4A).[16] When intravenous contrast is administered, the graft enhances homogenously (Fig 4B).[15,16] CT Angiography (CTA) involves appropriate intravenous contrast bolus timing for arterial and/or venous phase imaging in order to clearly delineate the vascular structures and assess for potential complications.[16] At our institution, the pancreatic transplant CT protocol normally consists of a non-contrast phase, an arterial phase (40 seconds after contrast bolus administration), and a venous phase (70 seconds after contrast bolus administration). Additionally, 3D multiplanar reconstructions of the vessels can be utilized for more information about the vascular supply (Fig 5A).[16] Enteric contrast can also be administered, with or without intravenous contrast,


**FIG 4.** Image A shows a homogenous soft-tissue density structure in the right lower quadrant of the abdomen of a 56-year-old male, consistent with the non-contrast CT appearance of a pancreas transplant. Image B is of a 36-year-old female with a normal homogenously enhancing pancreatic transplant in the right lower quadrant of the abdomen. Enteric contrast is noted in both images, in order to fully assess for bowel pathology. (Color version of figure is available online.)

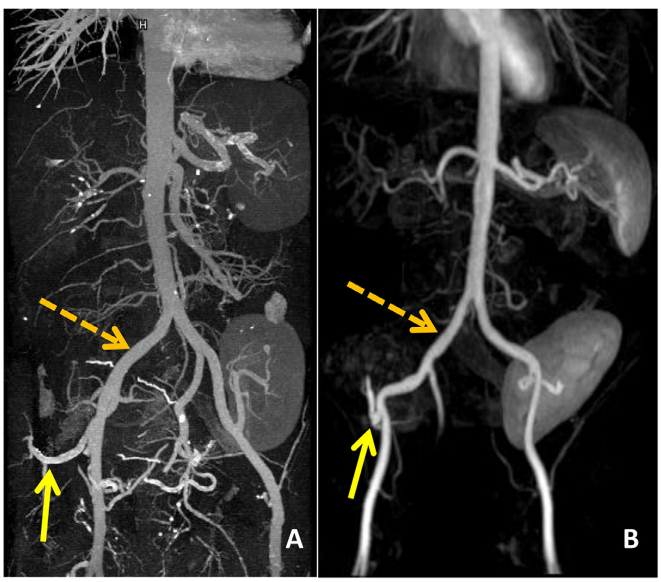


**FIG 5.** 3D reconstructions of the abdominal organs and vasculature after angiography can provide more information about the graft's vascular supply. Image A is an arterial phase reconstruction from a CTA of a 56-year-old male status post Simultaneous Pancreas and Kidney transplants, which demonstrates the transplanted graft artery (solid arrow) arising from the recipient right common iliac artery (dashed arrow). Image B is from the same patient, two years later, demonstrating the same normal vascular anatomy, only this time the patient received an MRA. The renal allograft is identified in the left iliac fossa. (Color version of figure is available online.)

in order to provide improved visualization of the bowel. In our experience, adequate bowel distention is useful for distinguishing collapsed bowel loops from post-operative fluid collections.

*Magnetic Resonance Imaging*

Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) are both useful tools in the arsenal of the radiologist to evaluate the graft and its vascular supply, respectively.[17] Benefits of MRI include: the lack of ionizing radiation, multi-planar capabilities and superior soft tissue contrast resolution. Pancreas parenchyma is best evaluated on fat-suppressed MR imaging. On non-contrast T1-weighted fat-suppressed imaging, the graft is hyperintense to the liver, while the intensity increases on post-intravenous contrast phase imaging (Fig 6A). On T2-weighted fat-suppressed imaging, the graft has intensity appearance between fluid and muscle intensity (Fig 6B). MRA and MRV allow for clear visualization of the graft's vascular supply and drainage, in addition to the iliac arterial and venous systems.[18] This modality can clearly demonstrate potential stenosis or thrombosis of the arteries or veins. Furthermore, 3D multi-planar reconstructions can be performed to better visualize the patient's entire vasculature (Fig 5B).

## Imaging Appearance of Pancreatic Transplant Complications

Potential complications in the setting of pancreas transplant are varied and can result from issues affecting the graft itself, the vascular supply, or organs unrelated to the pancreas, although these categories are for simplicity in classification and in actuality, many of these complications are related or occur simultaneously.[16] Complications may occur in the peri-transplant setting or many years later, depending on the patient's clinical status.

*Graft Related Complications*

*Rejection*

Pancreas transplant rejection is an autoimmune mediated response and is the single most common cause of graft failure, with rates varying between 5% to 25%.[1] Early detection and treatment with immunosuppressive agents is critical to ensure graft survival. Based on the time of the transplant, rejection can be classified as either hyperacute, acute, or chronic.[1,16] Hyperacute rejection is rare and occurs immediately after transplantation. Acute rejection usually occurs within 1 week to 3 months of post-transplant and chronic rejection generally occurs after 3 months post-transplant. The immune -mediated response causing rejection may be antibody-mediated, T-cell mediated with worsening acinar inflammation and auto-immune arteritis (acute), or interstitial fibrotic reaction with small vessel endarteritis and acinar atrophy (chronic).[1,19,20]

Ultrasound is useful in characterizing rejection.[12,14] In the earliest phases of rejection, there may be no imaging difference than normal; however, as the disease progresses, the pancreatic graft will become increasingly heterogeneous and echogenic as compared to the graft's normal appearance. (Fig 7A). On CT and MR, there will be less uniform enhancement of the transplanted pancreas due to the parenchymal dysfunction leading to decreased uptake of contrast (Fig 7B).[16] Furthermore, the organ may appear edematous and enlarge in size. Once the rejection becomes more severe and increases its chronicity, that pancreas may atrophy, and that can also be reflected in imaging.[1] While the imaging findings of rejection can be suggested with US, CT, or MR, a final diagnosis typically requires tissue sampling, often using image guidance.[13] This is because the differential diagnosis for rejection on imaging includes pancreatitis and graft thrombosis, so

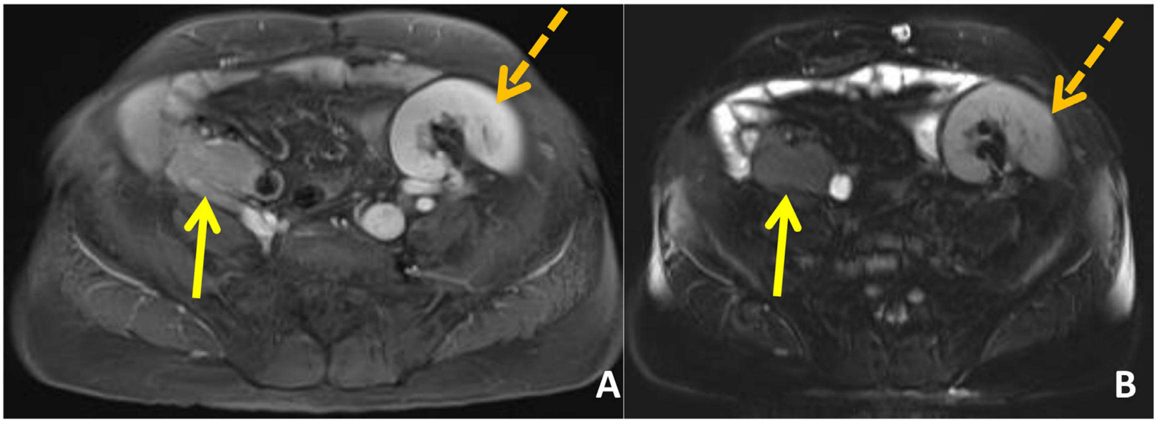


**FIG 6.** T1-weighted post-contrast (A) and T2 weighted (B) fat-suppressed images of a 58-year-old male status post Simultaneous Pancreas and Kidney transplants demonstrating normal appearing pancreas (solid arrow) and kidney (dashed arrow) transplants. Pancreas transplants are hyperintense on T1 and hypointense to fluid, but hyperintesne to muscle on T2. (Color version of figure is available online.)

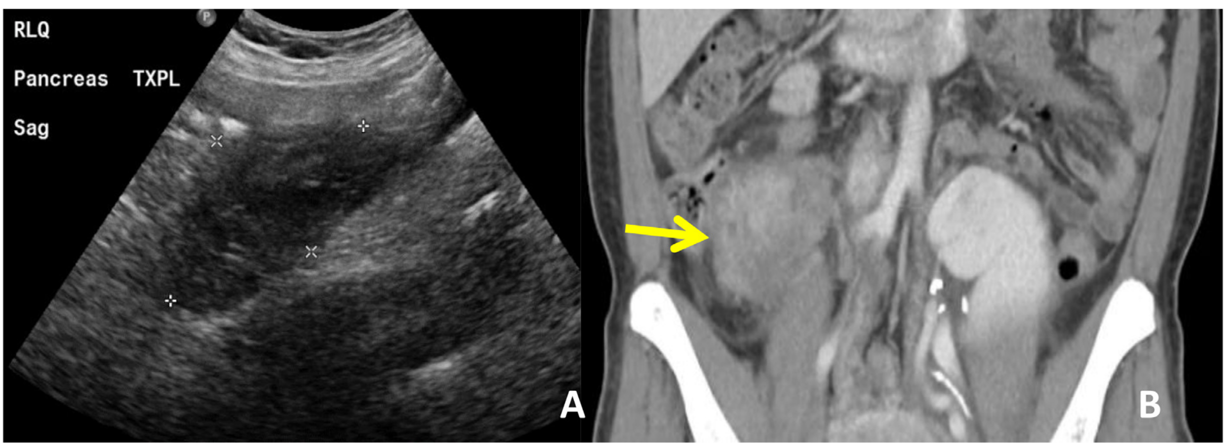


**FIG 7.** Ultrasound and CT can both be used to demonstrate pancreatic transplant rejection. Image A is the ultrasound of a transplanted pancreas of a 32-year-old female which demonstrates heterogeneous and increased echogenicity compared to the normal appearing graft in Figure 2. Image B is a contrast enhanced CT scan of the lower abdomen of a 37-year-old female showing a transplanted pancreas (arrow) in the right lower quadrant which has heterogeneous enhancement pattern with areas of low attenuation consistent with edema. These imaging findings are seen in the setting of rejection, but are non-specific, and may be seen in other clinical situations, such as graft pancreatitis. Both of these patients underwent percutaneous biopsy demonstrating chronic rejection. (Color version of figure is available online.)

histologic differentiation is necessary to ensure the patient is appropriately treated to optimize graft survival. Laboratory analysis of serum amylase and lipase (or urinary amylase in the setting of bladder drainage) is also not helpful in differentiating rejection from other potential diagnoses, like pancreatitis, and may not correlate to graft dysfunction at all.[21]

*Pancreatitis*

Graft pancreatitis is the second most common complication in pancreas transplants; however, like rejection, its imaging appearance is not specific.[1,14,16,22] Clinical presentation is also non-specific, as it is associated with pain, pancreatic dysfunction, and fever.[22] The causes of pancreatitis may be related to arterial or venous insufficiency, as it is believed that 100% of immediately post-transplant patient undergo an acute inflammatory response related to ischemic reperfusion injury within the first few days of transplantation, which spontaneously resolves within a few days (Fig 8A). Similar to rejection, the graft becomes more heterogeneous in echogenicity on US and has a heterogeneous enhancement pattern with peri-pancreatic inflammatory stranding on CT or MR in the setting of pancreatitis (Fig 8B).[14,16] US of pancreatitis in transplanted organs is similar in appearance to pancreatitis in the native pancreas, despite different etiologies.[10] Because of its imaging and lab value similarity to rejection, post-transplant pancreatitis can only be diagnosed after a biopsy, although this procedure may also rarely cause pancreatitis.[13,21] Complications of graft pancreatitis are similar to non-transplant pancreatitis and include hemorrhage, necrosis, peri-pancreatic fluid collection, pseudocyst formation, abscesses, and arterial pseudoaneurysm.[3] Venous thrombosis can also result from graft pancreatitis.[10]

*Infection*

Any intra-abdominal infectious process can affect the transplanted pancreas; however, superinfection of other conditions may be seen in the setting of pancreatitis and necrosis.[14,16] Imaging findings will be similar to rejection or pancreatitis on US, CT, or MR and clinical course will dictate the need for antibiotic therapy. Immunosuppression due to graft placement puts this patient population at increased risk of infection throughout the body over the course of their lifetime.[10]

*Necrosis*

Pancreatic transplant necrosis is a severe complication of multiple potential etiologies including, but not limited to, severe pancreatitis, arterial thrombosis, venous thrombosis, infection and rejection.[14,16,23] Imaging appearance is similar to rejection and pancreatitis including increased echogenicity on US and decreased enhancement on CT or MR.[14,16] Additionally, foci of air may be noted

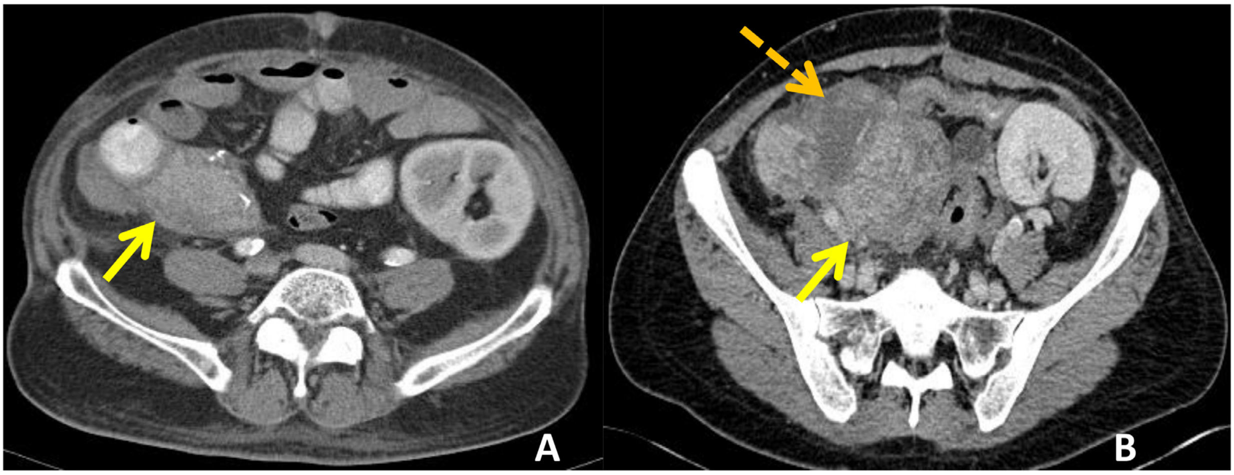


**FIG 8.** Graft pancreatitis can range from mild to severe in terms of its clinical presentation. Image A is an axial CT slice of a 55-year-old male 24 hours post-transplant which shows a transplanted pancreas (arrow) mild edema and heterogeneity of enhancement. This mild pancreatitis was asymptomatic and subsequently resolved without treatment. Conversely, Image B is an axial CT slice of a 41 year old female 2 months post-transplant with pain and fever demonstrating an enlarged, edematous graft (solid arrow) with heterogeneous enhancement and a peri-pancreatic fluid collection (dashed arrow). The patient underwent percutaneous biopsy demonstrating pancreatitis, and the patient was treated accordingly. (Color version of figure is available online.)

within the graft, which will appear echogenic with dirty shadowing on US and can be confirmed on subsequent CT evaluation.[14,16]

### *Vascular Complications*

#### *Arterial Complications*

The arterial supply of the pancreas requires multiple surgical anastomoses, which allows for potential complication.[6,13] These findings include arterial stenosis, arterial thrombosis, and pseudoaneurysm formation.[14,16,24] Stenotic vessels can be visualized on CT angiography, MR angiography, or direct angiography, although both CT and MR provide comparable visualization with an invasive procedure.[16,18] Arterial stenosis may be seen indirectly on Doppler US with evidence of turbulent flow.[14] Arterial thrombosis is typically characterized by an abrupt cut-off of the pancreatic artery graft on either CT, MR, or direct angiographic imaging (Figs 9A and 9B).[16] On US, thrombosis is characterized by absence of a wave form on Doppler.[14] Arterial thrombosis can lead to pancreatic necrosis (Fig 9A). Pseudoaneurysms are commonly visualized on CT or MR at the site of anastomosis with a narrow neck and arising from the vessel, with the characteristic "yin-yang" appearance on Doppler US imaging.[14,16,24] Pseudoaneurysms may result from the surgical procedure itself, subsequent trauma to the patient, or after a biopsy procedure. Pseudoaneursyms may also have associated arterio-venous fistulas.[24]

#### *Venous Complications*

Similar to arterial complications, venous complications, such as venous thrombosis or stenosis, can be characterized on US, CT, and MR and may lead to graft failure or necrosis.[25] These findings may be characterized on Doppler US by absent venous flow and reversal of diastolic flow in the artery. Venous thrombosis is more common than arterial thrombosis and may result from stasis caused by compression from adjacent organ/fluid collections or secondary to phlebitis related to pancreatitis/rejection.[10,25] If there is stasis in a stump of the donor SMV, this may act as a potential cause of venous thrombosis.[10] The imaging appearance of the pancreatic parenchyma on CT, MR, or US in the setting of venous thrombosis may be similar to rejection and pancreatitis, requiring careful assessment of the transplant vasculature and in some circumstances, confirmatory biopsy (Fig 10).[12-14]

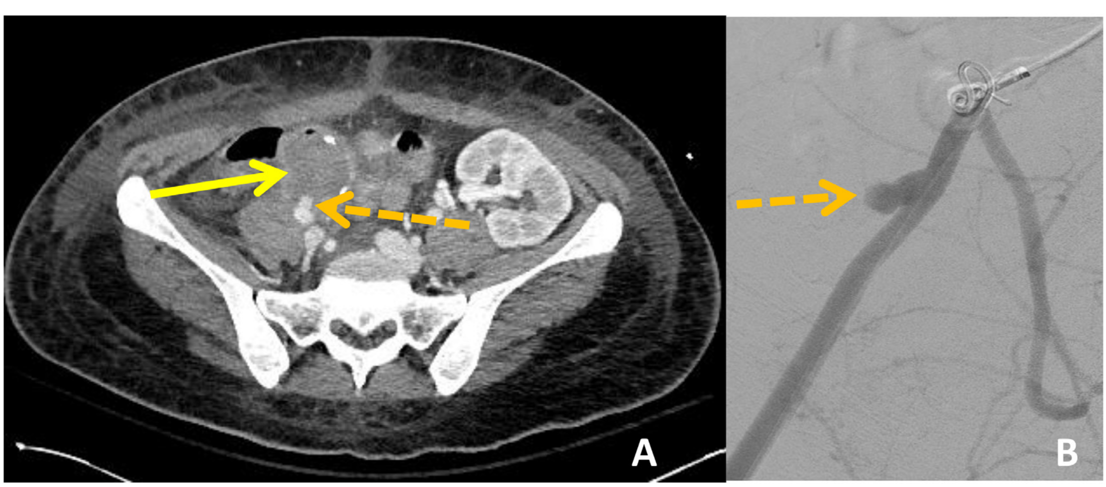


**FIG 9.** Pancreatic necrosis is a major complication of multiple other pancreatic complications. The graft (solid arrow) in the right lower quadrant of this 33-year old female demonstrates little to no enhancement of the pancreatic parenchyma on this post-contrast axial CT image, consistent with liquefactive necrosis (Image A). A focus of air is also noted within the graft, a finding denoting increased severity and possible superinfection. This patient's necrosis was cause by arterial thrombosis, characterized by abrupt cut-off of the vessel (dashed arrow). Direct catheter based angiography (Image B) of the same patient shows same abrupt termination of the pancreatic artery graft (dashed arrow). (Color version of figure is available online.)

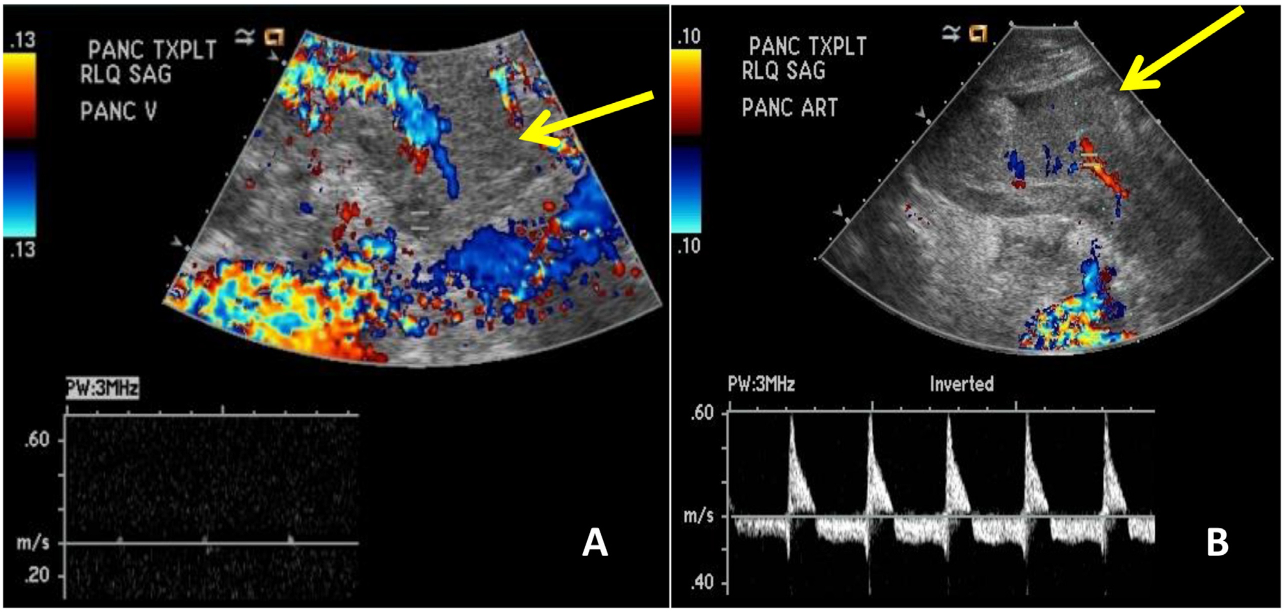


**FIG 10.** Color Doppler US images of the transplanted pancreas in a 44-year-old female demonstrate absent wave form in the pancreatic vein (Image A), reversal of diastolic flow of the pancreatic artery (Image B), and heterogeneous echotexture of the pancreas (arrow). These findings are consistent with pancreatic vein thrombosis.

Graft thrombosis, either arterial or venous, is seen in up to 19% of patients, and is the second most common cause of graft loss after rejection.[10]

*Non-Pancreatic Complications*

*Peri-Transplant Fluid Collection*

Fluid collections at the time of transplantation are a common post-surgical occurrence.[13] The collections formed during the placement of the graft, are usually from bleeding due to the multiple vascular anastomoses. Most of these are small seromas or hematomas, which resolve on their own; however, because these patients are immunosuppressed, superinfection and abscess formation may occur.[10,13] In this situation, these patients may require percutaneous drainage or, if more severe, surgical re-intervention.[13,18] On US, these collections appear hypoechoic, when they are simple fluid (Fig 11A), with increased echogenicity in the setting of hematoma or abscess.[12,14] On CT, these collections will have simple fluid attenuation (Fig 11B), while hematomas will demonstrate hyper-attenuation.[15,16] Abscesses will demonstrate rim enhancement on CT or MR imaging. Fluid collections may also result from pancreatitis, pancreatic necrosis, or duodenal leak, although not often in the immediate post-operative setting.[3,10]

*Bowel Complications*

Given that implantation of the pancreas transplant commonly involves connection with nearby bowel loops for enteric drainage, complications involving the bowels are not uncommon in the post-surgical setting.[26] Obstruction of the bowel loops may occur secondary to suture stricture, surgical adhesions, or internal hernias (Fig 12). This finding can be well seen on CT, with enteric contrast causing opacification of the bowel loops.[27] Like in other clinical settings, small bowel obstruction in transplant patients are at risk for bowel

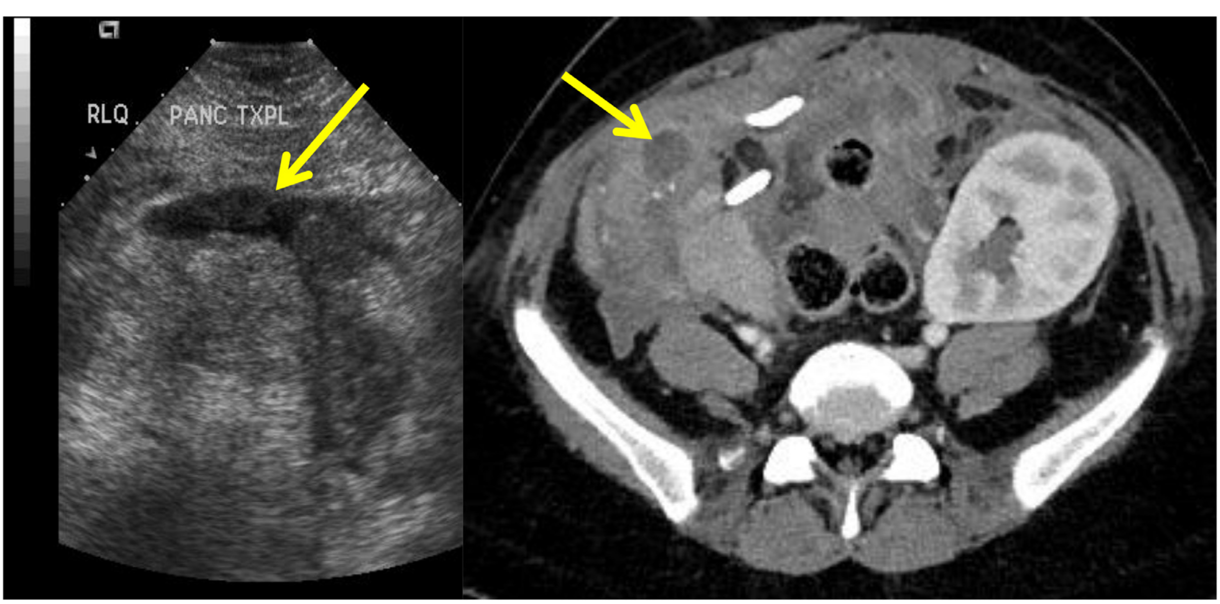


**FIG 11.** Post-operative fluid collections (arrow) may be characterized on either US (Image A) or CT (Image B). On US, the collection is a hypoechoic structure adjacent to the graft, while on CT it appears as a hypoattenuating fluid density structure near the pancreas. (Color version of figure is available online.)

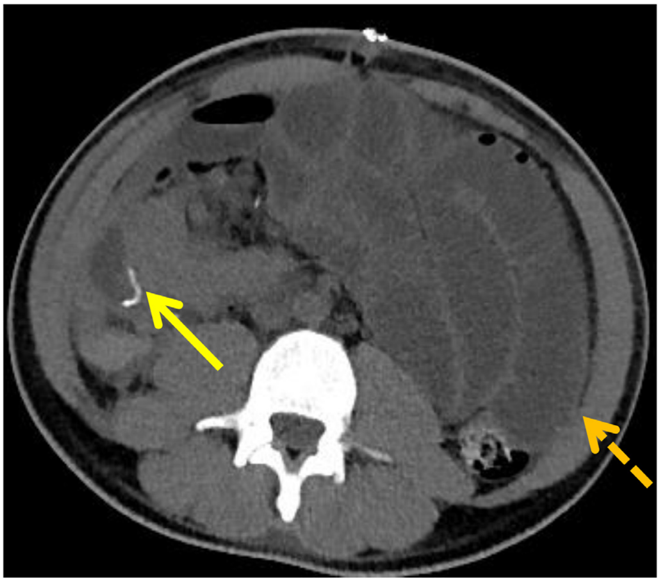

**FIG 12.** Post-transplant small bowel obstruction may occur due to a complication related to the bowel anastomosis of pancreatic enteric drainage. This 22-year-old male demonstrates multiple dilated small bowel loops (dashed arrow), with a transition point (solid arrow) noted at the level of the suture between the pancreatic graft and small bowel, on this non-contrast CT image, likely secondary to a stricture at the anastomosis. (Color version of figure is available online.)

ischemia.[26,27] Additional bowel related complications include leaking at the site of anastomosis, which would require surgical correction.

### *Post-Transplantation Lymphoproliferative Disorder (PTLD)*

PTLD may occur in up to 6% of pancreatic transplant recipients and varies in severity from patient to patient.[28] PTLD may range from benign lymphoid hyperplasia to malignant B-cell lymphoma. Most frequently, PTLD is seen in the lymph nodes, liver, or gastrointestinal tract; however, lesions can be seen throughout the body and may involve the graft itself.[29] PTLD can be characterized on CT or MR, but notably has increased radiotracer uptake on Positron Emission Tomography (PET) scans (Fig 13).[30]

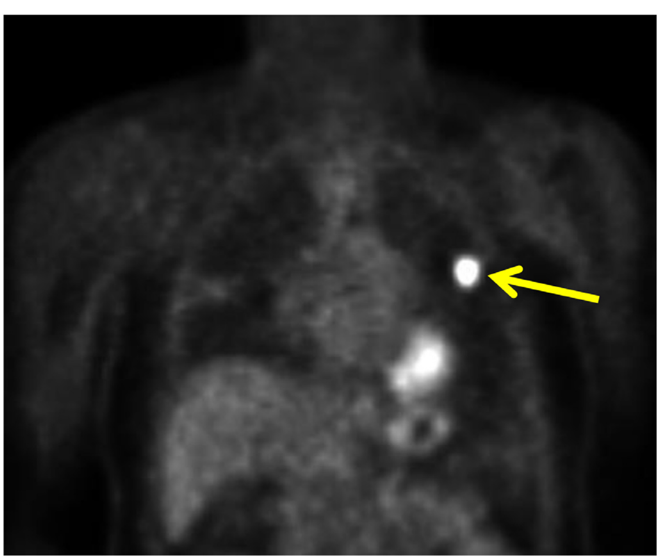

**FIG 13.** PTLD may occur anywhere in the body. This 45-year-old male had lung nodules noted on an unrelated CT scan of his chest many years after transplant. The subsequent PET image shows a PET positive nodule (arrow) in the left upper lobe, which on biopsy was revealed to be PTLD. No other areas of PTLD were identified on this patient. (Color version of figure is available online.)

## Conclusion

Pancreatic transplantation is potentially a life-saving treatment option for many patients and is a well-established procedure with reported potential complications. Imaging using a variety of modalities including US, CT and MRI plays an important role in the evaluation of pancreas allografts, the transplant vasculature and for characterization of complications. Awareness and knowledge of multitude of possible, and often inter-linked, appearances of pancreatic transplants and complications is important for both the radiologist and referring clinicians to inform patient management and prognostication.

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