



Comparison of color Doppler ultrasonography and computed tomography angiography (CTA) and computed tomography venography (CTV) in the diagnosis of arteriovenous thrombosis after simultaneous pancreas-kidney transplantation: a retrospective diagnostic accuracy study

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Background: Simultaneous pancreas-kidney transplantation is an important treatment approach for diabetic renal insufficiency, but pancreatic arteriovenous thrombosis is among the early serious surgical complications that can lead to graft loss and even be fatal. Ultrasound is considered to be a safe and non-invasive approach, but it is often affected by intestinal gas interference and operator proficiency, partial thromboses may be easily missed. Computed tomography angiography (CTA) and computed tomography venography (CTV) are highly accurate but radiative, requiring the use of contrast agents.

Methods: A total of 194 patients with end-stage diabetic nephropathy who underwent simultaneous pancreas-kidney transplantation from September 2016 to May 2021 were selected, among which 32 patients with highly suspected arteriovenous thrombosis were enrolled as the research subjects. All patients were examined by color Doppler ultrasonography, CTA and CTV. CTA and CTV are the gold standard for diagnostic imaging. The diagnostic value of color Doppler ultrasound, CTA and CTV in the diagnosis of pancreatic arteriovenous thrombosis was compared. and Kappa coefficient was used for consistency test.

Results: Among the 32 patients with high clinical suspicion of transplanted pancreatic arteriovenous thrombosis after simultaneous pancreas-kidney transplantation, 9 patients were diagnosed by CTA/CTV and 10 patients were diagnosed by color Doppler ultrasonography, of which 2 cases were false positive and 1 case false negative. After transplantation, the normal diameter of the donor splenic vein was 3.96 ± 0.16 mm. The difference in the diameter of the donor splenic vein between those with and without donor splenic vein thrombosis was statistically significant ($P < 0.05$). The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of color Doppler ultrasound in the diagnosis of arteriovenous thrombosis were 88.9%, 91.3%, 90.6%, 80%, and 95.5%, respectively. There was no significant difference between color Doppler ultrasound diagnosis of arteriovenous thrombosis and CTA and CTV results (McNemar test $P = 1$). The diagnosis of arteriovenous thrombosis by color Doppler ultrasonography was consistent with that of CTA and CTV (Kappa coefficient = 0.776).

Conclusions: Color Doppler ultrasonography has the advantages of safety and radiation-free, and can be used as the first choice for diagnosis of pancreatic arteriovenous thrombosis after simultaneous pancreas-kidney transplantation.

Keywords: Color Doppler ultrasonography; simultaneous pancreas-kidney transplantation; transplanted pancreas; thrombosis

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Introduction

Simultaneous pancreas-kidney transplantation is an important treatment approach for diabetic renal insufficiency. It is one of the most common procedures at many organ transplantation centers as well as one with the longest tradition (1). However, complications are still relatively inevitable. Transplanted pancreatic arteriovenous thrombosis is among the early serious surgical complications that can lead to graft loss and even be fatal for the recipient (2). Timely prevention and detection that could guide follow-up treatment are of great clinical importance.

At present, computed tomography angiography (CTA) and computed tomography venography (CTV) are still the gold standard for the diagnosis of graft arteriovenous thrombosis after simultaneous pancreas–kidney transplantation, but they are radiative and require the use of contrast agents, which are not suitable for patients with renal insufficiency (3) and iodine allergy, and cannot be performed bedside in early postoperative patients in intensive care.

Ultrasound is considered a safe, non-invasive, non-radiative, simple, quick, repeatable, and removable approach. It is also the preferred initial imaging modality for evaluating the transplanted pancreas, whereby grayscale assesses the parenchyma and fluid collections, and color Doppler ultrasonography delineates the vascular anatomy and patency and assesses graft perfusion and viability (4,5). However, ultrasound is often affected by factors such as intestinal gas interference and operator proficiency, partial thromboses may be easily missed (4). The purpose of this study was to compare the clinical value of color Doppler ultrasound with CTA and CTV in the diagnosis of transplanted pancreatic arteriovenous thrombosis after simultaneous pancreas-kidney transplantation. We present the following article in accordance with the STARD reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-3134/rc>).

Methods

Study design

Between September 2016 to May 2021, a total of 194 patients with endstage diabetic nephropathy, who had received combined pancreas–kidney transplantation for the first time and had normal preoperative coagulation function were selected for a retrospective study. Among them, 32 patients with high suspected arteriovenous thrombosis were enrolled as the research subjects. Inclusion criteria were: (I) patients with diabetes mellitus complicated with endstage renal disease; (II) undergoing first pancreas–kidney transplantation; and (III) normal preoperative coagulation function. Highly suspicious clinical criteria included: high-risk factors for thrombosis such as obesity, intraoperative arteriovenous intima injury caused by vascular compression and folding, postoperative anticoagulation, observation of blood glucose, amylase, urinary amylase, and other laboratory indicators, and existing abnormalities. Exclusion criteria were: (I) pulmonary or urinary tract infection, hematuria, cytomegalovirus and/or BK virus infection; (II) renal graft rejection; and (III) poor compliance during treatment and uncooperative with treatment.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of the Second Affiliated Hospital of Guangzhou Medical University (No. 2019-268). Informed consent was taken from all the patients.

Equipment and methods

VIVID E9 (GE), LOGIQ E9 (GE) and S2000 (SIEMENS) color ultrasound diagnostic devices were selected. An abdominal protruding array probe was used with a probe frequency of 3.5–5 MHz. Color Doppler examination and CTA/CTV examination were performed routinely in all 194 patients after simultaneous pancreas-kidney transplantation. Color Doppler ultrasonography was

Table 1 Baseline recipient characteristics

Characteristics	Data
Age (years)	49.79±8.53
Sex	
Male	27 (84.4)
Female	5 (15.6)
BMI (kg/m ²)	25.45±3.09
Dialysis modality	
None	2 (6.2)
Peritoneal	1 (3.1)
Hemodialysis	29 (90.6)
Induction	
ATG	3 (9.3)
Thymoglobulin + basiliximab	27 (84.3)
Multiple	2 (6.2)
Calcineurin inhibitor	
Cyclosporine A	3 (9.3)
Tacrolimus	29 (90.7)

Data are presented as n (%) or mean ± SD. BMI, body mass index; ATG, anti-thymocyte globulin.

performed routinely in accordance with the Technical Specifications for Ultrasonic Image Diagnosis of Organ Transplantation in China (2019 edition) (6) to observe the size, shape, internal echo, pipeline structure and blood flow filling of the graft. For the 32 patients with suspected transplanted pancreatic arteriovenous thrombosis, urgent ultrasound examination and CTA/CTV were required, focusing on scanning to reconstruct the intracavity structure and blood flow filling of the arteriovenous vessels, and comprehensive evaluation of the graft. Color Doppler ultrasonography was performed by ultrasonographers with more than 10 years' experience and systematic training who were unaware of all patient information, including the final histopathological diagnosis.

Baseline data, such as age, sex, and body mass index (BMI), were collected, and the inner diameter of the donor splenic vein, the location, size, echo, and blood flow of the thrombus were measured.

Diagnostic criteria and comparative analysis

Siemens 64-slice spiral CT was used for CTA and CTV, and iodoform served as the contrast agent; a dose of 1.2 mL/kg was injected via the precubitus vein. The diagnostic results of color Doppler ultrasound and CTA/CTV were compared and analyzed to determine the accuracy of diagnosis of graft pancreatic arteriovenous thrombosis.

Statistical analysis

IBM SPSS25.0 software was used for the statistical analyses. Measurement data are expressed as mean ± standard deviation, and a *t*-test was performed for comparison between groups. Count data are expressed as N (%); Sensitivity, specificity, accuracy, positive predictive value, negative predictive value were used to describe the diagnostic accuracy parameters. Kappa coefficient was used to evaluate the consistency between color Doppler ultrasound and CTA/CTV diagnosis *P*<0.05 was considered statistically significant.

Results

Baseline characteristics

This study included a total of 194 patients who underwent pancreatectomy and kidney transplantation, among whom were 32 cases of highly suspected transplanted pancreatic arteriovenous thrombosis, including 27 males and 5 females, with an average age of 49.79±8.53 years. Patients' age, sex, BMI, dialysis mode, immune induction regimen, and basic immunosuppression regimen are shown in *Table 1*.

CTA and CTV confirmation of arteriovenous thrombosis of grafts and clinical outcomes

CTA and CTV confirmed that 9 patients had developed transplanted pancreatic arteriovenous thrombosis, reaching an incidence of 4.6%. There was no arteriovenous thrombosis of transplanted kidney among 194 patients with pancreas-kidney combined transplantation. Among the 9 cases of graft pancreatic arteriovenous thrombosis, 8 were diagnosed by color Doppler ultrasound, comprising 6 cases of donor splenic vein thrombosis (*Figure 1*), 1 case of donor

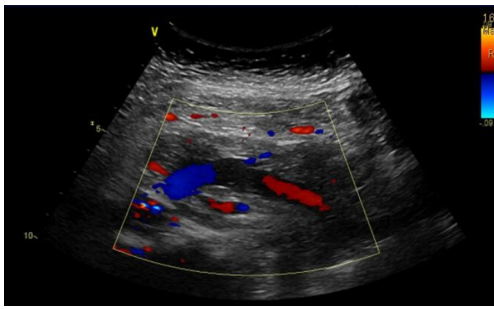


Figure 1 Donor splenic vein thrombosis seen as a slightly hypoechoic mass in the lumen, CDFI shows a filling defect. CDFI, Color Doppler Flow Imaging.

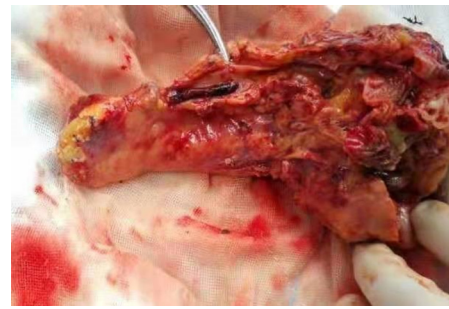


Figure 3 Donor splenic artery thrombus of the pancreatotomy graft.

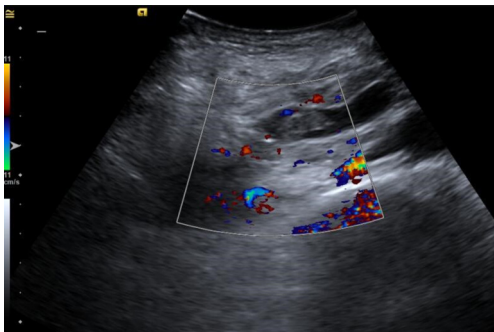


Figure 2 Donor splenic artery thrombosis seen as a slightly hyperechoic mass in the lumen, CDFI shows a filling defect. CDFI, Color Doppler Flow Imaging.

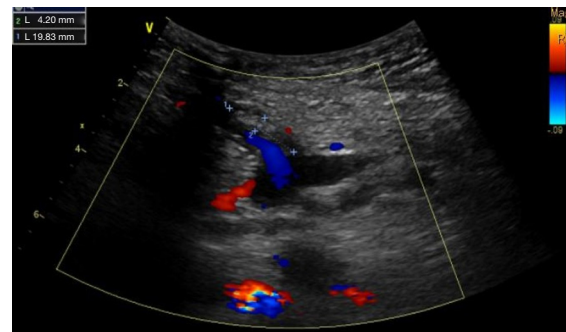


Figure 4 Donor superior mesenteric vein thrombosis seen as isoechoic masses in the lumen, CDFI shows a filling defect. CDFI, Color Doppler Flow Imaging.

splenic artery thrombosis (*Figures 2,3*), and 1 case of donor pancreatic arteriovenous thrombosis.

The following ultrasonographic characteristics were found among the 6 cases of donor splenic vein thrombosis: abnormal echo mass in the lumen of the donor splenic vein (isoechoic in 4 cases, hypoechoic in 2 cases). Color Doppler ultrasound showed a filling defect in the abnormal mass in 5 cases (*Figure 1*) but no obvious color blood flow signal in the lumen in 1 case. In the case of donor splenic artery thrombosis, the ultrasonographic features were an isopolytic mass in the lumen of the donor splenic artery, and a filling defect in the blood flow at the mass on color Doppler ultrasound showed (*Figure 2*). Also, the blood flow velocity of the donor splenic artery was significantly slowed. In the 1 case of pancreatic arteriovenous thrombosis, the ultrasonographic characteristics were a lack of an obvious blood flow signal in the transplanted pancreas, no blood flow in the donor pancreatic artery, and no obvious color blood flow signal in the lumen of the donor portal

vein and the donor splenic vein. During the surgical exploration of the transplanted pancreas, it was observed that the transplanted pancreas was black, the pulse of the reconstructed blood vessel could not be touched and the donor splenic artery thrombosis could be seen after vascular incision (*Figure 3*). The results of the ultrasonic examination in the 8 cases were consistent with the results of CTA/CTV. In the case of transplanted pancreatic arteriovenous thrombosis, ultrasound examination only showed superior mesenteric vein thrombosis (*Figure 4*), whereas CTA/CTV results showed the superior mesenteric vein thrombosis as well as the superior mesenteric artery thrombosis.

In addition to the 8 cases of transplanted pancreatic arteriovenous thrombosis indicated by color Doppler ultrasound, there were 2 cases of widened donor splenic vein on grayscale ultrasound, while no obvious color blood flow signal was found in the lumen on color Doppler ultrasound (*Figure 5*). Also, the possibility of thrombosis could not be ruled out by ultrasound. CTA/CTV results

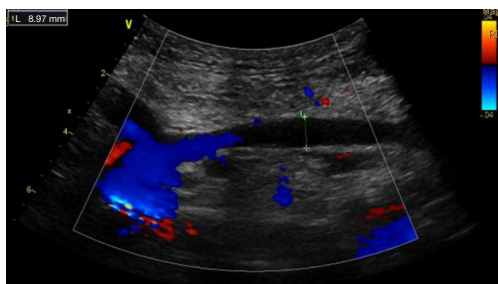


Figure 5 The inner diameter of the donor splenic vein is widened, there is low echo in the lumen. CDFI shows no blood flow signal in the lumen. CDFI, Color Doppler Flow Imaging.

Table 2 Comparison of gender, age, and donor splenic vein diameter in patients with and without donor splenic vein thrombosis

Characteristics	Donor splenic vein thrombosis	
	With (n=6)	Without (n=23)
Male/female	4/2	20/3
Age (years), mean \pm SD	56.16 \pm 3.14	50.50 \pm 1.19
Donor splenic vein diameter (mm), mean \pm SD	11.71 \pm 0.43	3.96 \pm 0.16

Table 3 Comparison of diagnostic results of color Doppler ultrasound and CTA/CTV

Method	Results of diagnosis	CTA/CTV		A combined
		Positive (n=9)	Negative (n=23)	
Color Doppler ultrasound	Positive	8	2	10
	Negative	1	21	22

CTA/CTV, computed tomography angiography/computed tomography venography.

showed no thrombosis in the donor splenic vein.

Comparison of donor splenic vein diameter between patients with and without donor splenic vein thrombosis

Among 194 patients with pancreatic-kidney combined transplantation, the inner diameter of the donor splenic vein was 3.96 (2.2, 5.9) mm in patients without donor splenic vein thrombosis and 11.7 (10.0, 14.3) mm in patients with donor splenic vein thrombosis. The difference in donor splenic vein diameter between those with and without donor splenic

vein thrombosis was statistically significant ($P < 0.05$, Table 2), although there was no significant difference in age ($P > 0.05$).

Comparison of color Doppler ultrasound and CTA/CTV in the diagnosis of transplanted pancreatic arteriovenous thrombosis

Following the diagnosis of graft pancreatic arteriovenous thrombosis by color Doppler ultrasound, 2 cases were false positive, and 1 case was false negative. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of color Doppler ultrasound in the diagnosis of transplanted pancreatic arteriovenous thrombosis were 88.9%, 98.9%, 98.9%, 80%, and 99.5%, respectively. There was no significant difference between the color Doppler ultrasound diagnosis of pancreatic arteriovenous thrombosis and CTA and CTV results (McNemar test $P = 1$). The diagnosis of pancreatic arteriovenous thrombosis by color Doppler ultrasonography was consistent with that by CTA and CTV (Kappa coefficient = 0.776) (Table 3).

Discussion

Pancreas-kidney combined transplantation is the operation with the highest incidence of surgical complications among all solid organ transplants. The transplanted pancreas is a hypoperfused organ, and thrombosis is a common postoperative surgical complication and the major surgical complication causing graft loss (7). Therefore, timely and accurate diagnosis before graft failure caused by pancreatic arteriovenous thrombosis and effective treatment that could increase graft survival is of great importance (8). A previous study has reported that the incidence of pancreatic arteriovenous thrombosis after transplantation is 6–17% (9). In this study, the incidence of pancreatic arteriovenous thrombosis after transplantation was 4.6% (9/194), which is lower than previously reported (9). Also, no thrombus occurred in the transplanted kidney. These results are closely related to our strict evaluation process and selection criteria for donors and recipients (10), emphasis on the core procedure of pancreas repair (11), and continuous use of low-molecular-weight heparin for anticoagulation after surgery.

In this study, among the 9 cases of transplanted pancreatic arteriovenous thrombosis, 6 were venous thrombosis, accounting for about 2/3. All cases occurred in the donor splenic vein, and none was missed by color Doppler ultrasound. Splenic vein thrombosis may easily occur because of the high coagulation state common in

simultaneous pancreas-kidney transplantation recipients due to splenic veins lacking spleen blood backflow (12). Previous studies have shown that vein thrombosis is the second most common cause of graft failure (8,13,14). Therefore, if patients are highly suspected of clinical graft thrombosis, it is first necessary to investigate thrombosis in the donor splenic vein. In this study, the 6 cases of donor splenic vein thrombosis were followed up and rechecked during the treatment process. Finally, all thrombi disappeared, direct imaging providing a basis for clinical guidance of thrombolytic therapy.

In the present study, color Doppler ultrasonography diagnosed 1 case of pancreatic donor splenic artery thrombosis and 1 case of pancreatic arteriovenous thrombosis. The ultrasonographic characteristics of transplanted pancreatic arteriovenous thrombosis included no obvious color blood flow signal in the pancreas, no blood flow signal in the donor pancreatic artery, and no obvious color blood flow signal in the lumen of the donor portal vein and the donor splenic vein, suggesting a possibility of pancreatic infarction, which was confirmed at surgery. The sonographic features were the same as those reported in the previous literature (8). The reasons for the formation of such ultrasonographic features are as follows: extensive arteriovenous thrombosis of pancreas transplantation leads to ischemia and infarction of the transplanted pancreas, and there is no blood perfusion in the transplanted pancreas, so the color Doppler ultrasound shows that there is no color blood flow signal in the gland of the graft.

In this study, color Doppler ultrasound diagnosis of pancreatic arteriovenous thrombosis was false positive in 2 cases and false negative in 1 case. In the false-positive cases the inner diameter of the donor splenic vein was widened, so sound penetration in the lumen was poor, and a blood flow signal in the lumen was not shown. Possible causes of misdiagnosis include the following: the transplanted pancreatic longitudinal is on the right side of the lower abdomen, so it will be affected by early postoperative (within 1 week) intestinal gas interference as well as the surgical scar and drainage tube occlusion, and the direction of the donor splenic vein is often perpendicular to the direction of the ultrasound beam, which makes it difficult to distinguish normal anechoic venous blood from a hypoechoic thrombosis in the lumen. The color blood flow signal display is not ideal, leading to misdiagnosis. The final diagnosis of the false-negative case was donor superior mesenteric vein thrombosis. The superior mesenteric artery is small, located in the rear of the head of the pancreas, and easily obscured by bowel gas, so its shape cannot be

detected by the color Doppler ultrasound (15).

Among the positive cases, 1 patient diagnosed by color Doppler ultrasonography with pancreatic arteriovenous thrombosis presented with no blood flow in the artery, and it could not be determined whether this was caused by embolism or by serious intestinal gas interference.

Conclusions

To sum up, this study showed that the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of color Doppler ultrasound in diagnosing transplanted pancreatic arteriovenous thrombosis after simultaneous pancreas-kidney transplantation is high. This imaging tool can be used to observe the blood flow in the parenchyma of the graft and can determine the location, size, and degree of embolization of transplanted pancreatic thrombosis. Our data proved that the results of color Doppler ultrasound did not significantly differ with CTA and CTV diagnosis (McNemar test $P=1$). However, color Doppler ultrasound has limitations in observing the reconstructed artery of the transplanted pancreas, which is highly susceptible to being obscured by intestinal gas (16), postoperative scar and drainage tube. Thus a combination of measurement of coagulation factors and urinary amylase and other laboratory tests, CTA and CTV, or contrast-enhanced ultrasound is highly recommended to confirm the diagnosis.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-3134/coif>).

The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of the Second Affiliated Hospital of Guangzhou Medical University (No. 2019-268). Informed consent was taken from all the patients.

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