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Value of magnetic resonance imaging in evaluating the pancreatic allograft transplant complications

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Abstract

Purpose: To retrospectively investigate the value of magnetic resonance imaging (MRI) in detecting complications following pancreas transplant.

Materials and methods: Institutional review board approved this retrospective HIPAA-compliant study and waived informed patient consent. We identified all allograft pancreas transplant patients at our institution from 2001 to January 2014 who had all pertinent post-transplant imaging and clinical data available. Transplant type was documented. Patients were divided into two groups according to post-transplant period (group A; <12 months, group B; ≥ 12 months). We evaluated the parenchymal enhancement using contrast-enhanced MRI of the allograft and determined the mean percentage of parenchymal enhancement (MPPE) overall and in various abnormalities, the vessel patency, any peripancreatic fluid collection, and the ductal anatomy. We correlated these with clinical results using t test, χ^2, and Fisher's exact test; $p < 0.05$ was considered significant.

Results: 51 patients (34 male, mean age 43.7 years) were identified, 28 (55%) of whom had abnormal imaging findings; transplant rejection-related necrosis ($n = 7$), fluid collections ($n = 7$), vascular stenosis ($n = 4$), isolated venous thromboses ($n = 3$), acute pancreatitis ($n = 3$), pancreatic and peripancreatic abscesses ($n = 2$), pseudoaneurysm ($n = 1$), and small-bowel obstruction ($n = 1$). Pre vs. post-contrast pancreatic MPPE at 1 min was 120% in the normal allografts and 115% in the allografts with pancreatitis and without necrosis ($p > 0.05$). MPPE at 1 min was only 9% in the allografts rejections with necrosis/infarction. More complications were found in group A than group B ($p < 0.05$).

Conclusions: Contrast-enhanced MRI is useful for the non-invasive assessment of pancreas transplant complications.

Key words: Pancreas transplant—Complication—Magnetic resonance imaging

Pancreas allograft transplant has proven to be reliable to normalize blood sugar level and to improve quality of life in patients with Type 1 diabetes [1]. Types of pancreas transplant include isolated pancreas transplant, pancreas after kidney transplant (PKT) or simultaneous pancreas and kidney (SPK) transplant, and multi-visceral transplant. PKT or SPK transplant is increasingly used for treating end-stage renal disease secondary to insulin-dependent diabetes mellitus.

Despite significant advancements made in recipient and donor selection, surgical techniques, post-operative treatment, and pancreas transplants still have a higher rate of postsurgical complications as compared to other solid organ transplants [2]. Unfortunately, no reliable clinical or readily performed laboratory tests directly related to the function of the allograft pancreas have

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been established for the diagnosis of complications, other than routine pancreatic enzyme tests. To avoid the perceived risk of complications, few pancreatic biopsy procedures for allograft pancreas are performed.

It can be challenging to interpret the various complications of allograft pancreas, using ultrasonography (US) or computed tomography (CT) [3–5]. US can detect the change in blood flow but cannot assess vessel contour abnormality. US is unable to reliably identify other complications including rejection or pancreatitis as it is often unable to visualize the transplanted pancreas due to overlapping bowel gas. While CT is widely available, relatively inexpensive, and allows rapid image acquisition, yet, the risk of contrast-induced nephropathy has limited its use in repeated examinations beyond the immediate post-operative period.

Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) with and without intravenous (IV) contrast medium have become an invaluable imaging modality in cases of impaired pancreatic function or suspected post-operative complications such as acute pancreatitis, parenchymal necrosis, pancreatic ductal injuries, and vascular complications [3–8]. The purpose of our study is to review our experience in MRI in evaluating complications after allograft pancreas transplant.

Materials and methods

Patients

Institutional review board (IRB) approved this retrospective HIPAA-compliant study and waived informed patient consent. Pancreas grafts were procured using an en-bloc technique with aortic flush [5–7]. The donor iliac artery "Y" graft was anastomosed to the recipient common iliac artery (usually on the right side) or rarely to the aorta, and systemic venous drainage was established to the recipient right common iliac vein or the vena cava. The enteric drainage of the pancreas was created using an end-to-end circular stapler to anastomose the donor duodenum to the proximal small bowel of the recipient.

We reviewed clinical and radiologic databases at our institution from January 2001 to January 2014, and identified all patients who underwent allograft pancreas transplant. We then identified those patients who underwent abdominal MRI examination following transplant, and who had all pertinent imaging available on our radiology archive and clinical follow-up information. Four patients with severe artifacts on MRI (e.g., due to motion) were excluded. The reason for examination was noted, and confirmation that the indication for MRI was likely attributable to post-transplant disorders was made. We documented the reason for transplant and the type of transplant surgery performed.

Magnetic resonance imaging

All MRI exams were performed with a 1.5 Tesla magnet (Avanto; Siemens Medical Solutions, Malvern, PA) or 3.0 Tesla magnet (TIM Trio; Siemens Medical Solutions, Malvern, PA) using surface phased-array coil. After three-plane scout view acquisition, axial T1-weighted unenhanced fast low-angle shot (FLASH) gradient echo (GRE) sequence and coronal and axial half-Fourier acquisition single-shot turbo spin-echo (HASTE) with relaxation enhancement sequences were employed. All patients underwent IV contrast enhancement exams, 10 patients had MRA exams, and 14 patients had MRCP exams.

For MRCP, the pancreatic duct was imaged using a single-shot fast spin-echo pulse sequence, with a single 40-mm-thick coronal "slab" positioned over the pancreas. The matrix size was 256 × 256; the field of view (FOV) varied from patient to patient and was typically 22 × 22 cm. Fat saturation was used in the sequence. Acquisition time was approximately 1–2 s per scan and obtained during breath holding. A thin slice coronal T2-weighted sequence was also employed along with a respiratory synchronized three-dimensional turbo spin-echo sequence.

Magnetic resonance angiography (MRA) and contrast-enhanced MRI were performed using a T1-weighted fat-saturation GRE sequence volumetric interpolated breath-hold examination (VIBE). MRA data were reconstructed with maximum intensity projection (MIP) and multi-planner reformation (MPR). For IV contrast material, 0.1 mmol of gadobenate dimeglumine (Multihance; Bracco, Princeton, NJ) per kilogram of body weight was injected at 2 mL/s. In order to remove the high signal from overlying stomach and duodenum, the patient either fasted for 4–6 h before the examination was given 300 mL of ferumoxsil oral suspension as a negative contrast agent (Gastromark, Mallinckrodt Medical, Raleigh, NC), or given pineapple juice [4]. Two-phase imaging was obtained at approximately 1 and 5 min after injection of the contrast agent.

Image and related data analysis

All the images were retrospectively reviewed by two experienced abdominal radiologists with 12 and 14 years of experience. The allograft mean percentage of parenchymal enhancement (MPPE) was analyzed, MPPE = [contrast-enhanced mean glandular signal intensity (MGSI) − unenhanced MGSI)/(unenhanced MGSI)] × 100%. The MGSI for the pancreas allograft was derived on the unenhanced T1 imaging by averaging two regions of interest (ROIs) from a representative image section that encompassed the allograft. Focal areas of signal intensity abnormalities were excluded from sampling due to heterogeneous pancreatic enhancement. The same

ROIs were measured on the post-contrast-enhanced images. Patients were divided into two groups: less than 12 months and greater than or equal to 12 months since the time of transplant. The differences in morbidities due to complications between the two groups were compared. MPPE was compared between normal allografts and particular disease states.

Statistical analysis

For analyzing categorical frequency data, the χ^2 and Fisher's exact probability procedures were applied. For comparing continuous variables in two independent groups, the t test and Mann–Whitney test were used. A value of $p < 0.05$ was considered significant. Receiver operating characteristic curve analysis was performed, and the area under the curve was determined for the MPPE variables. Based on this analysis, a threshold was determined for the most accurate measurement.

Results

51 allograft pancreatic transplant patients (34 male, mean age 43.7 years; age range 20-61 years) were identified. Among those 51 patients, 32 (63%) underwent SPK transplant; 9 (18%) patients had an isolated pancreas transplant; 5 (10%) patients underwent a PKT; 4 (8%) patients had a multi-visceral transplant including the pancreas, liver, and small bowel; and 1 (2%) patient had a simultaneous pancreas and lung transplant. All patients were referred for MRI exams because of abnormal laboratory assay results such as elevated blood glucose, amylase and lipase, or clinical findings such as abdominal pain, fever, or increased venous pulsation.

There was no evidence of glandular parenchymal or peripancreatic allograft-related complications in 23 patients.

Pancreatic allografts removals were performed in 7 patients due to infarction/necrosis, severe hyperglycemia that required insulin administration, and severe unremitting abdominal pain. The MRI findings were correlated with the histopathologic evidence of severe necrosis or infarction of the 7 allograft specimens. Four patients with an allograft rejection without necrosis or infarction were treated with corticosteroids and were followed up for more than 1 year.

Table 1 displays all MPPE measurements. MPPE measurements at 1 min were 120% in the normal allografts and 9% in the allograft rejections with necrosis or infarction. The MPPE in normal allografts rose approximately 20% from 120% at 1 min to 139% at 5 min measured time intervals (Fig. 1). There was a sensitivity of 74% when the MPPE cutoff value was set at 100% to represent the normal value. The specificity was 100% when the MPPE cutoff value was set at 20% to determine allograft necrosis or infarction.

The pancreas allograft was hyperintensity on T2WI and showed no enhancement when it was in a state of complete necrosis or infarction. These removed allografts with necrosis or infarction had a mean MPPE well below that of normal patients, and remained at 9% and 14% at 1 and 5 min, respectively (Fig. 2).

In three patients with acute pancreatitis, the MPPE measurements in the allografts at 1 and 5 min were 115% and 149%, respectively (Fig. 3). There was no significant difference in this group compared with the normal allografts ($p > 0.05$). All the patients with acute pancreatitis showed similar imaging findings of non-allograft pancreatitis such as edema, peripancreatic fluid collection, enlargement and heterogeneity of the glandular parenchyma, and elevated amylase. The peripancreatic fluid collections were more common and extensive in the allograft pancreatitis patients than in the rejection allograft patients. All the acute pancreatitis patients recovered with treatment.

Other complications included 7 patients with fluid collections alone, 4 patients with vascular stenosis at the anastomotic sites, and 3 patients with non-allograft venous thrombosis. These included one patient with left

Table 1. Results of mean percentage of parenchymal enhancement (MPPE) at 1 and 5 min

MRI findings	*N*	MPPE 1 (1 min)	*p* value MPPE 1 (vs. normal)	MPPE 2 (5 min)	*p* value MPPE 2 (vs. normal)	*p* value MPPE 1 vs. 2
Normal	23	119.7 ± 45.5		139.2 ± 41.3		0.78
Fluid collection alone	7	126.7 ± 65.4	0.76	156.7 ± 59.5	0.41	0.56
Necrosis	7	9.1 ± 9.3	<0.05	13.7 ± 14.3	<0.05	0.31
Vascular stenosis	4	130.1 ± 49.1	0.68	136.1 ± 54.8	0.90	0.42
Pancreatitis	3	114.9 ± 20.9	0.86	139.1 ± 47.7	0.97	0.63
Venous thrombosis	3	100.4 ± 18.5	0.48	104.5 ± 19.0	0.23	0.95
Abscess	2	91.7 ± 102.9	0.45	98.4 ± 100.8	0.77	0.84
Pseudoaneurysm	1	22.3 ± 0.0	<0.05	26.6 ± 0.0	<0.05	0.72
Small-bowel obstruction	1	109.8 ± 0.0	0.83	108.9 ± 0.0	0.48	0.51
Total	51	101.5 ± 57.8		119.0 ± 60.8		0.13

N refers to number of patients, MPPE data are mean ± SD. Within MPPE 1 (1 min) group, there is significant difference between necrosis and normal group ($p = 0.00$), and there is significant difference between pseudoaneurysm and normal group ($p = 0.048$). Within MPPE 2 (5 min) group, there is significant difference between necrosis and normal group ($p = 0.00$), and there is significant difference between pseudoaneurysm and normal group ($p = 0.00$)

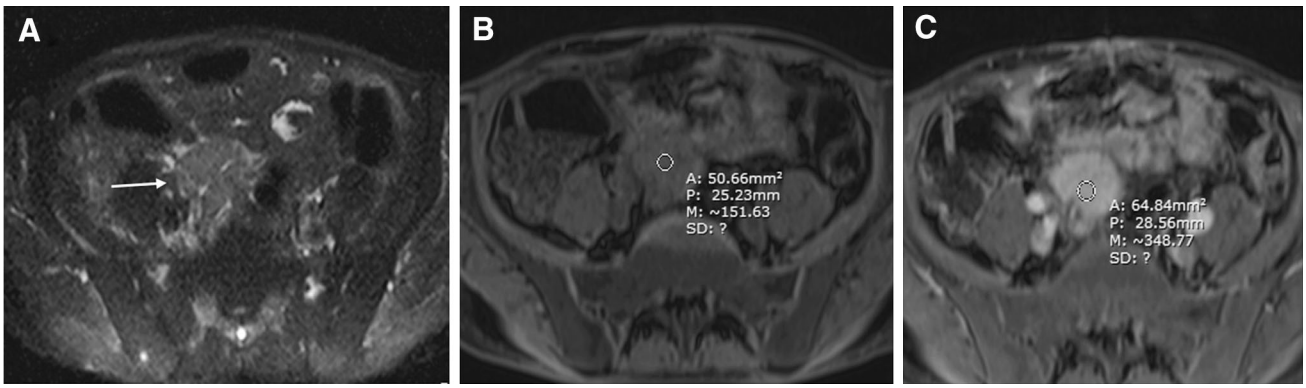

Fig. 1. 47-year-old man with normal transplanted pancreas. **A** Transverse T2-weighted image with fat saturation shows a normal transplanted pancreas with normal size and homogeneous signal intensity (*arrow*). **B**, **C** Transverse T1-weighted image with fat saturation (**B**) shows mean signal intensity (SI) of 151.6 at 1 min post-contrast enhancement (**C**) shows mean SI of 348.8 at 5 min, providing a mean percentage of parenchymal enhancement (MPPE) of 130.0%.

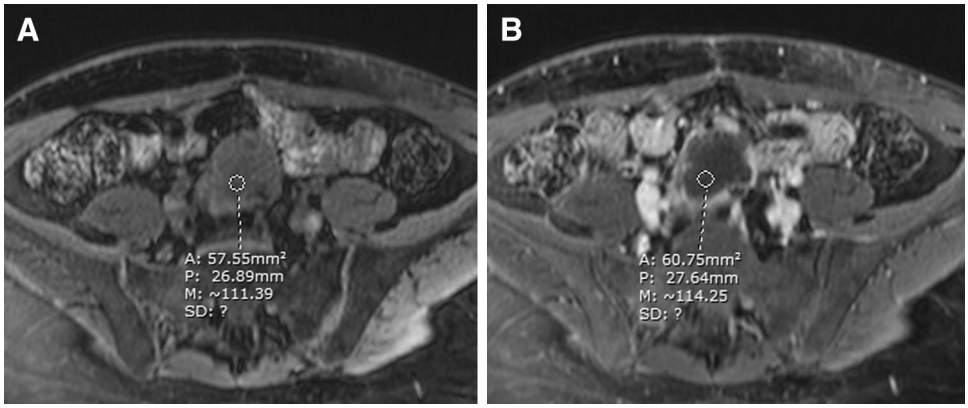

Fig. 2. 20-year-old woman with complete pancreatic necrosis of the transplanted pancreas. **A**, **B** Transverse T1-weighted image with fat saturation (**A**) shows mean signal intensity (SI) of 111.4 at 1 min post-contrast enhancement (**B**) shows mean SI of 114.3 at 5 min providing a mean percentage of parenchymal enhancement (MPPE) of 2.6%.

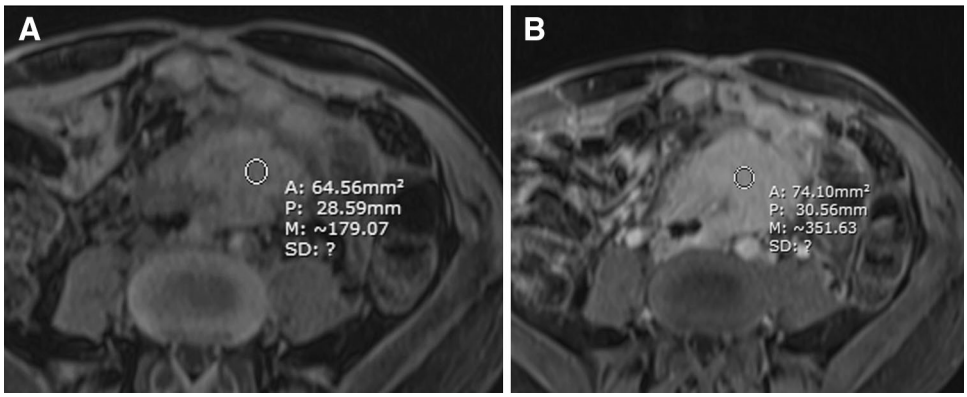

Fig. 3. 25-year-old woman with acute pancreatitis of the transplanted pancreas. **A**, **B** Transverse T1-weighted image with fat saturation (**A**) shows edema of pancreas with a mean signal intensity (SI) of 179.1 at 1 min post-contrast enhancement (**B**) shows mean SI of 351.6 at 5 min providing a mean percentage of parenchymal enhancement (MPPE) of 96.4%.

portal vein thrombosis, one patient with main portal vein thrombosis, and one patient with middle hepatic vein thrombosis. 2 patients developed pancreatic parenchymal and peripancreatic abscesses (Fig. 4). One patient had a pseudoaneurysm. One patient developed a partial small-bowel obstruction due to extensive adhesions. There were no abnormal pancreatic ductal abnormalities on secretin-stimulated MRCP exams.

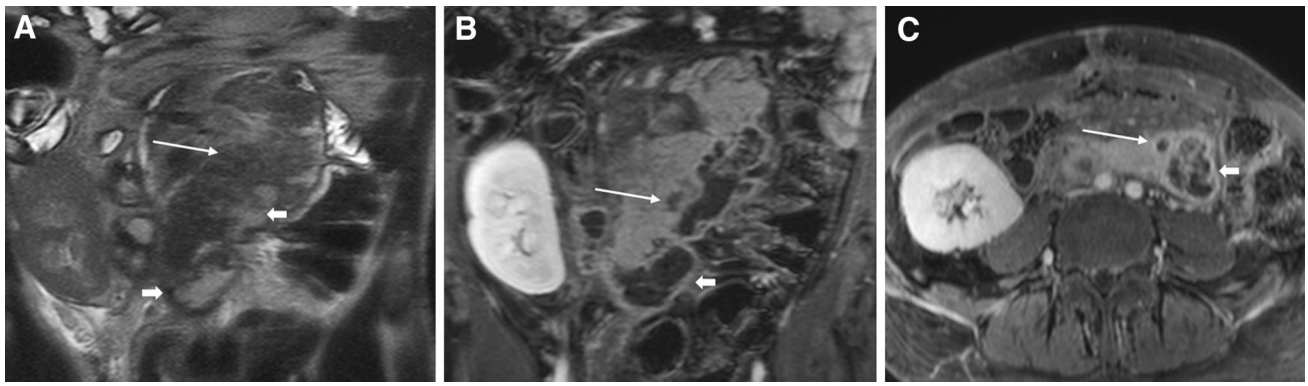

Fig. 4. 40-year-old man with abscess of transplanted pancreas and peripancreatic tissue. **A** Coronal T2-weighted image shows edema of pancreas (*long arrow*), heterogeneous hyperintensity of pancreas (*short arrow*). **B**, **C** Coronal (**B**) and transverse (**C**) T1-weighted image post-contrast enhancement shows rim enhancement of transplanted pancreatic parenchyma (*long arrow*) and peripancreatic tissue (*short arrow*).

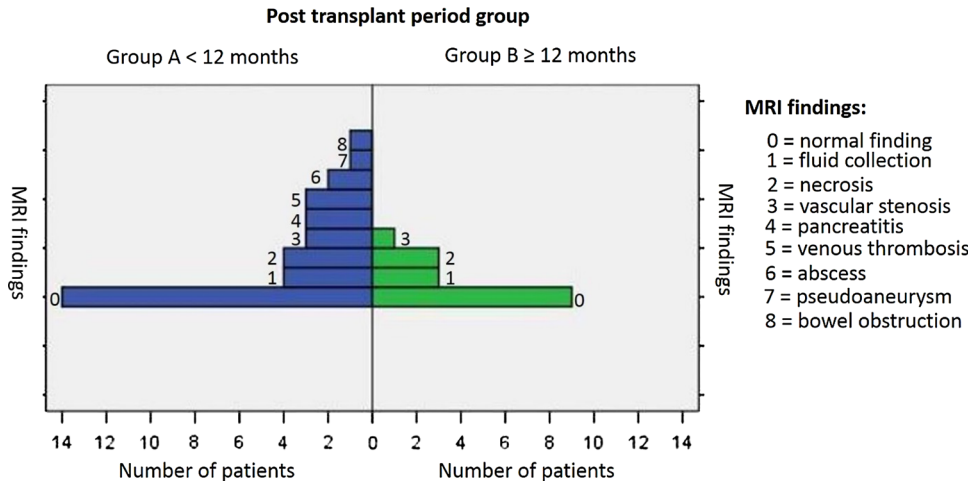

Fig. 5. Population pyramid graph of MRI findings in different group patients with post-pancreas transplant. *X* axis refers to number of patients, *Y* axis refers to MRI findings (0 = normal finding, 1 = fluid collection, 2 = necrosis, 3 = vascular stenosis, 4 = pancreatitis, 5 = venous thrombosis, 6 = abscess, 7 = pseudoaneurysm, 8 = bowel obstruction). There is significant difference in rate of complications before and after 12 months of pancreas transplant ($p < 0.05$).

When the patients were divided into two groups (<12-month group and ≥12-month group) according to the time of post-transplant (Fig. 5), the <12-month group was significantly more likely to have an abnormality on MRI ($p < 0.05$).

Discussion

Pancreas transplant is the most reliable method to achieve normoglycemia in a select group of Type 1 diabetics that qualify for this procedure. With improvements in surgical technique, preservation solutions, and immunosuppression, enteric drainage rather than bladder drainage in combination with systemic venous drainage has become the preferred implantation technique at most centers. In order to decrease tension on the enteric anastomosis, many centers have also begun to place the pancreas with the head facing upward rather than toward the pelvis, and have moved the vascular anastomoses cephalad as well using common iliac artery and the vena cava or the common iliac vein rather than the external iliac vessels. As a result of this modified placement, the pancreas is now situated deeper, higher, and more posteriorly in the abdomen rendering the allograft more difficult to visualize with US imaging. And it is difficult to detect complications using CT without IV contrast enhancement.

Therefore, it is important to develop a sensitive and non-invasive technique to detect complication in a pancreas allograft. Small cohort studies have shown that MRI has become valuable in detecting pancreatic allograft complications [7–13]. Currently, in our institution, MRI is used as a second-line imaging modality for post-

allograft patients who could not be adequately evaluated by CT or US.

MRI without IV contrast enhancement can reveal abnormalities of pancreatic allograft, but there is no specificity. Prior studies [14–18] demonstrated that the unenhanced MRI had variable results and limitations in evaluating dysfunctional pancreatic allograft. The allograft edema and heterogeneity that occurs in rejection can be identified by conventional sequence including T1- and T2-weighted imaging [10, 11, 13–19], parenchymal edema alone is not a specific finding of allograft rejection, and it is difficult to differentiate rejection from acute pancreatitis or ischemia using the finding of edema. Fernandez et al. [15] demonstrated that the percentage of post-contrast enhancement in normal allograft was greater than that in dysfunctional allograft. In their study, the mean percentage of enhancement at 1 min was 98% in 6 normal allografts as compared with 42% in 6 dysfunctional allografts. Krebs et al. [11] compared the results of MRI with histopathologic analysis in 25 patients and found that the percentage of enhancement (at 1 min) in the normal group was greater, 106%, compared with 50% enhancement in the dysfunctional group. In our study, the percentage of enhancement in the normal allografts was greater, 120%, compared with 9% in the necrotic allografts. These results are similar to those of Fernandez et al. [15] and Krebs et al. [11].

Allograft pancreatitis usually occurs secondary to impaired microcirculation. It may be suspected in the presence of elevated serum amylase and lipase levels. The diagnosis of allograft pancreatitis is suggested when changes isolated to the pancreas including peripancreatic fluid associated with an ill-defined pancreas and edema are shown [12]. A peripancreatic fluid collection, elevated amylase without elevated glucose, and imaging follow-up after pancreatitis is suspected may be important in differentiating acute pancreatitis from rejection.

Graft thrombosis either venous or arterial that leads to allograft necrosis or infarction is one of major causes of allograft loss. It can occur secondary to a vascular graft anastomotic abnormality or microvascular disease [11]. Another reason for thrombosis usually due to severe rejection with alloimmune arteritis and occlusion of small vessels. The relatively smaller microcirculatory blood flow of transplanted pancreas (1.3% of cardiac output) may account for the accordingly higher incidence of thrombosis involving the pancreatic graft [20].

It is important to detect total allograft thrombosis with necrosis/infarction, if it is identified, then allograft pancreatectomy is usually required to avoid severe systemic complications [21]. In our study, the earliest thrombosis identified specifically by MRI occurred at transplant post-op day 5 and the furthest post-transplant episode occurred at 20 months. The allograft with an MPPE of 9% had necrosis or infarction and were identified using contrast-enhanced MRI. In our study, 7 allografts were explanted secondary to allograft thrombosis that resulted in necrosis.

MRA was found to be a reliable imaging technique to identify vascular complications such as occlusion, stenosis, and infarction [22, 23]. In our study, 4 patients with stenosis of vascular anastomosis were detected.

Fluid collections are the most common complication after a pancreas transplant. The clinical presentation and imaging findings are similar to those of an enteric leak. MRI can also be helpful to identify fluid collection and distinguish it from a hematoma by detecting T1 hyperintensity. Infection may occur in 50% patients of pancreatic allografts [24, 25]. Pseudoaneurysm is associated with a risk of hemorrhage and a higher incidence of graft loss [26–30]. Pseudoaneurysms typically develop in the early post-operative period as either a technical complication or as a result of infection or abscess adjacent to the arterial anastomosis. In our study, one pseudoaneurysm resulted in bleeding presenting at transplant post-op day 5.

The most common intestinal complications following the pancreas transplant are small-bowel obstruction, anastomotic leak, and pseudomembranous or cytomegalovirus colitis. Small-bowel obstruction due to adhesion or internal herniation secondary to intraperitoneal placement of the allograft can also occur. These obstructions secondary to adhesions tend to occur in the anterior abdomen and are usually low grade [31].

This study had several limitations. In our institution, MRI examination is not the primary imaging modality for evaluating the complications of pancreas allograft. MRI is used only for the cases that could not be adequately evaluated using US or CT. In order to review MRI features of a pancreas allograft, we had to exclude abundant CT and US exams of the patients after pancreas transplants. Some patients had to be excluded due to severe MRI artifacts or the inability to administer contrast enhancement. Thus our patient population may not reflect the distribution of complications of pancreas transplants in our institution.

In conclusion, this study demonstrates that MRI evaluation is a valuable non-invasive, accurate imaging modality to differentiate, and detect post-transplant complications.

Disclosures This project was performed at Department of Radiology and Imaging Sciences, Indiana University School of Medicine.

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