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New insight of pancreatic imaging: from ''unexplored'' to ''explored''

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Abstract

Pancreatic cancer remains one of the most difficult neoplasms for early diagnosis and treatment. Recent advances of imaging including 3D volume data setting in multidetector-row CT (MDCT) and MRI are urging us to focus on the imaging of normal and pathological conditions of pancreatic parenchyme and peripancreatic structures, which are frequently involved by pancreatic cancers and are affecting the prognosis of patients with pancreatic cancers. In this Feature Section, five main topics of pancreatic imaging are addressed: pancreatic arterial territories, imaging of the intra- and peripancreatic venous anatomy and its clinical significance, imaging of the peripancreatic lymphatic network and its clinical significance for staging of pancreatic cancer, perfusion characteristics of pancreatic cancer to differentiate chronic mass-forming pancreatitis, and development of intraductal papillary mucinus neoplasms of the pancreas (IPMNs) to adenocarcinoma and pancreatic invasion. Recognition and understanding of the imaging anatomy of the pancreas might lead to precise staging of pancreatic cancer and to new approaches of less-invasive treatment. Follow-up of patients with IPMNs of the pancreas on imaging seems, at this time, to be the most valuable strategy in the high-risk group selection.

Key words: Pancreatic arterial territories—Pancreatic venous anatomy—Peripancreatic—Lymphatic network—Perfusion characteristics of pancreatic cancer—Intraductal papillary mucinus neoplasms of the pancreas

Pancreatic cancer remains one of the most difficult neoplasms for early diagnosis and treatment. During the past few decades, the incidence of pancreatic carcinomas has increased all over the world, and these tumors have become the 4th or 5th most common cause of death from cancer. Only 10%–30% of patients with pancreatic carcinoma have resectable disease at diagnosis. Therefore, long-term survival is extremely rare. Many researchers have been making every effort to find a way for early diagnosis, accurate staging, and effective treatment of pancreatic cancers. However, it was recently reported that use of the brand-new molecular-targeted drug with gemcitebine for systemic chemotherapy of patients with advanced pancreatic cancers could extend median survival by only one month [1]. So, when considering the strategy of diagnosis and treatment of pancreatic cancer, the following questions arise: How and what do we know about the anatomy of the pancreas? Do we miss something very basic?

The term pancreas is derived from Greek and means literally ''an organ colored like beef or meat.'' The Chinese character representing pancreas in Japanese means ''an organ which consists of glands.'' On the other hand, the original Chinese character representing pancreas means ''an organ of remote region or unexplored territory'' (Fig. 1). It is indeed true that the pancreas is still an unexplored organ, compared to the liver whose arterial, portal venous, hepatic venous, and segmental anatomy had been well established many years ago [2]. Little attention has been paid to the arterial territory of the pancreas, the anatomy of intra- and peripancreatic veins, and the anatomy of peripancreatic lymphatic networks.

In this Feature Section, five main topics of pancreatic imaging are addressed: pancreatic arterial territories, imaging of the intra- and peripancreatic venous anatomy and its clinical significance, imaging of the peripancreatic lymphatic network and its clinical significance for staging of pancreatic cancer, perfusion characteristics of pancreatic cancer to differentiate chronic mass-forming pancreatitis, and development of IPMNs (Intraductal papillary mucinus neoplasms of the pancreas) to adenocarcinoma and pancreatic invasion. The content is outlined here with some supplements.

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膵 An organ consisting of "glands"

膸 An organ of "remote region"
An organ of "unexplored territory"

Fig. 1. Pancreas as unexplored territory. *Upper row*: Japanese Kanji (Chinese character) representing pancreas means "an organ consisting of glands." *Lower row*: Chinese character representing pancreas means " an organ of remote region" or " an organ of unexplored territory".

Imaging anatomy of the pancreas and its clinical significance

Arterial territories or segmental anatomy of the pancreas

It is not surprising that there had been no solid concept of the arterial territories or segments of the pancreas [3], because there was little clinical need for pancreatic segmentectomy or segmental resection; also there had been little clinical success of the less-invasive targeted therapy. As shown in this Feature Section, follow-up by imaging of patients with intraductal mucinous neoplasms (IPMNs) of the pancreas may be the most effective way to find the early-stage pancreatic cancer. Pancreatic segmentectomy has precisely been discussed for the IPMNs [4, 5]. Clinical application of the less invasive targeted therapy such as intra-arterial chemotherapy [6] or gene therapy [7–9] is in the early stages. In the near future, knowledge of the arterial territories or segmental anatomy of the pancreas will be appreciated for both surgery and locally targeted less-invasive therapy. In this Feature Section, Dr. Okahara and colleagues describe the anatomical variations and arterial territories (segments) of the pancreas using CT during selective arterial injection of contrast medium.

Anatomy of the pancreatic veins

The assessment of tumor invasion to the portal-superior mesenteric veins is crucial for surgical planning in patients who are potentially resectable. The criteria for evaluation of cancer extension to Portal-SMV were proposed in several previous reports [10]. Observing the pancreaticoduodenal veins is valuable for obtaining additional information regarding curability, because they have a close relationship with the extrapancreatic nerve plexus and the root of the small bowel mesentery. The anatomy of the peripancreatic veins of the pancreatic head has been well established [11–13]. CT assessments of the small pancreaticoduodenal veins in patients with pancreatic carcinoma can help to reliably identify vascular invasion earlier in the course of invasive carcinoma. Understanding the normal CT anatomy of the peripancreatic and intrapancreatic veins, not only in the pancreatic head but also in the body and tail areas, is a prerequisite for evaluating these veins in patients with pancreatic disease.

Recently, multiplanar reformation (MPR) in dynamic contrast-enhanced studies facilitated by multidetector-row CT (MDCT) has allowed confident and accurate three-dimensional assessment of small pancreatic veins. Specifically, high-resolution MDCT images obtained using the MPR technique, especially the thin-slice images (1 or 2 mm in thickness) acquired by MDCT and MPR using high iodine concentration contrast media, have allowed the identification of these small pancreatic veins. In this Feature Section, Dr. Hongo and colleagues describe detailed anatomic variation of the venous drainage of intrapancreatic veins by analysis of the venous phase of multidetector-row CT (MDCT).

Extrapancreatic neural plexus and peripancreatic lymphatic networks

The new UICC TNM classification published in 2002 reflects the influencing prognostic factors of patients with pancreatic cancer [14]. In clinical practice, there are very few patients with stage I pancreatic cancer because there is no screening method established (nor risk-group setting) for pancreatic cancer at this point. Furthermore, it is very important to know that even T1 pancreatic cancer can infiltrate surrounding peripancreatic tissue including regional lymph nodes [15]. Despite recent advances of imaging including 3D volume data setting in multidetector-row CT (MDCT) and MRI, little attention has been paid to imaging of normal and pathological conditions of peripancreatic lymphatic networks, peripancreatic neural plexuses, and pancreatic veins, which are frequently involved by pancreatic cancers and affect the prognosis of patients with pancreatic cancers.

Retroperitoneal infiltration via extrapancreatic nerve plexuses is one of the major causes of postoperative recurrence. The second portion of the pancreatic head nerve plexus is frequently involved and is contiguous to the root of the small bowel mesentery. The normal extrapancreatic nerve plexus can hardly be seen on CT, but it is known that the inferior pancreaticoduodenal artery (IPDA) and vein (IP) pass through the second portion of the pancreatic head nerve plexus [16, 17]. Recently, evaluation by CT is reported to be able to demonstrate tumor invasion to the extrapancreatic nerve plexus showing obliteration of the IP and/or the first jejunal trunk (JT) [18].

Imaging findings of peripancreatic lymphatic invasion by pancreatic cancer have not been described before, though lymphatic networks exist around the pancreas having close anatomical relationship with neural plexuses and blood vessels. On pathologic examinations, there may be two ways of peripancreatic lymphatic invasion by

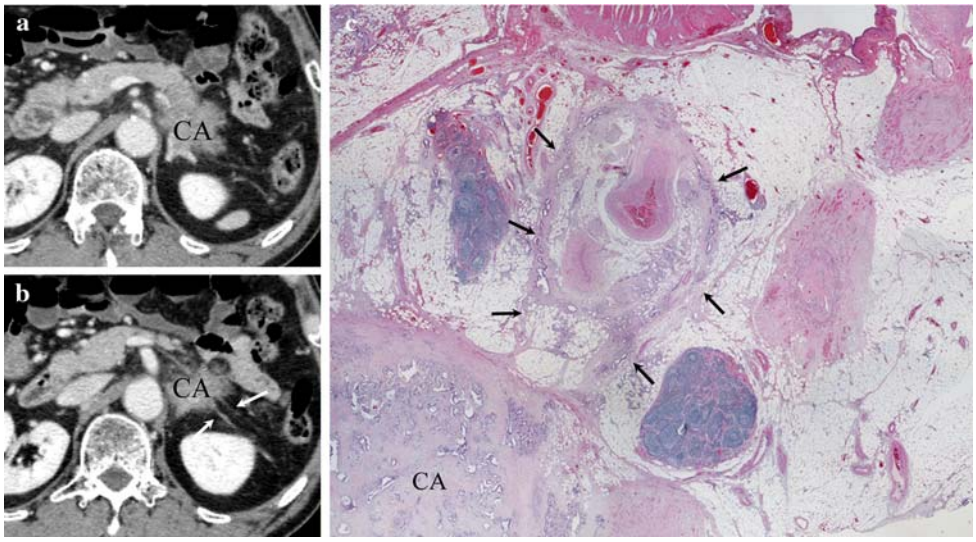

Fig. 2. Lymphatic spread of pancreatic cancer. Axial images of postcontrast CT showed some linear areas of increased attenuation (*arrows*, **b**) in the retroperitoneal fat planes which are contiguous to the cancer of pancreatic tail (*CA*, **a**, **b**). Resected specimen revealed cancer invasion along the lymphatic channels (*arrows*, **c**) which are contiguous to the cancer of the tail (*CA*, **c**). The foci of cancer cells in the peripancreatic fat are associated with fibrous stroma similar to the primary cancer (*CA*, **c**).

pancreatic cancer; tumor emboli that fill up the dilated lymphatics [19] and tumor extension along the lymphatic channels (Fig. 2). In this Feature Section, Dr. Sai and colleagues describe the CT features of normal peripancreatic lymphatic networks, and state that areas of increased attenuation in the peripancreatic fat plane corresponding with anatomical networks in the patients with known pancreatic cancer may indicate cancer invasion to lymphatics.

Differentiation of pancreatic cancer from pancreatic fibrosis by perfusion characteristics on CT and MRI

In some clinical cases, difficulties can arise in the differentiation of autoimmune pancreatitis (AIP) and mass-forming chronic pancreatitis from pancreatic cancer [20, 21]. Late enhancement of pancreatic carcinomas has been observed on CT by a few investigators [22, 23]. On delayed phased MRI, significant differences between enhancement of cancer and benign fibrosis have been reported [24]. Rich fibrotic stroma in pancreatic adenocarcinoma would play a major role in these perfusion characteristics along with architectures of so-called tumor vessels [25] and vascularity of the cancer. In this Feature Section, Dr. Hata and colleagues describe the time-attenuation curve (TAC) pattern of pancreatic cancer on triple-phase postcontrast CT with correlation to histopathologic features including amount of fibrotic stroma and vascularity. Dr. Yamada and colleagues describe TAC patterns of normal pancreatic parenchyma, chronic pancreatitis, and pancreatic cancer. Chronic pancreatitis and pancreatic adenocarcinoma could be differentiated according to TACs of the second and third phases obtained during triple-phase CT with diagnostic accuracy of around 90%.

IPMNs as a clue for detecting early-stage pancreatic cancer

The risk of developing pancreatic cancer for patients with hereditary pancreatitis (HP) is extremely high [26]. This poses opportunities for secondary screening in those patients. Otherwise there has been no effective screening method for detecting early-stage pancreatic cancer, though a lot of clinical efforts have been made. Periodic checkups by imaging and/or EUS (endoscopic ultrasound) for patients with main pancreatic duct dilatation or cystic lesions are considered to be an effective method for the early detection of pancreatic cancer [27]. The possibility of clinical utility of genomic abnormalities including tumor suppressor genes such as Ki-67, p53, and DPC4 remains unclear. Stool K-ras analysis has been reported as a potential screening method for the early detection of pancreatic adenocarcinoma and precursor lesions such as pancreatic ductal mucinous cell hyperplasia [28]. Identifying the responsible gene abnormalities for early pancreatic cancer using array-based comparative genomic hybridization is just in the early stages.

Intraductal papillary mucinous neoplasm (IPMN) is a relatively new entity and has been increasingly recognized recently as belonging to a well-characterized group of intraductal mucin-producing neoplasms of the pancreas with malignant potential [29]. Thin-section dynamic CT has been shown to be a useful modality for follow-up of IPMNs, especially those that have progressed into invasive carcinomas [30, 31]. When a solid mass in the pancreatic parenchyma surrounding the dilated pancreatic ducts appears on follow-up CT, progression to an invasive carcinoma should be considered and surgical resection is recommended. In this Feature Section, Dr. Yamada and colleagues describe the

imaging features of the invasive carcinoma originating from intraductal papillary mucinous neoplasms of the pancreas.

Conclusion

Recognition and understanding of the imaging anatomy of the pancreas, including pancreatic veins, lymphatic pathways, and extrapancreatic neural plexuses, might lead to the accurate staging of pancreatic cancer. Knowledge of arterial territories or segmental anatomy of the pancreas might be useful for locally targeted treatments for pancreatic cancer. Understanding perfusion characteristic of pancreatic cancer, which is determined by the vascularity and presence of fibrotic stroma, can differentiate cancer from benign pancreatic fibrosis. Careful follow-up of IPMNs leads to detection of early-stage pancreatic cancers.

I sincerely hope that the knowledge communicated in this Feature Section will be shared by many clinical researchers and will underscore the next step in pancreatic imaging and treatment.

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