

Surgical complications after pancreatic transplantation: A computed tomography imaging pictorial review

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Abstract

Pancreatic transplantation is considered by the American Diabetes Association and the European Association for the Study of Diabetes an acceptable surgical procedure in patients with type 1 diabetes also undergoing kidney transplantation in pre-final or end-stage renal disease if no contraindications are present. Pancreatic transplantation, however, is a complex surgical procedure and may lead to a range of postoperative complications that can significantly impact graft function and patient outcomes. Postoperative computed tomography (CT) is often adopted to evaluate perfusion of the transplanted pancreas, identify complications and as a guide for interventional radiology procedures. CT assessment after pancreatic transplantation should start with the evaluation of the arterial Y-graft, the venous anastomosis and the duodenojejunostomy. With regard to complications, CT allows for the identification of vascular complications, such as thrombosis or stenosis of blood vessels supplying the graft, the detection of pancreatic fluid collections, including pseudocysts, abscesses, or leaks, the assessment of bowel complications (anastomotic leaks, ileus or obstruction), and the identi-

fication of bleeding. The aim of this pictorial review is to illustrate CT findings of surgical-related complications after pancreatic transplantation. The knowledge of surgical techniques is of key importance to understand postoperative anatomic changes and imaging evaluation. Therefore, we first provide a short summary of the main techniques of pancreatic transplantation. Then, we provide a practical imaging approach to pancreatic transplantation and its complications providing tips and tricks for the prompt imaging diagnosis on CT.

Key Words: Diabetes mellitus; Type 1; Pancreas transplantation; Complications; Computed tomography; Diagnostic imaging

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Core Tip: Pancreatic transplantation is a complex surgical procedure and, similarly to any major surgical intervention, may lead to a range of postoperative complications that can significantly impact graft function and patient outcomes. Computed tomography offers non-invasive and accurate visualization of the transplanted pancreas and surrounding structures, providing detailed anatomical information and aiding in the detection of complications.

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INTRODUCTION

Pancreatic transplantation is considered by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) an acceptable surgical procedure in patients with type 1 diabetes (T1D) also undergoing kidney transplantation [*i.e.* simultaneous pancreas and kidney (SPK) transplant] in pre-final or end-stage renal disease if no contraindications are present[1]. Pancreatic transplantation has been considered for years the only treatment for T1D that consistently establishes an insulin-independent, normoglycemic state, with 5-year graft survival of 83%, 55% and 70%, in case of SPK, pancreatic transplantation alone (PTA) or pancreas after a kidney transplantation (PAK), respectively [2-4]. The main indication of PTA is presence of T1D and normal or near-normal renal function in patients who suffer from hypoglycemia unawareness, which results in impaired quality of life or with difficulty adhering to the requirement of insulin injection[5]. In few selected cases, transplantation of pancreatic islet – a less invasive procedure consisting in the transplantation of islets of Langerhans in the recipient hepatic portal system – is indicated as an alternative to pancreatic transplantation by ADA and EASD[1]. However, intrahepatic islet transplantation for T1D is limited because of the need of multiple infusions and poor islet viability after transplantation, and more recently intracutaneous transplantation of islets has also been investigated[6]. In a 20-year span from 2000 to 2020, only about 4365 islet allotransplants have been performed according to a recent worldwide survey[7], while the number of pancreatic transplantations in the 10-year span from 2010 to 2019 is of about 23000 procedures[8].

Pancreatic transplantation is a complex surgical procedure and, similarly to any major surgical intervention, may lead to a range of postoperative complications that can significantly impact graft function and patient outcomes[9,10]. The occurrence of postoperative complications may vary depending on factors such as the type of transplantation (SPK, PAK or PTA) and the specific patient population. Cross-sectional imaging – *i.e.*, Doppler ultrasound (US), contrast-enhanced US (CEUS) and computed tomography (CT) – plays a pivotal role in the evaluation of the transplanted pancreas. US is the preferred initial imaging modality for evaluating the transplanted pancreas due to its safe, non-invasive, radiation-free, simple, quick, and repeatable approach. However, US is often affected by factors such as intestinal gas interference and operator proficiency, and partial thrombosis may be easily missed[11]. CT offers non-invasive and accurate visualization of the transplanted pancreas and surrounding structures, providing detailed anatomical information and aiding in the detection of complications. Indeed, CT allows for the identification of vascular complications, such as thrombosis or stenosis of blood vessels supplying the graft as well as bleeding or pseudoaneurysms, the detection of pancreatic fluid collections, including pseudocysts, abscesses, or leaks, the assessment of bowel complications (anastomotic leaks, ileus or obstruction), while it has a limited role in the evaluation of graft rejection[12,13]. Magnetic resonance imaging (MRI) is rarely uncommonly used for examination the assessment of pancreatic graft-related complications, and it is preferred particularly in patients with declining renal function. The main adoption of CT compared to MRI is based on different reasons, including wider availability of CT compared to MRI particularly in the emergency and urgent settings, the lower acquisition time of CT exams compared to MRI which is important in imaging acutely ill and intensively monitored patients, but also to the lower spatial and temporal resolution, creating difficulties in the evaluation of the enteric anastomosis and vascular complications. Contrast medium administration in CT should not be a contraindication in kidney transplant recipients. Fananapazir *et al*[14] demonstrated that the incidence of acute kidney injury in patients with transplanted kidney submitted to CT scans with low-osmolality iodine-based contrast material was 7% when considering the threshold of ≥ 0.3 mg/dL for the increase in serum creatinine levels. The incidence of contrast induced nephropathy after contrast-enhanced CT was similar (6.1%) in a study by Cheungpasitporn *et al*[15]. However, in a study involving

about 6175 patients, McDonald *et al*[16] demonstrated lack of significant difference in the onset of contrast induced nephropathy between patients with a solitary kidney, including kidney transplant recipients (4.1%), and those with bilateral kidneys (4.2%). The assessment of serum creatinine for calculating the estimated glomerular filtration rate is recommended before contrast medium administration within 7 d before CT in patients with an acute disease, an acute deterioration of a chronic disease or in hospitalized patients, and preventive hydration protocols need to be considered in at-risk patients as indicated by guidelines[17-19].

This pictorial review is aimed at illustrating CT findings of surgical-related complications after pancreatic transplantation. A comprehensive knowledge of surgical techniques allows understanding the postoperative anatomic changes that are identified on CT images. Therefore, this review will first a short summary of the main techniques of pancreatic transplantation and, then, will discuss imaging tips and tricks for the prompt diagnosis of complications after pancreatic transplantation on CT.

SURGICAL TECHNIQUES

After organ procurement from a deceased donor, a meticulous graft back-table surgery is necessary before pancreatic transplantation. Main steps are: Splenectomy, removal of the excess fat surrounding the pancreas and ligation of small vessels and lymphatics along the inferior margin of the pancreatic tail, coursing anteriorly around the surface of the neck and head of the pancreas to the proximal duodenal staple line. A suture of the vessels at the root of the mesentery and inferior mesenteric vein is performed followed by an oversewing of the mesenteric staple line. A vascular preparation is necessary using a Y conduit of donor iliac artery which is anastomosed to the superior mesenteric and splenic arteries of the graft (Figures 1 and 2). Assessment of blood supply to the entire pancreas graft exclusively *via* cross-circulation between splenic artery and superior mesenteric artery is mandatory in order to guarantee blood supply to all the pancreas graft. By flushing the superior mesenteric artery and not looking for back-flushing through the gastroduodenal artery is possible to recognize the need for vascular reconstruction of the gastroduodenal artery to guarantee blood supply to head of the pancreas graft and duodenal segment, and possibly reduce the incidence of duodenal complications [20]. A duodenal shortening with stapler and oversewing of the staple line is then completed. At this stage, the graft is ready for implantation.

Through a midline incision, the pancreas allograft is usually placed intraperitoneally, on the right side with the head in a cranial position, and receives arterial inflow from the iliac artery (Figure 1). Venous anastomosis can be performed through systemic vein technique with the graft portal vein (PV) anastomosed to the recipient inferior vena cava or iliac vein, or through the PV technique with the graft PV anastomosed to the recipient inferior vena cava or iliac vein. In the PV technique, the graft PV is connected to the recipient superior mesenteric vein. Systemic drainage theoretically may lead to hyperinsulinemia[21], while portal drainage could allow a more physiological “first pass” effect through the liver since insulin is immediately extracted by the liver. However, the arterial anastomosis to the iliac artery tends to be more difficult using the PV technique and it requires a very long Y graft. Moreover, obesity, thickened mesentery, or an inadequate caliber of the superior mesenteric vein can make the portal drainage even harder[22]. Long-term studies comparing the two techniques have not demonstrated clear metabolic advantages with portal drainage and the use of the PV has remained marginal over the years[23]. For the exocrine pancreas drainage, anastomosis between the donor duodenum and recipient small bowel loop (*i.e.*, jejunal or an ileal loop) is performed side-to-side with a circular stapler. After firing the stapler (trans-oral anvil delivery system EEA), the end of the donor duodenum is closed using a linear stapler. Alternatively, a bladder diversion can be performed[24]. Bladder drainage can be particularly advantageous in case of PTA, for the assessment of the concentration of urinary amylase as a marker of rejection. Disadvantages of this technique include both urologic complications such as hematuria (16%), leaks (14%), reflux pancreatitis (11%), recurrent urinary infections (10%), urethritis (3%), urethral stricture/disruption (3%), and metabolic complications due to the urinary loss of the bicarbonate-rich pancreatic juice, including hyperchloremic metabolic acidosis and dehydration[23, 25]. When these complications became intractable, conversion from bladder to enteric drainage is often necessary[26]. Enteric drainage is currently the predominant technique in pancreatic transplantation[23].

Usually, recipients start receiving immunosuppression during surgery, consisting in antibody induction and a triple drug immunosuppressive therapy is started immediately postoperatively. Most of the Centers utilize a regimen consisting of tacrolimus, mycophenolate mofetil and steroid.

Heparin prophylaxis is recommended with intravenous heparin administered as a single dose during surgery after pancreas revascularization and it is continued after surgery with low molecular weight heparin or continuous infusion, at the discretion of the Transplant Centre.

Some days after transplantation, a CT scan is advisable to early recognize vascular thrombosis or any signs of vascular alterations, not yet clinically relevant.

COMPLICATIONS AFTER PANCREATIC TRANSPLANTATION

Postoperative surgical complications of pancreatic transplantation are still common despite many improvements in surgical techniques, and may be distinguished based on time of onset[27-28]. Postoperative monitoring of the pancreatic graft by CT is requested in about 89% of cases according to a recent series of 230 pancreatic transplantations and is helpful for optimizing patient management[29].

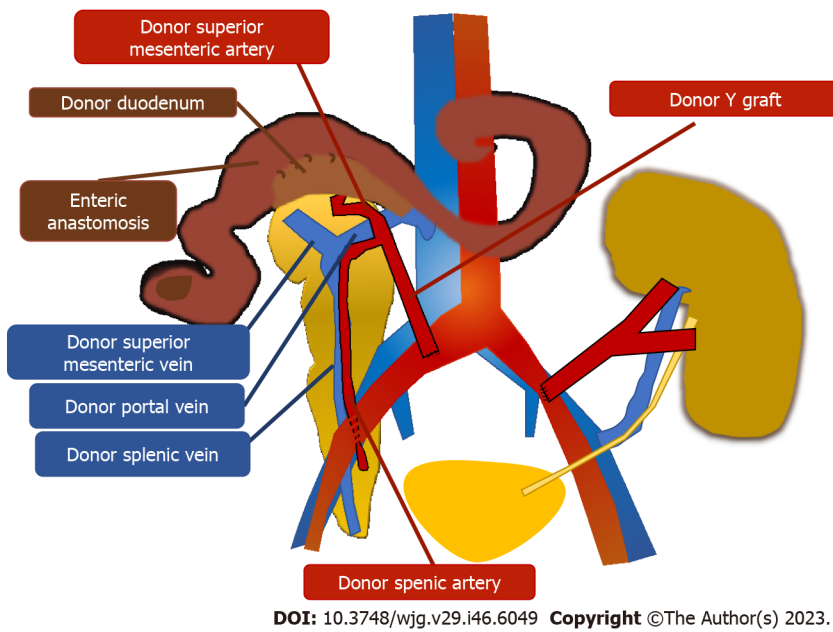


Figure 1 Schematic imaging representation of simultaneous pancreas and kidney transplantation.

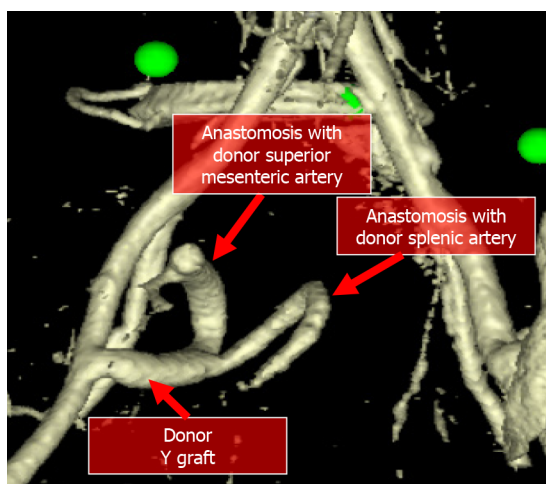


Figure 2 Volume rendering reformat of computed tomography images in the arterial phase demonstrates the Y conduit of donor iliac artery to the superior mesenteric and splenic arteries of the graft.

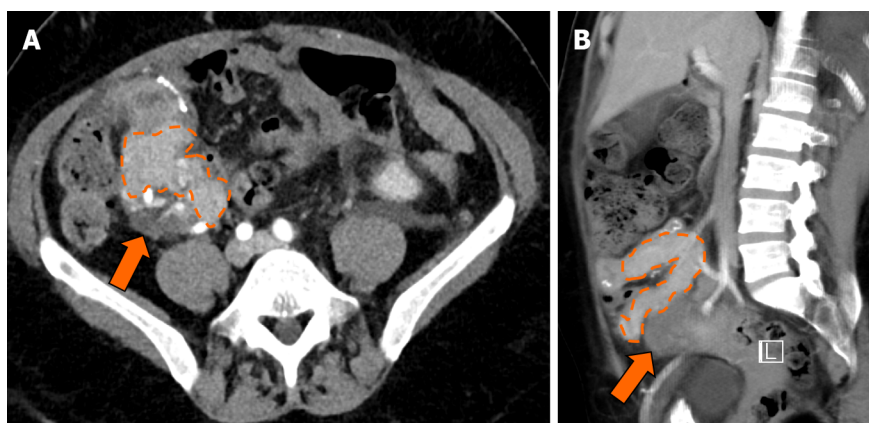
The main reasons for requesting imaging are related to the indication per protocol even without acute clinical indication, sudden progressive hyperglycemia, persistent or abdominal tenderness[29]. However, the adoption of CT needs to be patient-tailored particularly in the context of SPK, due to the potentially nephrotoxic effect of contrast agents which is reported to be as low as 5.6% in kidney transplant recipients with the use of hypo-osmolar contrast agent[30].

Initial complications of pancreatic transplantations are largely related to technical factors, including vascular thrombosis, bleeding, enteric anastomotic leak or graft pancreatitis, and urologic complications[8]. Late complications include pseudocyst formation, post-transplant lymphoproliferative disease, pseudoaneurysms, artero-venous fistulas and rejection (Figure 3).

Graft thrombosis is the most common complication after transplant and may lead to graft failure in about 3.7%, 4.1% and 5.9% of SPK, PAK and PTA, respectively[8]. Graft loss due to infection, pancreatitis, bleeding, leaks, and other reasons occur in up to 0.5%, 0.5%, 0.5%, 0.4%, and 0.6%, respectively[8].

Graft thrombosis

Graft thrombosis occurs in 7%-34% of patients after pancreas transplant, with high body mass index being a risk factor, may affect arteries or veins and can be partial or complete[10,12,29,31]. Partial graft thrombosis occurs in about 25% of cases after pancreatic transplantation, is subclinical in the majority of cases, and may resolve spontaneously with medical therapy[29]. Venous thrombosis is far more common than arterial thrombosis, but arterial thrombosis is the most



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Figure 3 A 51-year-old woman, one month after simultaneous kidney-pancreatic transplantation is admitted to the emergency department for abdominal pain; final diagnosis at biopsy of the pancreatic graft was rejection. A: Contrast enhanced computed tomography in the axial plane shows a minimally inhomogeneous pancreatic graft (dotted orange line) with peripancreatic fluid (arrows) posteriorly to the graft; B: Sagittal plane of the same contrast enhanced computed tomography.

dangerous leading to rapid graft loss[29,32]. Acute rejection and CT finding of pancreatitis are risk factors for graft thrombosis[12].

Contrast-enhanced CT with angiographic phase and venous phase demonstrates thrombosis as a filling defect in a vessel during the vascular phase, and allows to clearly indicate the extension of the filling defect. Arterial thrombosis (Figure 4) may lead to graft dysfunction, pancreatitis, leakage of pancreatic enzymes, sepsis, necrosis and even emphysematous transformation of the graft if it is left untreated. Pancreatic graft venous thrombi (Figure 5) can remain relatively localized possibly maintaining normal graft function, or may propagate into the PV, iliac vein, or vena cava (in case of systemic venous drainage) or superior mesenteric veins (in case of portal venous drainage). In case of vascular thrombosis, a decreased enhancement of the transplanted pancreas usually occurs due to the organ ischemia, and the main differential diagnosis between arterial and venous thrombosis is made by direct visualization of the thrombus in the vessel.

Percutaneous thrombectomy, followed by anticoagulation, is considered a therapeutic option to remove the thrombus, with low complication rate[33].

Graft thrombosis may be graded on contrast-enhanced CT based on the system proposed by Hakeem *et al*[12] into:

Grade 0 – Lack of thrombosis.

Grade 1 – Peripheral thrombosis: Thrombus is located at the transected margin of the superior mesenteric vein/splenic vein or superior mesenteric artery and it is present only in a single branch.

Grade 2 – Intermediate nonocclusive thrombosis.

Venous: Thrombus extends into parenchymal vessels/main trunk of the superior mesenteric vein or splenic vein to the superior mesenteric vein/splenic vein confluence but not into the PV.

Arterial: Thrombus extends into the main trunk of the superior mesenteric artery/splenic artery to the “Y” graft but not into the Y graft.

Grade 3 – Central occlusive thrombosis.

Interestingly, despite the diagnosis of vascular thrombosis seems quite straightforward Hakeem *et al*[12] showed some discrepancies among radiologists in the detection with 28 new thrombosis identified on retrospective imaging review, with the grade 1 thrombosis being underestimated at initial diagnosis by the reporting radiologists.

Pancreatitis

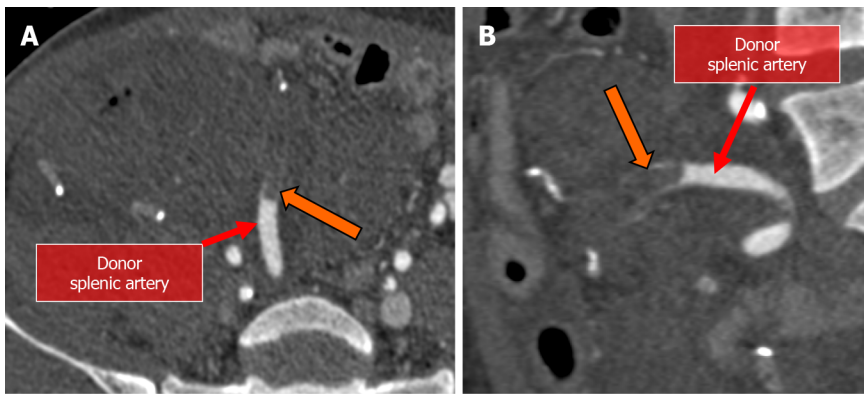
Graft pancreatitis is amongst the most frequent complications following pancreatic transplantation, the third most common cause for re-operation following bleeding and pancreas graft thrombosis, and a common histologic feature identified in up to 61% of rejected allografts[34,35]. Graft pancreatitis is distinguished in early if it occurs within 3 mo and later after 3 mo, while physiological acute graft pancreatitis occurs within the first 72 h after reperfusion of the transplanted organ secondarily to an acute inflammatory response related to ischemic reperfusion injury[36].

Common findings in CT include focal or diffuse enlargement of the pancreatic parenchyma, with edematous changes (usually is noted a decrease in HU value), indistinct pancreatic margins due to inflammation, and surrounding fat stranding (Figure 6). CT imaging allows to differentiate between edematous and necrotizing pancreatitis, to assess the presence of collections and to evaluate long-term evolutions including pseudocyst and walled-off necrosis[37].

Notably, graft pancreatitis and vascular thrombosis may occur simultaneously; indeed, pancreatitis can predispose to vascular thrombosis, and vascular thrombosis can also lead to graft inflammation, thus leading to some overlapping CT imaging features as shown on Figure 7.

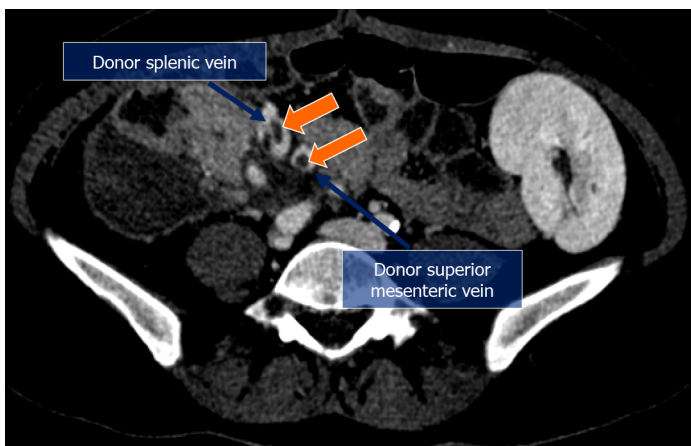
Peripancreatic collection and Infection

Infection may occur in the form of peripancreatic fluid collections (Figure 6), pseudocysts (Figure 8), leakage at the level



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Figure 4 A 46-year-old woman, few days after surgery had low prothrombin time; final diagnosis was graft arterial thrombosis. A: Contrast enhanced computed tomography in the angiographic phase demonstrated arterial thrombosis of the donor splenic artery. In this patient, the transplanted pancreas was explanted thereafter; B: Coronal plane of the same contrast enhanced computed tomography in the angiographic phase.



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Figure 5 A 35-year-old woman is admitted to the emergency department for abdominal pain; final diagnosis was venous thrombosis. Contrast enhanced computed tomography in the venous phase demonstrates venous thrombi (orange arrows) in the donor splenic vein and in the donor superior mesenteric vein.

of the enteric anastomosis (Figure 9), or infection of the abdominal wall surgical wound[21,38].

Fluid collections are the most common abnormality after pancreatic transplantation, may occur early or late after transplant, are clinically significant in about 16% of patients, and may lead to superinfection[38,39]. Intraabdominal collections also include seroma, hematoma, lymphocele, urinoma, or pseudocyst[11,38].

CT demonstrates an abnormal fluid collection of low attenuation with surrounding rim-enhancement and possible intralesional gas[38]. Soft tissue edema and fat stranding in the adjacent tissues may also be present. Percutaneous drainage is safe and effective for management of peripancreatic fluid collections after pancreas transplant[38].

Enteric or Pancreatic Leaks

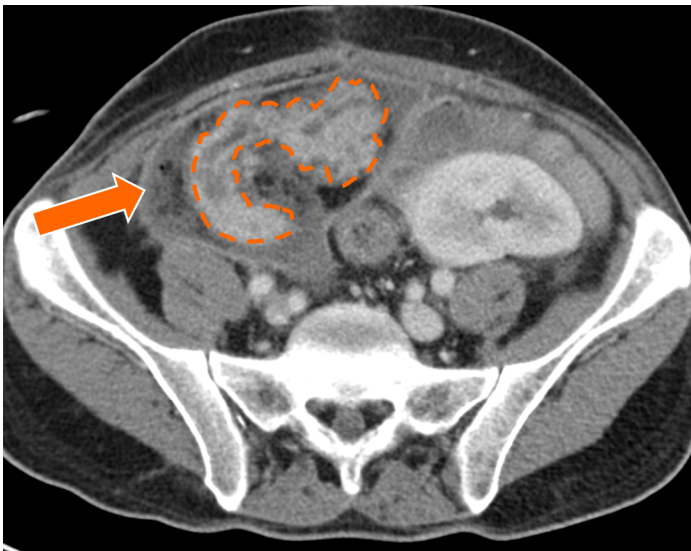
Duodenal leaks represent about 2.5%-2.9% of complications after pancreatic transplantation[40,41] and represent the cause of re-laparotomy in about 2.1% of cases[34]. Enteric leaks after pancreatic transplantation are usually characterized by extravasation of pancreatic juice from the duodenojejunostomy site leading to focal peritonitis and collections (Figure 9), and eventually abscess formation[26]. Duodenal leaks usually occur early in the postoperative course, but may also be seen late post-transplant and increase 6-mo graft loss risk with a hazard ratio of 13.9[40-42]. Pancreatic duct fistula after focal pancreatitis or ischemia leading to duct disruption, may also result in the development of a peripancreatic collection[42].

Bleeding

In the early postoperative period, the occurrence of bleeding is the most common cause of reoperation[29].

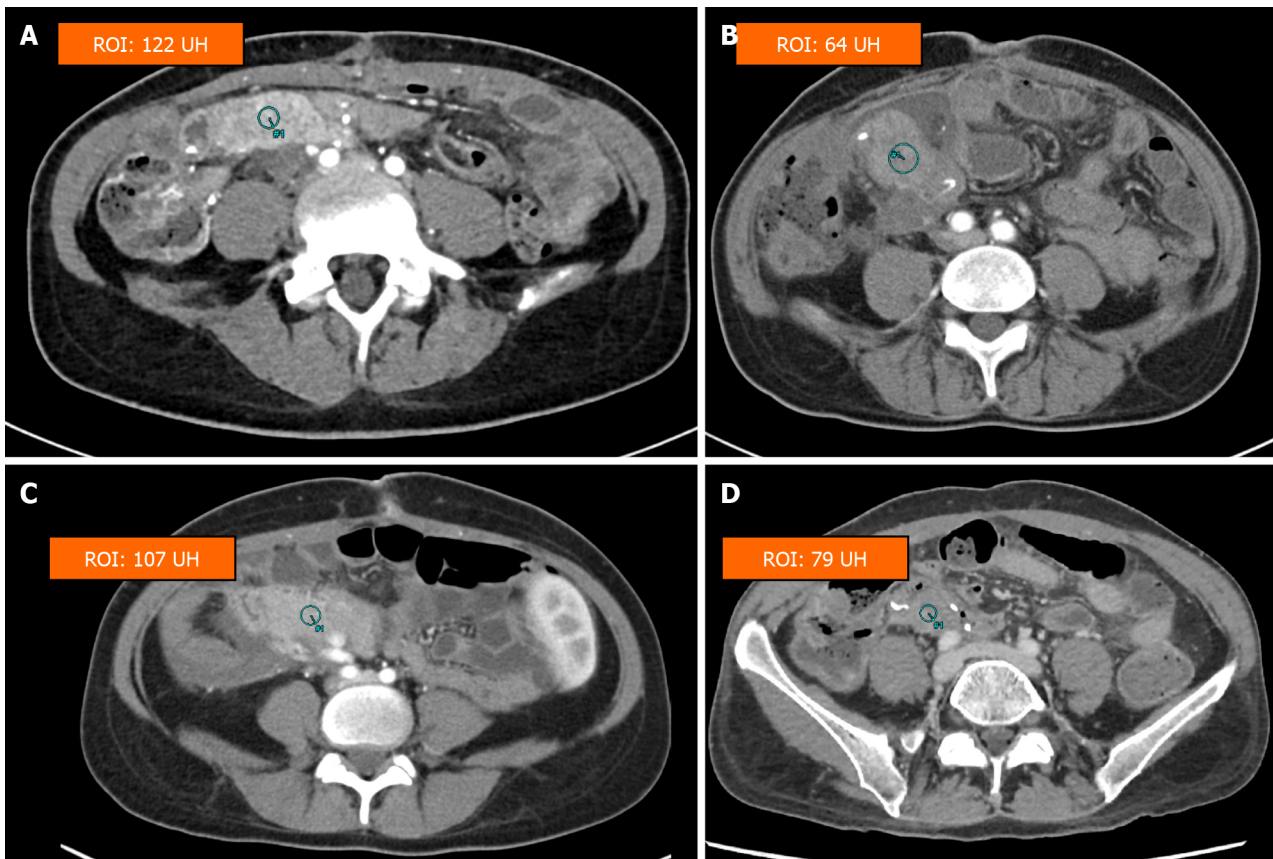
The source of bleeding in the early post-operative period may be:

Intra-abdominal: It is usually related to damage of the peripancreatic vessels or vascular anastomosis, enhanced by the antithrombotic prophylaxis or antithrombotic therapy in patients with vascular thrombosis.



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Figure 6 A 35-year-old man is admitted to the emergency department presenting hyperpyrexia and abdominal tenderness; final diagnosis was edematous pancreatitis with acute peripancreatic fluid collection. Contrast enhanced computed tomography in the axial plane shows inhomogeneous transplanted pancreas (dotted orange lines) with slightly enlarged Wirsung duct and acute peripancreatic fluid collection (arrow) with thick wall and fat stranding surrounding the transplanted pancreas. A diagnosis of edematous pancreatitis was made.



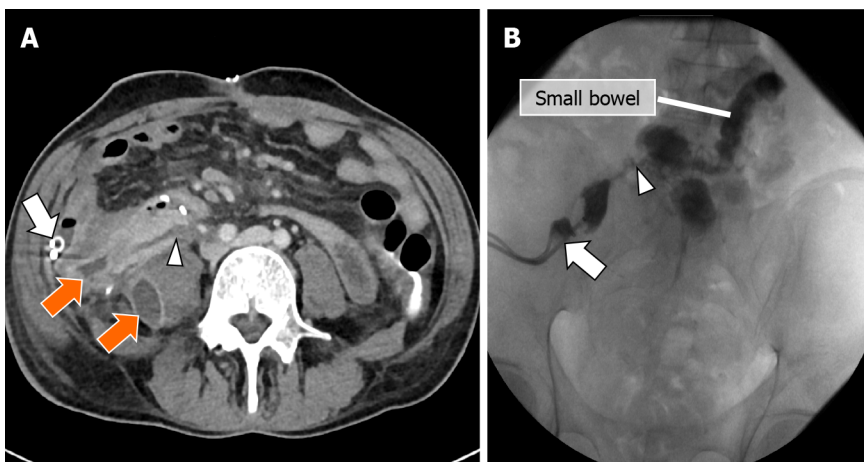
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Figure 7 Contrast enhanced computed tomography in four different patients after pancreatic transplantation. A region of interest is drawn in the pancreas in the four patients. A: Normal pancreatic parenchyma; B: Inflammatory pancreatitis; C: Decreased parenchymal enhancement from venous thrombosis; D: Decreased parenchymal enhancement from arterial thrombosis.



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Figure 8 A 35-year-old man after four weeks from edematous pancreatitis. Contrast enhanced computed tomography in the coronal plane shows an encapsulated fluid collection (arrow) of homogeneously low attenuation surrounded by a well-defined enhancing wall consistent with pancreatic pseudocyst.



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Figure 9 A 43-year-old man admitted to the emergency department for hyperpyrexia and abdominal tenderness; final diagnosis was enteric leakage. A: Contrast enhanced CT demonstrated the presence of an enteric leakage as a fistulous tract (arrowhead) from the small bowel at the level of the duodenojejunostomy, which resulted into fluid collections (orange arrows). Abdominal drainage (white arrow) was inserted and the analysis of the fluid was consistent with the diagnosis of enteric leakage; B: Fluoroscopic image demonstrate the presence of an enteric leakage as a fistulous tract (arrowhead) from the small bowel at the level of the duodenojejunostomy. Abdominal drained is also evident (white arrow).

Digestive: It comes from the digestive anastomosis or the staple line of the duodenal ends. Gastrointestinal bleeding after pancreas transplant usually occur at the duodenojejunostomy due to reduced blood flow to the graft or due to ulcers at the anastomosis. Digestive bleeding may resolve after conservative measures such as correction of coagulation abnormalities, heparin withdrawal and transfusion; surgical revision may be indicated if the bleeding does not resolve.

Precontrast CT may indicate the presence of an acute hematoma as a hyperattenuating (usually above 60 UH) collection on precontrast CT in case of intrabdominal bleeding or hyperattenuating content in the GI lumen in case of gastrointestinal bleeding. In case of active bleeding, contrast-enhanced CT acquired in the arterial and venous phases demonstrates pooling/extravasation of the contrast agent within the hematoma or within the bowel lumen and may allow to identify the culprit vessel in case of intrabdominal hemorrhage.

Bleeding due to other arterial complications (*e.g.* arterio-venous fistula, pseudoaneurysm, arterioenteric fistula, arterio-urinary fistula) have been reported but are infrequent, with occurrence of pseudoaneurysm being more common as a late complication[32,43]. Management can be endovascular or surgical and should be individualized[43].

Pseudoaneurysm may develop particularly at the level of anastomoses as a consequence of chemical damage due to leak of pancreatic enzymes[26]. On CT imaging, pseudoaneurysm appears as a saccular enhancing outpouching from the injured artery, with enhancement similar to other arteries, but does not increase in size on delayed phases and follows the



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Figure 10 A 42-year-old woman admitted in the hospital for elevation of pancreatic amylase 6 mo after transplant; final diagnosis was venous stenosis. Contrast enhanced computed tomography in the sagittal plane with Maximum Intensity Projection reconstruction demonstrates venous stenosis (arrowhead) at the anastomotic site. The pancreatic graft is enlarged with inhomogeneous enhancement which likely reflects graft dysfunction.

blood pool on all phases. Arterio-venous fistula is a very rare complication of pancreatic transplantation[32,43] which may result from the postoperative or post-biopsy laceration of both arterial and venous walls and may potentially lead to major bleeding or graft loss if untreated[43-45]. On CT, arterio-venous fistula will be demonstrated on arterial phase as enlarged Y-graft arteries with an early opacification of the donor draining vein.

Graft vascular stenosis

Vascular stenosis is relatively uncommon with an incidence of about 2.5% and more commonly occur at the anastomotic level[40]. Early detection of vascular stenosis is critical to avoid complications, including thrombosis, ischemia, and graft dysfunction[46]. The multiplanar reconstruction of the vascular tree provides a reliable method of visualizing the entire vascular anastomoses, detecting a focal decrease in caliber of the vessel (Figure 10).

CONCLUSION

In conclusion, pancreatic transplantation is a complex surgery with high morbidity often related to postoperative complications, which may occur during hospitalization, early in the first three months or in the late period. Cross-sectional imaging with CT plays a critical initial role in the diagnosis and management of postoperative complications in many transplanted patients who present to the emergency department for suspected transplant dysfunction. Therefore, radiologists should be aware of surgical techniques and normal imaging appearance of pancreatic transplantation and should be well-trained to recognize identify acute findings and provide key imaging information to optimize patient management.

FOOTNOTES

Author contributions: D'Alessandro C, made the literature search, wrote the first draft of the manuscript, and prepared most of the figures; Todisco M conceptualized the manuscript, helped with figures preparation and provided inputs; Di Bella C and Furian L wrote the first draft of the manuscript for the surgical paragraph, provided inputs and revised the draft of the manuscript; Crimi F provided inputs and revised the draft of the manuscript; Quaia E conceptualized the manuscript, provided inputs, and revised the draft of the manuscript; Vernuccio F conceptualized the manuscript, helped with the literature search, wrote the outline of the manuscript, prepared some of the figures and extensively revised the draft of the manuscript.

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