ORIGINAL PAPER

e-ISSN 2329-0358 © Ann Transplant, 2019; 24: 199-207 DOI: 10.12659/AOT.912005



Received: 2018.07.08

Endovascular Interventions in Vascular Accepted: 2018.11.19 **Complications After Simultaneous Pancreas** Published: 2019.04.12 and Kidney Transplantations: A Single-Center **Experience** ABCDEF 1,2 Agnieszka Surowiecka-Pastewka Authors' Contribution: 1 Department of Gastroenterological Surgery and Transplantation, Medical Centre Study Design A of Postraguade Medicine, Warsaw, Poland ADE 1 Marta Matejak-Górska Data Collection B 2 Department of Surgical Research and Transplantology, Mossakowski Medical ABCDF 3,4 Michał Fraczek Statistical Analysis C Research Center of the Polish Academy of Sciences, Warsaw, Poland E 3,4 Katarzyna Sklinda Data Interpretation D 3 Diagnostic Radiology Department, Central Clinical Hospital of the Ministry of the Manuscript Preparation E Interior in Warsaw, Warsaw, Poland DE 3.4.5 Jerzy Walecki Literature Search F 4 Centre of Postgraduate Medical Education, Warsaw, Poland DEG 1,2 Marek Durlik Funds Collection G 5 The Committee on Medical Physics, Radiobiology, and X-Ray Diagnosis of the Polish Academy of Sciences, Warsaw, Poland **Corresponding Author:** Agnieszka Surowiecka-Pastewka, e-mail: agnieszkasurowiecka@op.pl Source of support: Departmental sources Background: Vascular failures are serious complications in pancreas transplantation. Open surgery is a reliable and quick intervention method, but it carries a risk of infection and bleeding. Endovascular procedures are rare among patients after a SPK, but are becoming more frequently used. One of the main risks of the endovascular approach is that the renal function impairment caused by contrast agent. Material/Methods: We performed a retrospective analysis of 200 transplanted pancreases at our center over the last 14 years. The analyses included those patients after pancreas transplantation who required the most challenging vascular interventions and ones that were non-standard for the procedure. Severe vascular conditions requiring endovascular intervention were observed in 3% of SPKs. In one retrans-**Results:** planted patient, there was an acute ischemia of the lower extremity due to the narrowing of the common iliac artery following a previous transplantectomy, above the new pancreas graft anastomoses. In another patient, local inflammation led to the disruption of the external iliac artery on the level of transplantectomy, caused severe bleeding, and we had to implement a stent-graft to reconstruct the iliac artery wall. A third patient had a pseudoaneurysm demanding further treatment with a stent-graft implemented into the femoral artery due to a pseudoaneurysm of the right external iliac artery. **Conclusions:** Intravenous interventions in patients with a transplanted or retransplanted pancreas are safe and feasible. It is a technically demanding procedure, but the risk of kidney graft function deterioration, as well as of bleeding due to the high dose of heparin used, is lower than with open vascular surgery. **MeSH Keywords:** Endovascular Procedures • Intraoperative Complications • Pancreas Transplantation Abbreviations: AEF – arteriometric fistulas; AVF – arteriovenous fistulas; CID – carbostent and implantable devices; CT - computed tomography; IDDM - insulin-dependent diabetes mellitus; PSA - pseudoaneurysm; PTA – pancreas transplantation alone; PVGT – pancreas venous graft thrombosis; RI – resistive index; **SPK** – simultaneous pancreas and kidney transplantation; **US** – ultrasonography Full-text PDF: https://www.annalsoftransplantation.com/abstract/index/idArt/912005 1 5 2 20 2 2855



Background

Pancreas transplantation is a standardized method that is safe and feasible. During simultaneous pancreas and kidney transplantation (SPK), we usually perform 7 vascular anastomoses. Vascular complications after SPK or pancreas alone (PTA) are severe conditions that can lead to early graft loss or even to the death of the recipient [1]. Vascular complications can be divided into venous and arterial. Early arterial complications potentially provoke acute bleeding or graft ischemia, and in most cases, they result from the surgical technique used [2]. Arterial failures are rare, and appear as arterial stenosis, arterial thrombosis, pseudoaneurysm (PSA), arteriovenous fistulas (AVF), or arterioenteric fistulas (AEF) involving the Y-graft or the recipient's arteries [1,3]. The incidence of PSA after pancreas transplantation is higher than after kidney transplantation [4,5]. Pseudoaneurysms of Y-grafts or the iliac arteries distal to the pancreatic arterial anastomoses can develop on a mycotic background, and have a high mortality rate [4]. There is a report of a rupture of the splenic artery of the pancreas (PSA) 6 years following an SPK procedure [6].

PSAs can be related to arterial anastomosis or may be non-anastomotic. Lesions of anastomoses often result from infections of mycotic or bacterial origin, whereas non-anastomotic ones are primarily caused by an infection or by fine-needle biopsy [7]. Endoscopic biopsies might be an alternative with a lower vascular complication rate. Other early surgical complications, like intestinal/duodenal leakage or intraabdominal infections, are other risk factors for vascular complications [2]. The site of the anastomoses and arterial flow need to be thoroughly evaluated with the use of Doppler ultrasonography. If any abnormal collection is revealed, a CT scan or angiography should be performed [7].

Vascular thrombosis, with or without severe pancreatitis, is the main reason for early graftectomies [8]. Moreover, AEF with severe bleeding is an indication to remove the pancreas graft. Late transplantectomy is often a life-saving procedure in the case of PSAs or AEF [8].

The literature concerning vascular complications after SPK is diverse, but in most cases, it consists of descriptions of single-center experiences, and presents various feasible methods, including open surgery and endovascular stenting and coiling, as well as hybrid methods. A review by Yadav et al. demonstrates how the surgical approach to serious vascular complication has changed over the last 3 decades [2]. In the 1990s, the criterion standard was to open the abdomen, whereas endovascular interventions are currently the first-choice method [2]. Open surgery is often combined with graftectomy [2]. Rupture of graft vessels, due to PSA or AVF, leads to massive bleeding, and the survival of the recipient depends on the specific diagnosis and definitive treatment. Quick and reliable intervention ensures blood supply to the graft and extremities, and also protects the graft from thrombosis. However, every intervention should be individualized, adjusted to both the patient's condition and technical possibilities. The endovascular approach is less invasive than open surgery, with a lower risk of blood loss and infection, but requires an experienced interventional radiologist. Potential kidney graft function deterioration, as well as bleeding associated with the high dose of heparin used and graft ischemia hazard, support the open approach, which is also a first-choice method for patients in hypovolemic shock. The aim of this report on a small series of cases was to present rare but serious vascular complications after pancreas transplantation.

Material and Methods

We retrospectively analyzed all cases of pancreas transplantations performed at our clinic, and chose those that required vascular interventions that were challenging and non-standard for the procedure. In January 2018, we transplanted our 200th pancreas.

The study was a retrospective analysis of medical records of 200 pancreas-transplanted patients. No risk for the patients was involved during the study and only non-identifiable data was used for publication. Our clinic has permission from the Polish Ministry of Health to conduct pancreas and kidney transplantations (date of current permission 22.12.2017, expires in 2022).

Surgical technique

The pancreas graft is prepared on the back table. Arterial blood supply to the graft is reconstructed into a common trunk with a Y-graft from the iliac artery of the donor anastomosed to the supra-mesenteric and splenic arteries. The portal vein is most commonly elongated with the donor's common iliac graft. If the graft's portal vein is long enough, we sometimes omit the reconstruction.

We perform a longitudinal midline incision and dissect right iliac vessels of the donor. During a transplantation of the pancreas, we usually perform 4 arterial and 3 venous anastomoses. An increasing number of re-transplantations led us to anastomose iliac vessels first, in order to leave an opportunity for a second or third graft anastomosis in the future. The most common approach to vessel anastomosis at our center is to create it between the reconstructed vessels of the graft, the right external iliac artery, and right common iliac vessel. Previously, we routinely performed duodeno-duodenal anastomosis. Now, we prefer to anastomose the donor's duodenum to the proximal jejunum, as we observe less early bleeding, which can



Figure 1. (A–C) CT scans after intravascular common iliac artery stenting. A patient after pancreas and kidney transplantation. Pancreas graft necrosis developed and the graft had to be removed. Pancreatic enzymes were released, which led to the destruction of the common iliac artery at the site of the former Y-graft anastomosis. The bleeding was stopped by implantation of a straight stent graft into right common iliac artery (green arrow). Residual fluid collection (blue arrow) at the site of the former graft location.

still be successfully managed with the endoscopic approach. We create a double-layered hand-sewn side-to-side junction.

For the kidney graft, we anastomose the organ while performing pancreas graft hemostasis. We transplant the kidney from the same median incision, with an additional "pocket" created from the retroperitoneal space behind the left iliac vessels. In almost all cases, we use the left kidney due to its longer renal vein and lack of demand for vascular reconstructions. We perform end-to-side anastomoses between the graft vessels and the recipient's left external iliac vein and artery. We do not routinely implement double J stents.

Management

We perform US examinations daily in the early period after the transplantation (day 0 to day 10), and then routinely every month. All of the patients had a computed tomography scan 3 months following the transplantation in order to assess the graft and its vasculature. Additional US and CT examinations where performed if complications were suspected.

Immunosuppressive therapy administered after pancreas transplantation consists of induction (monoclonal or polyclonal antibodies) and steroids, calcineurin inhibitors, and anti-proliferative agents (mycophenolate).

Results

We observed severe vascular complications in 3% of the patients after pancreas transplantation. In 3 cases, there was massive bleeding from ruptured pseudoaneurysms after graftectomies. Only 1 of these patients survived, and 2 died due to septic complications. There were 2 patients with acute lower-extremity ischemia. In both cases, we achieved good results with satisfactory pancreas function. Five patients in our cohort died suddenly due to massive bleeding in different hospitals. We presume that vascular fistulas might have been responsible for acute and severe bleeding from the upper gastrointestinal tract. One patient was diagnosed with AVF on the splenic vessels, manifesting as delayed graft function, that was successfully stented. After the procedure, the patient was insulin-free.

External iliac artery wall dissection, pseudoaneurysm

In our cohort, we had 1 patient who required endovascular stenting of the ruptured external iliac artery. A month following SPK, and after 2 surgical revisions due to a duodenal leak, we decided to remove the pancreas graft because of massive bleeding. The identified source of the bleeding was a damaged wall of the external iliac artery. A mass of inflammatory tissue was surrounding the iliac vessels, which were fragile and had extremely thin and bleeding walls. We decided to add sutures, but this was not sufficient. An additional incision was made in the left groin with the use of the X-ray c-arm, and a stent-graft was implemented to the external iliac artery through the femoral artery (Figure 1A–1C). No further episodes of bleeding or extremity ischemia were observed. The patient was discharged from the clinic in good condition, and with a functional kidney graft.

Massive bleeding from arterial fistulas

In our series, a single patient developed AEF 6 months following SPK. We observed deterioration of the function of both pancreas



Figure 2. (**A**, **B**) Inflammatory aneurysm found in CT. (**C**, **D**) Arteriography showing stent-graft implantation. Pancreas transplanted into the right middle-abdomen. Broad Y-graft anastomosis with the common iliac artery (green arrow). Synchromous kidney transplantation (white arrow). Radiological signs of graft inflammation at the site of the arterial anastomosis (blue arrow). A graftectomy prodedure had to be performed eventually, due to acute inflammation. An inflammatory aneurysm has developed at the site of the previous Y-graft anastomosis (yellow arrow). The stent graft implantation procedure was performed with the use of a straight stent graft (red arrow).

and kidney grafts. In the biopsies, acute humoral rejection was diagnosed and graft-versus-host antibodies (B27, DSA) were identified. Severe upper gastrointestinal bleeding occurred 11 months following the transplantation. The endoscopic approach failed; therefore, the patient was referred for laparotomy. The source of the bleeding was an arterial fistula from the distal branch of the Y-graft, and a concomitant inflammatory aneurysm of the right common iliac artery (Figure 2A–2D). Due to the patient's severe condition, a hybrid intervention was performed. After the graftectomy, a straight stent was implemented intravenously from a small incision in the left groin to the sac of the aneurysm. However, 2 weeks later the stent became clotted (Figure 3A–3F) and a right femoral–femoral bypass was performed (Figure 4A–4D). A similar



Figure 3. (A–E) CT scans revealing stent-graft thrombosis. (F) Pseudoaneurysm (blue arrows). The patient developed clinical symptoms of right-lower limb ischemia a month following the implantation of the stent graft. A CT scan revelaed thrombosis of the stent graft (green arrows) which was confirmed intraoperatively. A bypass procedure with a Dacron prosthesis connecting the right common iliac artery to the right external iliac artery was performed (white arrows). Formation of pseudoaneurysm above the stent graft insertion site can be appreciated in CT and fluorowcopy images.

case has been described by Fridell et al., in which AEF was first diagnosed with endoscopy, and then the patient was qualified for the open approach. After the transplantectomy, they had to manage massive bleeding from gastrointestinal anastomosis. Due to the iliac artery stenosis, the patient required a femoral-femoral bypass [1].

Critical iliac artery stenosis

In 1 case, a critical stenosis of the artery was an indication for endovascular intervention. We performed pancreas re-transplantation in a patient with insulin-dependent diabetes mellitus (IDDM) who had previously undergone SPK, but lost the pancreas graft due to early venous thrombosis. The kidney graft function remained very good. The grafting procedure was routine, with arterial blood supply to the graft reconstructed with a Y-graft from the iliac artery of the donor, and anastomosed to the supra-mesenteric and splenic arteries. The portal vein was elongated with a caval graft. In this case, the vessel anastomoses were created below the previous junctions: to the right common iliac artery and vein. One hour after the surgery, the symptoms of an acute ischemia developed in the right lower extremity. In the initial ultrasound, the pancreas graft showed homogenous echogenicity, good arterial supply, and normal restrictive index values (RI 0.85). Doppler ultrasound revealed critical stenosis of right common iliac artery. We decided to perform computed angiography, which confirmed ultrasound findings, showing a short (4 mm) critical stenosis of the right common iliac artery located 10 mm below the bifurcation of the aorta; therefore, we qualified the patient for intravenous stenting.

Arteriography was performed, and confirmed critical stenosis of the right common iliac artery (Figure 5A–5D). The stenting procedure was performed with CID Isthmus 8/29 mm. In control angiography, the artery was patent, without signs of restenosis. The site of the stenosis was located several millimeters below the new arterial anastomosis, which was the location of the previous one. We did not observe kidney graft function deterioration after the procedure. Functioning of the pancreas graft was very good; the patient remained insulin-free, with positive c-peptide. No further episodes of extremity ischemia and no hemorrhagic complications were observed.



Figure 4. (**A**, **B**) Pseudoaneurysm of the internal iliac artery. (**C**, **D**) CT scans showing femo-femoral bypass. The internal iliac artery pseudoaneurysm was treated with the implantation of a right-sided aortoiliac stent graft (green arrows). The stent graft connected the common iliac artery to the Dacron bypass, and closed blood inflow to the thrombosed stent graft in the common iliac artery (blue arrows). Blood inflow to the left common iliac artery was also stopped, therefore a femorofemoral crossover bypass procedure was performed at the same time (yellow arrows). In order to prevent retrograde flow to the proximal part of the left common iliac artery, on occluder was placed in the left common iliac artery (white arrows).

Another case was an acute lower extremity ischemia due to the critical stenosis of the right common iliac artery above the Y-graft. The right common iliac artery was stented with the CID 6×100 . Due to the dissection of the right external iliac artery, a combining stet CID 6×60 was implemented. A well-developed collateral vascularization was present. In the early period, the patient's pancreas graft function was deteriorated as he demanded insulin. Six months after the transplantation, he is insulin-free, with excellent pancreas graft function and no symptoms of extremity ischemia.



Figure 5. (**A**, **B**) CT scans of re-transplanted patient. (**C**, **D**) Arteriography showing stent-graft implantation. Broad arterial anastomosis on the right common iliac artery. Apart from Y-graft (blue arrow), another artery, the pancreatic artery (green arrow), arises from the common vascular patch. Unfortunately, venous thrombosis of the graft developed, and a gastrectomy procedure had to be performed. Figure 5B shows the same patient after pancreas retransplantation. A large Y-graft was anastomosed to the anterior wall of the adbominal aorta (red arrow). Arterial stenosis developed on the right inernal iliac artery, at the site of the previous graft arterial anastomosis (yellow arrow). An arteriographic examination confirmed critical stenosis of the right common iliac artery. A stenting procedure was performed with CID Isthmus 8/29 mm (black arrow). The artery was patent in control angiography, with no signs of restenosis.

Discussion

Pancreas graft venous thrombosis is not only more often associated with arterial thrombosis [6,7], with prevalence as high as up to 10–20% of cases [9,10], but also much more difficult to treat endovascularly. Due to its rapid progression, the diagnosis is usually too late for endovascular treatment to be successful. Thus far, we have been unable to select a patient for this procedure, but the literature proves that PVGT can be successfully treated with interventional radiology. Venous thrombosis remains the main cause of graft failure and is the primary indication for transplantectomy [9]. Both partial venous thrombosis and complete venous thrombosis can result in graft loss [11]. Complete venous thrombosis is most frequently observed within the first 48 h following the transplantation [12]. In our series, graftectomies were performed in 20% of the analyzed cases, due to complete venous thrombosis in 50% of the cases and partial thrombosis in 25%.

Arterial complications of pancreas grafts have better prognosis, and intravascular management is usually more feasible.

External iliac artery dissection is a rare arterial complication [13]. Kimura et al. reported a case of a SPK complicated with external iliac artery dissection that occurred immediately after the vascular clamps were removed. To provide blood supply to the right lower extremity, they implemented a vascular stent from the femoral artery [13]. In most cases, early pseudoaneurysms lead to early graft loss and severe bleeding, whereas late forms are associated with mycotic infections, pancreatitis, or mechanical injury [1,14,15]. The endovascular or hybrid approach (with an additional incision in the groin) can be an alternative solution to excision of the Y-graft and graft re-transplantation, or even transplantectomy [14,15].

Severe bleeding may be the first symptom of arterial wall dissection and rupture of the pseudoaneurysm. The bleeding can flow into the abdomen or to the duodenum. Valle reported a case of massive bleeding to the upper gastrointestinal tract from a Y-graft PSA. Severe hypovolemic shock indicated that a quick and reliable solution was necessary. During the angiography, they embolized the Y-graft, stopped the bleeding, and decided to resort to a second open procedure – a graftectomy – after the patient was stabilized [16]. Another problematic case was reported by Yiannoullou et al., in which massive bleeding from a mycotic PSA occurred 9 months following SPK. They performed an open procedure, removed the pancreas graft, and supported the arterial defect with a bovine pericardial patch [5]. Furthermore, polypropylene patches can be used to reconstruct an arterial lumen [6].

Arteriovenous fistulas are a very rare complication in SPK, and are often accompanied with a pseudoaneurysm of the reconstructed arterial supply to the head pancreas graft [6]. Iliac artery pseudoaneurysm and arterial fistulas can also be a consequence of chronic infections, whereas the significance of chronic thrombotic microangiopathy and humoral graft rejection is still not proven [17,18]. Also, transcutaneous needle biopsy carries the risk of AVF [18,19]. It is a rare complication, occurring in 1.4% of cases presented in literature, and it sometimes coexists with graft inactivity [1]. It is a life-threatening and late complication, which in most cases requires a transplantectomy to save the recipient. A case described by Bartton showed an AVF between the superior mesenteric artery and the superior mesenteric vein of the head of the transplant with a simultaneous aneurysmatic dilatation of the Y-graft. Massive bleeding to the upper gastrointestinal tract 9 years after the SPK was the first syndrome [3]. The Y-graft was cannulated (right iliac artery access), and the aneurysm was successfully embolized [3]. Coils and detachable balloons, as well as also vascular plugs, can be used to treat AVF; however, this involves a risk of vein thrombosis, migration of the embolizing agent, and potential consequences of ionized radiation [19].

Yadav reported 13 cases of PSA and AVF approached endovascularly. In 8 patients, they embolized the lesion with coils or plugs and 37.5% of this group re-bled. Two of these patients underwent subsequent laparotomy with pancreas graftectomy, and 1 patient had an additional endovascular procedure with stenting. The remaining 5 patients from the analyzed cohort had primary endovascular stenting performed [2].

Arterioenteric fistulas are another, potentially fatal, arterial complication. They have a rapid course, and in most cases the final diagnosis and intervention are delayed. The endoscopic approach is often a first-choice method for cases in which bleeding from the upper gastrointestinal tract is present. However, a massive hemorrhage results in poor visibility and low chance of performing hemostasis correctly. If AEF is suspected, it is feasible to perform embolization during angiography [6]. Most articles reported AEF and PSAs between the superior mesenteric vessels. There is a report on PSA of a gastroduodenal artery, which was successfully embolized with coils [20].

Conclusions

Pancreas transplantation is a technically demanding procedure. Vascular reconstruction including Y-graft for superior mesenteric artery and splenic artery, as well as portal vein reconstruction, have increased risk of complications. Severe vascular conditions are a rare complication of pancreas transplantations. Intravenous interventions in patients with a transplanted pancreas are safe and feasible. Vascular methods are preferable in managing postoperative complications. However, an open or combined approach is inevitable. The risk of kidney graft function deterioration, as well as of bleeding due to the high dose of heparin used, is lower in endovascular procedures than in vascular surgery. Nevertheless, a multidisciplinary and experienced team of surgeons and radiologists is required. Surgeons performing pancreas transplantation must bear in mind that diabetic patients are encumbered with micro- and macrovascular complications as a result of the long-term consequences of the disease. Each patient is different and poses an individual surgical challenge. The transplantation procedure is often affected by the recipients' vascular conditions. Moreover, severe

vascular complications can occur after the transplantation. On the other hand, donors undergo minimal imaging examinations, which do not always reveal anatomical abnormalities. Such anomalies will not be exposed before the back-table work,

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but need to be addressed nevertheless in order to assure sufficient blood supply to the grafts. The surgeons' vascular skills determine the outcome of the transplantation.

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