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Pancreatic autotransplantation in the pig: variations in epigastric arterial blood supply

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Abstract. A major problem in pancreatic autotransplantation is the vascular supply of the left segment, which serves as the graft. We therefore examined the arterial blood supply of the epigastric organs in 36 German landrace pigs. In 19 pigs (anatomical variation 1) there was a pancreatic branch of the splenic artery supplying the left segment. After splenectomy the splenic artery could be used as the graft-supplying vessel. In 14 pigs (anatomical variation 2) the arterial branch for the left segment was the first branch out of the hepatic artery distal to the coeliac trunk. In these cases a splenohepatic bypass was performed to ensure delivery of the blood to the epigastric organs. Thereafter, the proximal part of the hepatic artery could be used as the vessel supplying the graft. The left segment could not be used for autotransplantation in 3 pigs (anatomical variation 3) because of the atypical vascular supply. During the 6-month observation period, no malfunction of the epigastric organs was evident.

Key words: Pancreas transplantation, in the pig - Experimental pancreas transplantation, pig, anatomy.

In pancreatic transplantation, the method of handling the duct that produces the best long-term function of the grafted organ is still a matter of debate [1, 2, 4, 8, 11]. Autologous models of pancreatic transplantation have the advantage of excluding rejection reactions. Therefore, it can be assumed that, in these models, loss of organ function and changes in organ structure are caused mainly by surgical techniques.

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We have developed a new model of segmental autotransplantation in pigs in which the right pancreatic segment is left in situ to maintain the digestive function of the organ for normal growth of the animal and to provide long-term functional studies of the grafts. In our model, the β-cells of this remaining right pancreatic segment are ablated by local perfusion with streptozotocin, a selective β-cell toxin [16]. Therefore, only the autotransplanted left segment anastomosed to the right iliac vessels is responsible for insulin production. The arterial supply of the pancreas is of great importance in autologous transplantation models because a sufficient blood supply of the epigastric organs has to be maintained after removal of the left pancreatic segment. In this paper, we describe variations in the blood supply of the left pancreatic segment in domestic pigs as well as the application of surgical techniques that allow for the removal of this left segment without disturbing the blood supply of other epigastric organs.

Methods

After approval from the local ethics committee on animal research, 36 locally supplied German landrace pigs, male and female, weighing 25 ± 3.5 kg ($\bar{x} \pm SD$), were studied.

Anesthesia

After premedication with atropine (0.01 mg/kg), azaperone (1 mg/kg), and methomidate (5 mg/kg), anesthesia was induced with ketamine (5 mg/kg) and methomidate (2 mg/kg) and the trachea was intubated. The lungs were ventilated with a nitrous oxide/oxygen (2:1) mixture (Draeger 19.1 Pulmomat, Draeger, Lübeck, FRG) and anesthesia was maintained by continuous infusion of thiopental (3-6 mg/kg per hour).

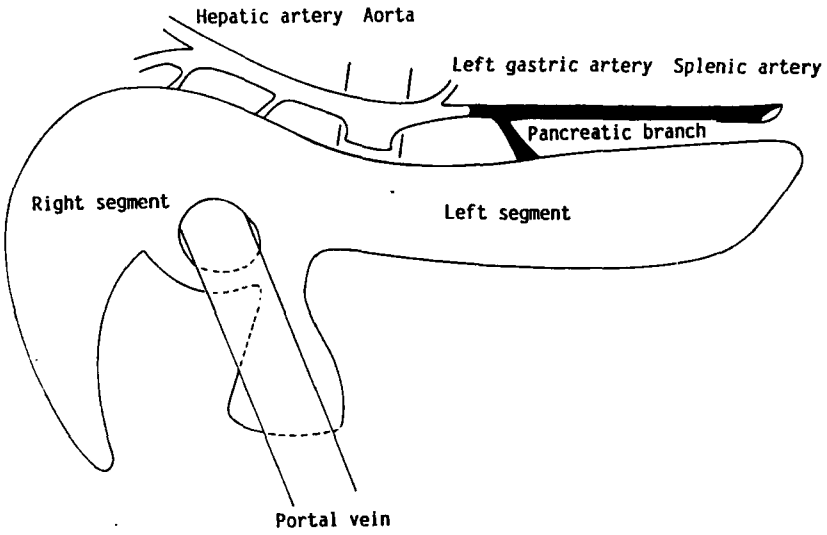

Fig. 1. Arterial supply of the left pancreatic segment (autograft) arising from the splenic artery (anatomical variation 1). After splenectomy the splenic artery is used as the graft-supplying vessel

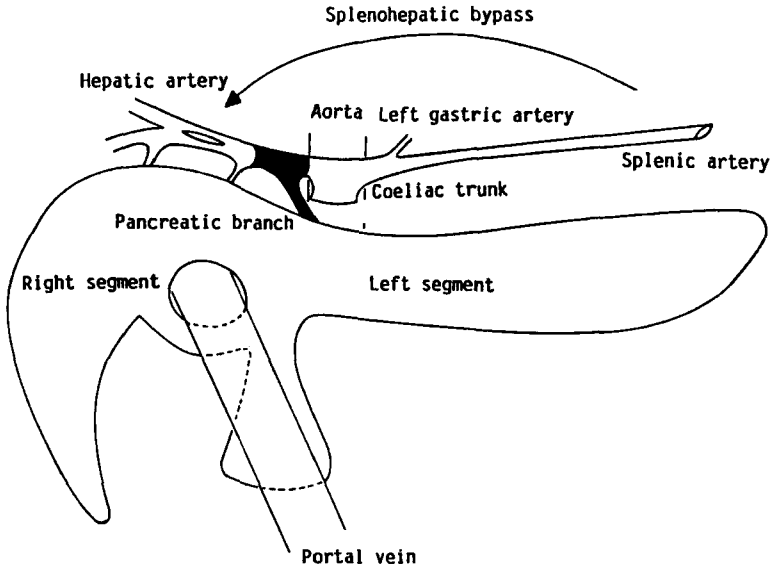

Fig. 2. Arterial supply of the pancreatic segment (autograft) arising from the hepatic artery (anatomical variation 2). The pancreatic branch for the left segment is the first branch coming out of the hepatic artery distal of the coeliac trunk

Surgical technique

After a long, vertical, midline incision, the gastrocolic omentum was divided and the front of the left pancreatic segment was exposed. Following mobilization of the spleen and division of the gastrosplenic ligament, the splenic artery and vein were dissected along the superior margin of the left pancreatic segment. Then, the coeliac trunk was exposed from its bifurcation into the splenic and hepatic arteries to its origin at the aorta. Next, the splenic artery was prepared from the coeliac trunk to its distal end, without damaging the left gastric artery branches, and the branch supplying the left pancreatic segment was exposed. Thereafter, the splenic vein was dissected to the point of confluence with the portal vein.

Streptozotocin perfusion

Our technique of local streptozotocin perfusion has been described in detail previously [16, 17] and can be summarized as follows: After removing the left pancreatic segment, the endocrine part of the right pancreatic segment was ablated by regional streptozotocin perfusion via the common hepatic artery and its pancreatic branches. During this procedure, the liver and stomach branches were occluded temporarily with vessel loops because streptozotocin is toxic to the liver. Before injection of 10 mg/kg streptozotocin, freshly dissolved in 20 ml saline, into the common hepatic artery, methylene blue was injected to confirm the vascular supply of the right pancreatic segment and the proper position of the cannula.

Vascular supply of the left pancreatic segment

Anatomical variation 1 (Supply out of splenic artery). When the left pancreatic segment was supplied by a pancreatic branch of the splenic artery, the following surgical technique was used. After splenectomy, the splenic artery was ligated and divided distal to the left gastric artery so that the distal part of the splenic artery could be used as the artery supplying the graft (Fig. 1). The splenic vein was transected at its confluence to the portal vein, and the blood of the graft was drained via the splenic vein. The pancreas was divided between the right and left segments along a line in

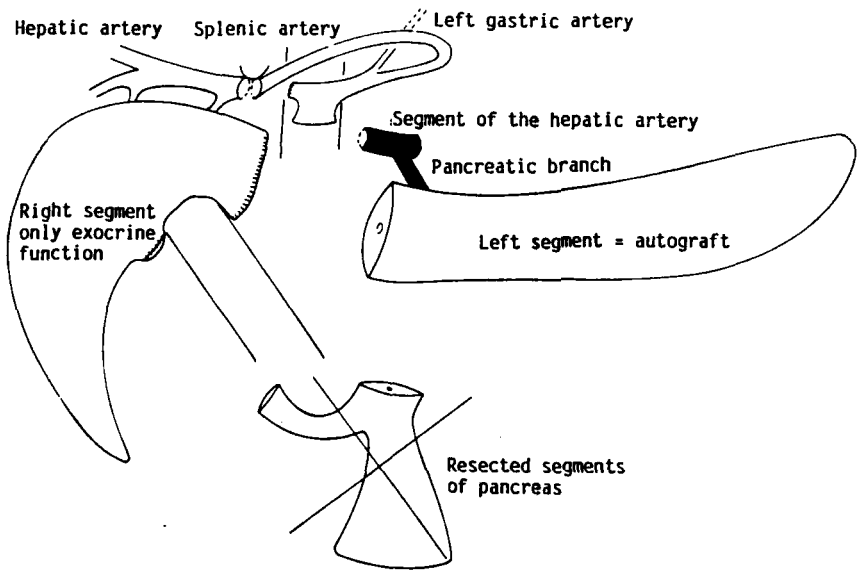

Fig. 3. Procedure for performing a splenohepatic bypass. The left pancreatic segment with the proximal part of the hepatic artery is resected and used as the graft

front of the aorta downwards from the coeliac trunk to the junction of the splenic and mesenteric superior vein. The dissection toward the right pancreatic segment was closed first by ligation of the pancreatic duct and a running suture using 4 × 0 polydioxanon (PDS, Ethicon, Norderstedt, FRG). After removing the left pancreatic segment, it was perfused at 4° C with Ringer's solution containing 10000 IU heparin. For transplantation of the graft, the distal end of the splenic vessels were anastomosed end-to-side with the iliac vessels.

Anatomical variation 2 (Supply out of hepatic artery). If no pancreatic artery coming from the splenic artery was identified, the hepatic artery was prepared to the point of the exit of the superior pancreaticoduodenal artery, looking for a branch supplying the left pancreatic segment. If there was a supplying branch, the proximal part (about 1-2 cm in length) of the hepatic artery had to be used as the arterial vessel supplying the graft (Fig. 2). To ensure an adequate blood supply to the liver and stomach, a splenohepatic bypass had to be performed; a direct end-to-end anastomosis was not possible, due to excessive traction of the artery. After systemic application of 5000 IU heparin, the spleen was removed and the distal end of the splenic artery was turned to the right side to be anastomosed with the hepatic artery distal of the pancreatic branch (Fig. 3). To anastomose the splenohepatic bypass, the splenic artery was temporarily clamped distal to the left gastric artery and the hepatic artery was divided distal of the pancreatic branch. Vascular anastomosis was performed end-to-end using a 7-0 polypropylene (Prolene, Ethicon, Norderstedt, FRG) running suture. Afterwards, the proximal part of the hepatic artery with the pancreatic branch was transected from the coeliac trunk. The rest of the procedure was performed as described above. The anastomosis of the hepatic artery segment and the right iliac artery was performed end-to-side.

Anatomical variation 3. If no pancreatic artery arising from the splenic artery or the hepatic artery was identified, the left pancreatic segment could not be used for autotransplantation.

In the 33 pancreatic autotransplantations that were performed, three different methods were employed to manage the exocrine part of the grafted pancreas: prolamine occlusion ($n = 10$), temporary fibrin sealing ($n = 13$), and pancreaticojejunostomy ($n = 10$) [16-18].

Results

A total of 36 pigs were operated on and the left pancreatic segment of each prepared for autotransplantation (Table 1).

Anatomical variation 1

In 19 out of 36 animals, the pancreatic artery supplying the left segment arose from the splenic artery. In each case, the origin of this pancreatic branch was found distal to the left gastric artery (Fig. 1). In one case, there were two major branches of the splenic artery supplying the left pancreatic segment.

Anatomical variation 2

Fourteen out of 36 animals had an arterial supply of the left pancreatic segment arising from the hepatic artery. In each of these animals, this pancreatic vessel was the first branch of the hepatic artery distal to the coeliac trunk (Fig. 2). In these cases, a splenohepatic bypass had to be performed, in which the splenic artery was anastomosed to the hepatic artery distal to the pancreatic branch (Fig. 3).

Anatomical variation 3

In three pigs the left pancreatic segment could not be used for autotransplantation due to its anatomical situation. In one animal the pancreatic artery supplying the left segment of the pancreas arose from

Table 1. Vascular supply of the epigastric organs in 36 German landrace pigs

Anatomical variation 1	Anatomical variation 2	Anatomical variation 3		
(n = 19)	(n = 14)	(*n* = 1)	(*n* = 1)	(*n* = 1)
Coeliac trunk	Coeliac trunk	Coeliac trunk	Coeliac trunk	Coeliac trunk
Splenic artery	Splenic artery	Splenic artery	Splenic artery	Splenic artery
Left gastric artery	Left gastric artery	Left gastric artery	Left gastric artery	Left gastric artery
Diverticular artery	Diverticular artery	Diverticular artery	Diverticular artery	Diverticular artery
Pancreatic branch for left segment				
Left gastroepiploic artery	Left gastroepiploic artery	Left gastroepiploic artery	Left gastroepiploic artery	Left gastroepiploic artery
		Pancreatic branch for left segment		
Hepatic artery	Hepatic artery	Hepatic artery	Hepatic artery	Hepatic artery
	Pancreatic branch for left segment			
Pancreatic branch for right segment	Pancreatic branch for right segment	Pancreatic branch for right segment	Pancreatic branch for right segment	Pancreatic branch for right segment
Right lateral hepatic branch	Right lateral hepatic branch	Right lateral hepatic branch	Right lateral hepatic branch	Right lateral hepatic branch
Gastroduodenal artery	Gastroduodenal artery	Gastroduodenal artery	Gastroduodenal artery	Gastroduodenal artery
Right medial hepatic branch	Right medial hepatic branch	Right medial hepatic branch	Right medial hepatic branch	Right medial hepatic branch
Right gastric artery	Right gastric artery	Right gastric artery	Right gastric artery	Right gastric artery
Left hepatic branch	Left hepatic branch	Left hepatic branch	Left hepatic branch	Left hepatic branch
Cranial mesenteric artery	Cranial mesenteric artery	Cranial mesenteric artery	Cranial mesenteric artery	Cranial mesenteric artery
			Pancreatic branch for left segment	
				Without a pancreatic branch for left segment

the coeliac trunk. In another pig, the pancreatic branch for the left segment had its origin in the superior mesenteric artery. In the third pig, it was not possible to identify and to isolate an arterial branch supplying only the left pancreatic segment.

No major variations were found in the venous outflow of the left pancreatic segment in any of the 36 pigs. The venous blood was drained in all cases via the splenic vein to the portal vein.

In one case, the splenohepatic bypass thrombosed during surgery a few minutes after anastomosis, and the anastomosis had to be corrected. This procedure was successful and no further complications were encountered. All animals in which a splenohepatic bypass (anatomical variation 2) was necessary for left segmental autotransplantation showed a normal enzyme profile of liver function during a 6-month observation period (unpublished data). The pigs thrived on a normal diet as do animals that have not been operated on and those that did not have a splenohepatic bypass (anatomical variation 1). Pathological anatomical examination did not reveal macroscopic or microscopic lesions resulting from disturbed vascular perfusion.

Discussion

Pancreatic transplantations are performed as a causal treatment for insulin-dependent diabetes mellitus. The survival rate of the graft in pancreatic transplantations is still lower than in transplantation of other organs [10], due to rejection reactions and complications of surgical techniques. Thus, more animal experiments will be necessary in the future. The pig seems to be a suitable laboratory animal since its physiology is comparable to that of humans [9] and because the cost of purchasing and maintaining pigs is lower than that of dogs [13].

In our autologous transplantation model, the left pancreatic segment is used as the graft. The main advantage of pancreatic segment autotransplantation is

the maintenance of a normal digestive function by the remaining right segment. Since the β-cells of the right segment are ablated by regional streptozotocin perfusion [16], insulin is produced only by the graft. This enables one to maintain control of the endocrine function of the graft for long-term studies. In an autologous pancreatic transplantation model, maintenance of the arterial blood supply of the epigastric organs is an important aspect of the surgical removal of the left pancreatic segment.

According to Ghoshal [6] and Wilkens and Münster [14], the left pancreatic segment of domestic pigs is supplied by a major pancreatic branch of the splenic artery. A similar vascular supply is found in the "Göttinger minipig" [5]. In our study, using locally supplied German landrace pigs, however, only 52% of the pigs had such a vascular supply of the left pancreatic segment. In their textbooks on the anatomy of domestic animals, Dobberstein and Hoffmann [3] and Zietzschmann [15] describe pancreatic branches of the splenic and of the hepatic arteries without assigning the branches to the pancreatic segments. Schiltsky [12] found in his examination of the blood supply of the epigastric organs of 11 pigs that at least one pancreatic branch arose from the splenic artery in all animals. However, in two animals, the left pancreatic segment was mainly supplied by a branch arising from the inferior pancreaticoduodenal artery. In one animal, the major branch arose from the proximal part of the hepatic artery.

In spite of this, we found an arterial supply of the left pancreatic segment not arising from the splenic artery in 17 of the 36 German landrace pigs studied. For most of these animals (14 out of 17), the arterial branch for the left pancreatic segment was the first branch out of the hepatic artery distal to the coeliac trunk. This pancreatic branch, arising from the hepatic artery, was short and small in diameter. This makes anastomosis of this branch with the iliac artery difficult and the risk of thrombosis high. To avoid these technical problems, removal of the proximal part of the hepatic artery with the origin of the pancreatic branch is necessary to obtain a sufficiently large vessel.

Under these conditions, maintaining the blood supply of the epigastric organs is often problematic. Kyriakides et al. [7] resolved this technical problem in the following way. In all animals they transected the coeliac trunk proximal to the division of the splenic and hepatic arteries, cut the hepatic artery further distal to the pancreatic branch, and anastomosed "the coeliac artery stump in the abdomen end-to-end to the distal hepatic artery." In this surgical procedure, the left gastric artery always had to be cut. Using Kyriakides' preparation, it is unimportant whether the pancreatic branch for the left segment arises from the splenic or from the hepatic artery. In our experiments, we performed a splenohepatic bypass for an adequate blood supply to the liver and stomach when the pancreatic branch of the left segment arose from the hepatic artery. In this way, we were able to remove the proximal part of the hepatic artery with the origin of the pancreatic branch without any risk of ischemia of the epigastric organs. In contrast to the procedure followed by Kyriakides and colleagues, we maintain the left gastric artery supplying the stomach. This technique has the additional advantage that it is not necessary to prepare and anastomose the hepatic artery when the left pancreatic segment is supplied by a branch out of the splenic artery, as we found in more than half of all the animals we studied. The operation time in these cases is shorter and there is no risk of insufficient perfusion of the liver and stomach. In a 6-month observation period after segmental pancreas transplantation, we were able to show that a splenohepatic bypass ensures a sufficient blood supply of the epigastric organs to thrive normally when resection of the proximal hepatic artery is necessary [17].

We conclude that, given these anatomical variations of the arterial blood supply of the left pancreatic segment in the pig and by applying a technique of splenohepatic bypass in selected cases, segmental autotransplantation is a reliable method for studying immunological and long-term graft function in pancreatic transplantation.

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