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ORIGINAL ARTICLE

Computer-assisted three-dimensional reconstruction of the fetal pancreas including the supplying arteries according to immunohistochemistry of pancreatic polypeptide

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Abstract
Purpose Computer-assisted three-dimensional reconstruction of the fetal human pancreas was prepared to reconsider topographical relation between the dorsal/ventral anlagen and the vascular supply.
Methods Tissue sections from the upper abdominal viscera of three fetuses were examined. Sections were immunohistochemically stained to determine pancreatic polypeptide expression, a marker of the ventral pancreas.
Results The immunohistochemical findings were used to create three-dimensional computer-assisted reconstructions to identify pancreatic arteries. The narrowest part of the pancreas, or the neck, corresponding to a part of the dorsal pancreas, was located on the left side of the common bile duct, portal vein and gastroduodenal artery (GDA). The posterior arterial arcade accompanied the ventral pancreas, whereas the anterior arcade did not. In contrast to the GDA, the splenic artery was clearly separated from the neck in fetuses. The GDA appears to be the primary and stable arterial supply for the neck of the pancreas.
Conclusions This observation may have implications for the preservation of the neck with the GDA during pancreaticoduodenectomy for benign and low-grade malignant diseases.

Keywords Gastroduodenal artery · Dorsal pancreas · Pancreatic polypeptide immunohistochemistry · Human fetus

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Introduction

The pancreas develops from the dorsal and ventral anlagen [1, 8, 13]. Computer-assisted three-dimensional (3D) reconstruction of the pancreas topographical anatomy has been limited to studies using early stage fetuses of humans [10] and rats [4]. Thus, to our knowledge, no study showed 3D reconstruction of vascular topographical anatomy as well as the dorsal and ventral anlagen. Krakowiak-Sarnowska et al. [7] demonstrated the fetal pancreaticoduodenal arteries using an injection method. However, they did not identify whether the arterial territory is the dorsal or ventral pancreas. In contrast to fetal studies, several Japanese surgical groups have used immunohistochemistry techniques to create reconstructions of the adult human ventral pancreas [12, 16, 18]. Those studies were based on the detection of pancreatic polypeptide (PP) in the

ventral pancreas-derived islets and acinus [9, 11]. Sakamoto et al. [12] concluded that, in adults, the dorsal pancreas is supplied by the anterior arterial arcade and the ventral pancreas by the posterior arcade. Consequently, to reconsider surgical treatments of vessels for the dorsal/ventral pancreas in adults, the aim of the present study was to present 3D reconstructions of the fetal pancreas including the vascular anatomy.

Materials and methods

Fetuses

The study examined tissue from three male fetuses of 15, 16 and 18 weeks of gestation (crown rump length, CRL 110–155 mm). The fetuses were donated by their families to the Department of Anatomy, Chonbuk National University in Korea. Examinations were in accordance of the provisions of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000), and use of the fetuses for research was approved by the university ethics committee.

Tissue preparation

Tissue blocks of approximately 5 × 5 × 3 cm in size containing upper abdominal viscera, ribs and vertebrae were removed from each fetus. After decalcification using EDTA (pH 7.5, 0.5 mol/L; decalcifying solution B, Wako, Tokyo, Japan), specimens were prepared for paraffin embedded histology. Horizontal paraffin sections of thickness 5 μm were cut at 50 μm intervals. Most sections were stained with hematoxylin and eosin (HE), and some sections of the pancreatic head (approximately 100 μm intervals) underwent immunohistochemical analysis for pancreatic polypeptide (PP) without microwave pretreatment. Approximately 100 immunohistochemistry sections were created from each block. The primary antibody was anti-human PP (rabbit polyclonal; Yanaihara Institute Inc., Fujinomiya, Japan). We chose the first antibody according to a personal communication from professor Mineko Fujimiya (Department of Anatomy, Sapporo Medical University School of Medicine). The second antibody (Dako Chem Mate Envison Kit, Dako, Glostrup, Denmark) was labeled with horseradish peroxidase, and antigen–antibody reactions were detected via an HRP-catalyzed reaction with diaminobenzidine. Counterstaining with hematoxylin was performed on the same samples.

Axial sectional dataset and registration

Stained sectional images were captured using a Canon 5D digital camera with a Canon 100 mm macro lens (1×). The field of view was 48.5 × 32 mm at a resolution of 4,368 × 2,912 pixels. Figure 1 shows enlarged sequential stained images from the sectional dataset. The dataset contained 249 images from the top of the liver to the bottom of the duodenum. The stained sectional images were examined by three authors (C.B.H., J.Z.W. and G.M.). The boundary of the pancreas was traced manually on each image. Image registration was accomplished by alignment with the center of the vertebrae. The orientation of the image was adjusted to fit with other organs in adjacent slices along with the spinal axis. The alignment process was repeated manually with respect to translation and rotation until all slices were aligned to the satisfaction of an experienced anatomist. Each odd-numbered image was stacked from the bottom for 3D reconstruction using 3ds Max 7 software (Autodesk Inc., LA, US).

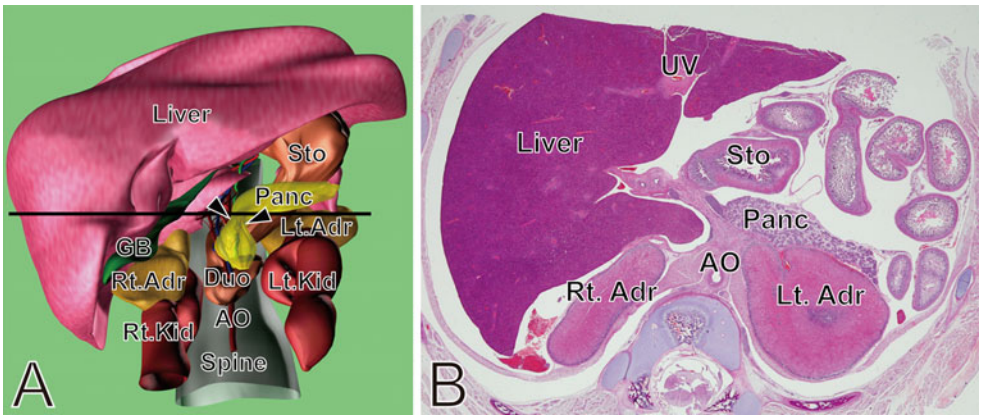

Fig. 1 Ventral 3D view of the fetal upper abdominal topographical anatomy. Upper abdominal organ sections of a CRL 155 mm fetus were used to create a 3D topographical reconstruction. The transverse line in **a** corresponds to the section shown in panel B (HE staining). Note the distinct neck of the developing pancreas (sandwiched by *arrowheads*). *Adr* adrenal glands, *AO* aorta, *Duo* duodenum, *GB* gall bladder, *Kid* kidneys, *Panc* pancreas, *Sto* stomach, *UV* umbilical vein

3D reconstruction

The selected images were set as background in 3ds Max. Experienced computer-aided design technicians placed a set of control points over the background image to construct the boundary of the pancreas slice by slice, excluding vascular tissues. The control points were carefully placed considering the curvature such that the set of points accurately reflected the shape of the pancreas. The pancreatic surface was recreated after the positioning of the control points was completed. If a region of the surface appeared unnatural, the corresponding control points were adjusted and another model created. The artery and bile duct were modeled using a profile function of 3ds Max. A set of control points was specified along with the center line of the artery. A tube-like surface was then generated based around the center line with a specific diameter.

Results

Each of the fetal abdominal viscera occupied a position similar to that found in adults, although the liver and adrenal glands were relatively larger than for adults (Fig. 1). The pancreatic head was located at the inferior side of the pancreatic body. Thus, the pancreas was bent and the convex surface faced the liver hilar region. The narrowest part, or neck, of the pancreas was seen immediately to the left side of the portal vein course. The contents of the hepatoduodenal ligament (i.e., the common bile duct, portal vein and hepatic artery) extended superiorly and rightward from the pancreatic head and crossed the superior side of the pylorus. Along the inferiorly protruded head of the pancreas, the third portion of the duodenum directed superiorly and leftward. The duodenum and pancreatic head did not attach to the dorsal body wall, but were enclosed by a mesentery.

Tissue sections were immunohistochemically stained to determine PP expression as a marker of the ventral pancreas. Areas of strong PP staining were observed in all three specimens. However, some areas likely to be ventral pancreas were not PP-positive in tissue from two of the three (15 and 16 weeks) fetuses. This was probably due to poor tissue fixation. Thus, only sections from the 18-week fetus were used for 3D reconstruction of the entire part of the pancreas. That fetus tissue showed a strong PP-positive area that was clearly demarcated even in lower magnification views (Fig. 2a–d). The border between the strong and weak positive areas was rough and curved rather than smooth. Tentatively, we call the area of the strong PP expression as the "ventral pancreas" in contrast to the no or weak reacted area as the "dorsal pancreas".

The ventral pancreas was located along the common bile duct and/or in the postero-infero-medial part of the pancreatic head. However, a small part (a ventral surface) of the common bile duct faced the dorsal pancreas. The ventral pancreas was situated in the posterior side of the upward courses of the superior mesenteric vein and portal vein. The gastroduodenal artery (GDA), after issuing the posterior superior pancreaticoduodenal artery (PSPDA), ran straight and inferiorly along the ventral surface of the dorsal pancreas. The main GDA trunk did not attach to the

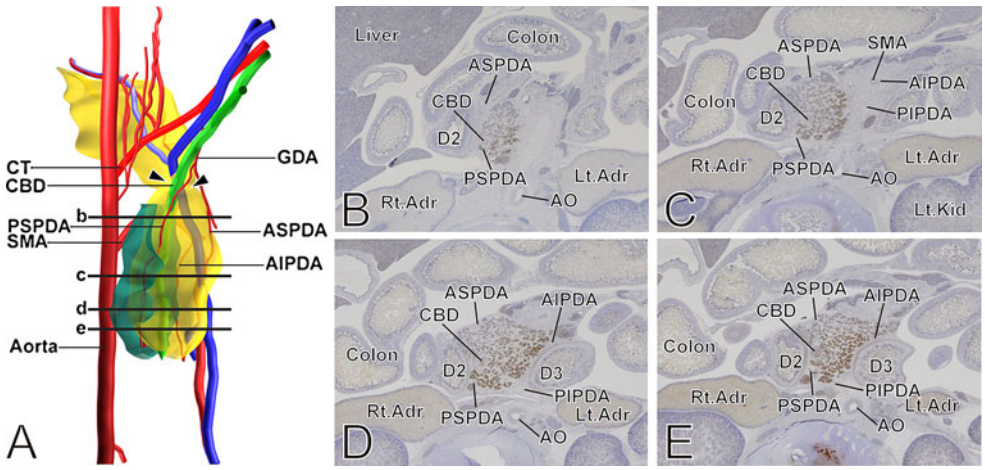

Fig. 2 Right-side view of a 3D reconstruction of the fetal ventral pancreas and pancreatic arteries. Upper abdominal organ sections of a CRL 155 mm fetus were immunochemically stained for pancreatic polypeptide (PP) expression (i.e., the ventral pancreas), and sections were then used to create a 3D topographical reconstruction. The *blue* color indicates strong PP expression. **a** The *transverse line* marked *b–e* correspond to the sections of immunostaining shown in **b–e**, respectively. Note the gastroduodenal artery (*GDA*) running alongside the neck of the pancreas (*arrowhead*). *AIPDA* and *PIPDA* anterior and posterior inferior pancreaticoduodenal artery, respectively; *ASPDA* and *PSPDA* anterior and posterior superior pancreaticoduodenal artery, respectively; *CBD* common bile duct, *CT* celiac trunk, *D2* and *D3* the second and third portions of the duodenum, *SMA* superior mesenteric artery. Other abbreviations are as for Fig. 1

ventral pancreas. In contrast, the PSPDA ran along the surface of the ventral pancreas and connected to the posterior inferior pancreaticoduodenal artery (PIPDA) passing between the ventral and dorsal pancreas. The neck of the pancreas corresponded to the dorsal pancreas and was located at the immediate superior side of the ventral pancreas. The course of the portal and superior mesenteric veins approximately corresponded to a border plane between the two anlagen of the pancreas. The splenic artery ran leftward on the dorsal side of the body and was distant from the neck of the pancreas (Fig. 3).

Discussion

The present study created 3D images of the human fetal pancreatic head using data from anti-PP-stained tissue sections. The neck of the pancreas was, when identified as the narrowest portion of the parenchyma, located in the right part of the dorsal pancreas. This observation was similar to those made in studies using later-stage fetuses [6]. The fetal GDA displayed a descending course along the right aspect of the neck of the pancreas. Thus, the portal and superior mesenteric veins ran near the GDA. In contrast, the splenic artery ran on the dorsal side of the pancreas body and it was clearly separated from the neck. Therefore, an arterial supply from the splenic artery to the neck of the pancreas in adults, such as the dorsal pancreatic artery, was likely to be due to topographical changes at later stages of fetal development [5]. Conversely, the GDA appeared to be the primary and stable feeder for the neck of the pancreas in fetuses.

We found that the border plane between the ventral and dorsal anlagen was rough and curved rather than smooth. Thus, the joining pattern for the ventral and dorsal pancreatic ducts is likely to vary among fetuses, as reported for adults [16, 17]. The posterior arterial arcade appeared to accompany the ventral pancreas, whereas the anterior arcade did not. The ventral pancreas seemed to be located along the common bile duct and/or in the postero-inferomedial part of the pancreatic head. However, a small part (a ventral surface) of the common bile duct appeared to face the dorsal pancreas. A course of the portal-superior mesenteric vein was likely to correspond to a border plane between the two anlagen of the pancreas.

The neck of the pancreas is the site for division in various pancreatic surgery procedures. However, the pancreatic stump is prone to morbidity and mortality after pancreaticoduodenectomy due to ischemia [14, 15]. The GDA and splenic artery are reported to be the major arteries supplying the neck of the pancreas, even though the neck lies between these two arterial territories [2, 3]. Despite a number of surgical studies, there remains limited information on the topographical relationship between arterial supply and the neck of the pancreas. The present findings suggest that the GDA is the main arterial feeder of the neck of the pancreas in both fetuses and adults, even though the topographical relationship between the pancreas neck and the GDA changes during development. The GDA lies in a groove that is located longitudinally between the head and neck of the pancreas. We suggest a modified surgical approach for patients with benign and very early stage malignant diseases whereby the GDA in situ position is preserved unless there is evidence of positive margins.

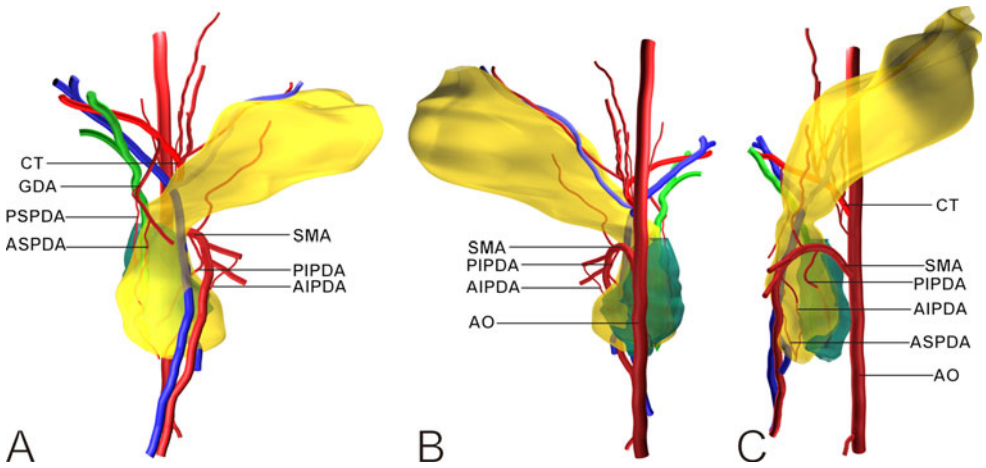

Fig. 3 3D reconstructions of the fetal ventral pancreas and pancreatic arteries. Upper abdominal organ sections of a CRL 155 mm fetus were immunochemically stained for pancreatic polypeptide (PP) expression (i.e., the ventral pancreas), and sections were then used to create a 3D topographical reconstruction. **a** Ventral view. Note the gastroduodenal artery (*GDA*) crossing the neck of the pancreas after the origin of the posterior superior pancreaticoduodenal artery (*PSPDA*). **b** Dorsal view. Note the ventral pancreas occupies a large volume in the dorsal aspect of the pancreatic head. **c** Left-side view. The *blue* color indicates strong pancreatic polypeptide expression (i.e., the ventral pancreas). Other abbreviations are as for Figs. 1 and 2

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