Review Article

Imaging of the pancreas: Recent advances

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ABSTRACT

A wide spectrum of anomalies of pancreas and the pancreatic duct system are commonly encountered at radiological evaluation. Diagnosing pancreatic lesions generally requires a multimodality approach. This review highlights the new advances in pancreatic imaging and their applications in the diagnosis and management of pancreatic pathologies. The mainstay techniques include computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), radionuclide imaging (RNI) and optical coherence tomography (OCT).

Key words: Computed tomography, endoscopic ultrasound, magnetic resonance imaging, optical coherence tomography, pancreatic imaging, radionuclide imaging, recent advances

Introduction

Pancreatic imaging is an essential tool in the early diagnosis and staging of pancreatic disease. The diagnosis of pancreatic diseases generally requires the combined use of different imaging modalities, allowing the evaluation of pancreatic ducts, the pancreatic parenchyma and adjacent soft tissues. This review analyzes the most recent advances in pancreatic imaging.

Techniques of Pancreatic Imaging

Since the introduction of computed tomography (CT) scan in late 1970s, there has been dramatic improvement in pancreatic imaging. With early conventional CT scanners, only 10-mm thick slices with a large acquisition time of 1 minute/slice were obtained; this resulted in motion artifacts and limited resolution. In addition, only ionic intravenous contrast agent was administered slowly over time. Helical (spiral) CT scanners, introduced in late 1980s, allowed much faster data acquisition with a slice thickness of 1–2 mm and a volume data set for three-dimensional imaging. Power injectors were introduced now, allowing bolus contrast administration for fast dynamic scanning. The better spatial resolution and dedicated pancreatic and portal venous phase (dual-phase helical CT) dynamic scanning increased the tumor conspicuity and allowed better detection and staging of pancreatic neoplasms. However, the multiplanar imaging still suffered from stair-stepping artifacts. This drawback was overcome with the introduction of multidetector computed tomography (MDCT) in late 1990s. In contrast to single-detector helical CT scanners, these scanners use multiple detector rows, are 10 times faster, and can obtain 16–64 slices per rotation at a slice thickness of 0.5 mm. The MDCT has improved volume coverage speed and spatial resolution along z-axis, and allows three-dimensional reformatting due to isotropic voxels and exquisite multiplanar reconstruction of pancreatic anatomy. High speed of MDCT also allows organ imaging in clearly defined perfusion phase.[1]

MDCT permits the acquisition in the arterial phase, pancreatic (parenchymal) phase and portal venous (hepatic) phase with a delay of 20, 40 and 70 sec, respectively, using 120 ml of iodinated contrast medium injected intravenously

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at a rate of 3 ml/sec. Maximum enhancement of pancreas and the maximum tumor-to-parenchymal attenuation difference is achieved during pancreatic phase followed by portal venous phase and the arterial phase. Therefore, for tumor detection, particularly adenocarcinoma [Figure 1], pancreatic and portal venous phases are superior to those obtained in the arterial phase. However, for detection of vascular invasion and liver metastases, the sensitivity of images obtained in the portal venous phase is better than those obtained in the pancreatic and arterial phases. Images of the pancreas obtained in the arterial phase are helpful in good visualization of the peripancreatic arterial supply. Using this image acquisition, it is possible to diagnose and characterize a small pancreatic lesion (less than 2 cm in diameter) more accurately, establish the level of peripancreatic vascular invasion and detect liver metastasis. Most of the authors are of opinion that the pancreatic parenchymal phase and the portal venous phase (dual phase) are sufficient for the detection of the pancreatic adenocarcinoma and the arterial phase may be reserved for those patients who require CT angiography (CTA). Thus, the biphasic contrast-enhanced MDCT is a very effective diagnostic tool in the detection and accurate preoperative staging of pancreatic malignancies, which remain a challenge for radiologists. The addition of multidetector CTA improves the accuracy of diagnosing unresectable pancreatic carcinoma. Features indicating vascular involvement include: tumor involvement for one half of the vessel's circumference, focal narrowing of the vessels and dilatation of peripancreatic veins. Criteria for unresectability include involvement of superior mesenteric artery or celiac trunk, involvement of superior mesenteric vein–portal vein confluence, and hepatic, peritoneal or lymph nodal metastases. The major limitation with the use of CT is that it cannot accurately differentiate between benign and malignant lymph nodal enlargement.[1-5]

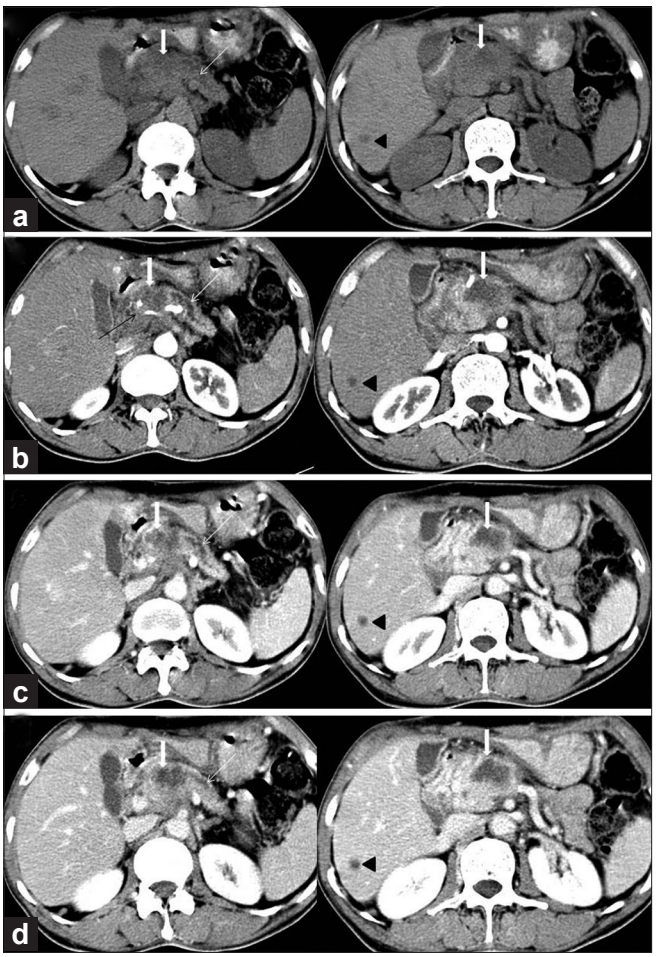

Figure 1: Pancreatic adenocarcinoma. Axial plain (a) and triple-phase contrast-enhanced CT upper abdomen obtained in arterial (b), pancreatic parenchymal (c) and portal venous (d) phase, in a 70-year-old male who presented with severe abdominal pain, demonstrates an ill-defined nonenhancing hypodense mass involving the head and proximal part of body of pancreas (thick vertical white arrow). Peripancreatic extension with encasement/attenuation of celiac axis branches (thin black arrow), infiltration and dilatation of main pancreatic duct (thin white arrow) and liver metastases (black arrow head) are also evident which make the tumor unfit for resection. Note that the pancreatic and portal venous phases are best for tumor detection, the hypovascular metastases stand out best in portal venous phase, while the arterial phase is good for demonstration of celiac axis encasement

Recently, a 320-detector CT scan has been introduced. Comparison of 320-detector volumetric and 64-detector helical CT images of the pancreas revealed no significant difference in CT numbers of pancreas. Signal-to-noise ratio (SNR) of the pancreas on biphasic images was significantly lower in the 320-detector group than in the 64-detector group. Image quality was acceptable in both the groups and was slightly better in the 64-detector group for pancreatic phase axial images and arterial phase multiplanar reformatted images. No significant difference was found in the depiction of pancreatic parenchyma, main pancreatic duct and focal pancreatic lesions.[6]

Majority of pancreatic endocrine tumors [Figures 2 and 3] are small and very vascular and will be best seen in arterial phase images; however, in some cases, portal venous phase imaging best demonstrates the tumor. Thus, dual-phase MDCT imaging, at 20 and 70 sec following intravenous contrast infusion, is recommended to optimize the detection of both the primary tumor and liver metastases.[7]

MDCT is the modality of choice for the diagnosis and staging of acute pancreatitis. It is highly sensitive in detecting the necrosis, the hallmark of severe acute pancreatitis and peripancreatic fluid collections. CT outclasses all imaging modalities in detecting calcifications [Figure 4], a specific sign of advanced chronic pancreatitis, and complications associated with chronic pancreatitis such as pseudocyst, intraductal calculi, inflammatory masses or

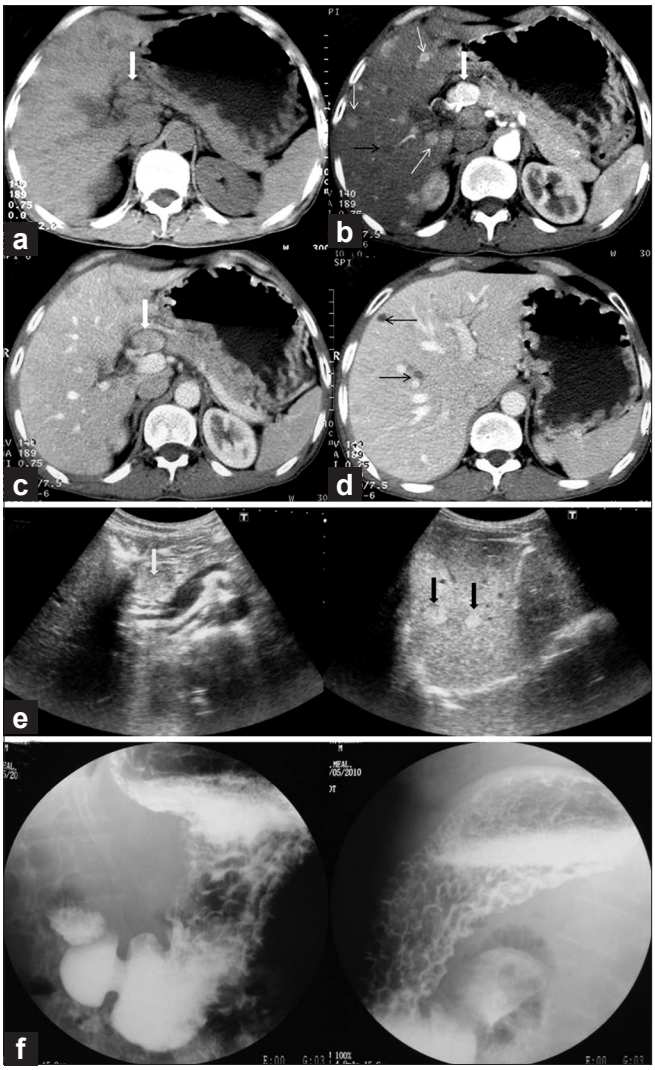

Figure 2: Functioning islet cell tumor: Gastrinoma in a 25-year-old male patient with Zollinger–Ellison syndrome (ZES). Axial plain (a) and dual-phase contrast-enhanced CT abdomen obtained in arterial (b) and portal venous (c, d) phase shows a small, well-defined mass of 1 × 0.5 cm size in the gastric triangle (thick vertical white arrow). The lesion is homogenous and hypodense on non-contrast CT, shows marked homogenous contrast enhancement in arterial phase image (suggesting hypervascular nature) and washout of contrast in portal venous phase. Majority of liver metastases from the tumor are hypervascular, appearing as homogenous hyperenhancing foci (thin white arrow) in arterial phase image, while a few are hypovascular appearing as non-enhancing foci both on arterial and portal venous phase images (thin black arrow). Due to hypervascular nature, both the tumor (thick vertical white arrow) and metastases (thick vertical black arrow) appear echogenic on ultrasound (e). Double-contrast barium meal (f) of the same patient demonstrates thickened gastric folds. Endoscopy revealed peptic ulceration of upper gastrointestinal tract. Patient also had hypergastrinemia

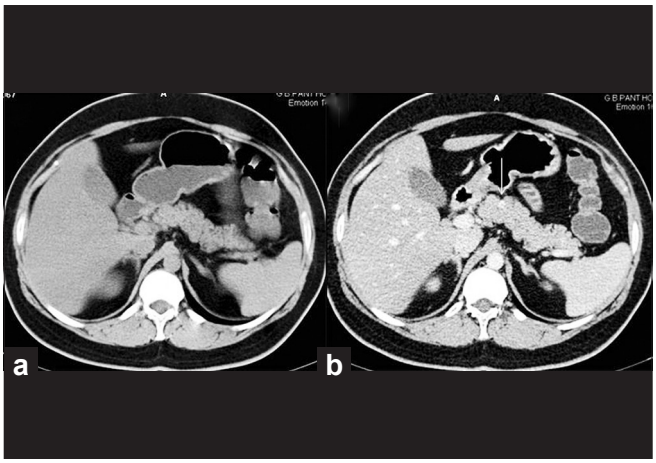

Figure 3: Functioning islet cell tumor: Insulinoma in a 55-year-old male patient who presented with hypoglycemic symptoms. Axial plain (a) and dual-phase contrast-enhanced CT abdomen obtained in portal venous phase (b) shows a well-defined intrapancreatic subcentimeter size mass (thin white arrow). The lesion is inconspicuous on non-contrast CT, however shows marked homogenous contrast enhancement in portal venous phase image

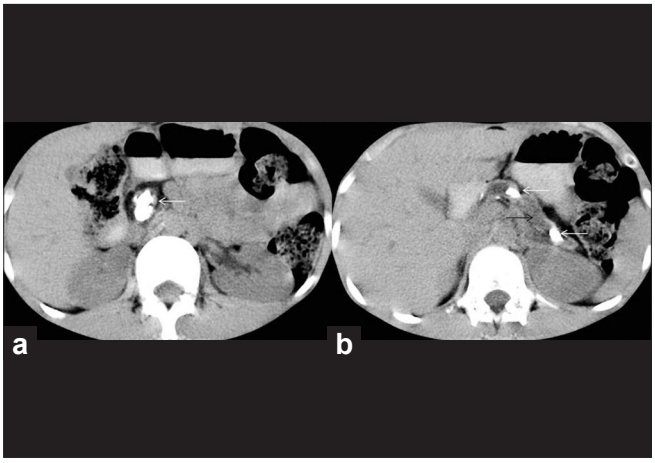

Figure 4: Chronic pancreatitis. Axial non-contrast CT abdomen shows features of chronic pancreatitis evidenced as atrophic pancreas, dilated main pancreatic duct (thin black arrow) and dense calcifications (thin white arrow) in pancreatic head region and within the dilated main pancreatic duct

pseudoaneurysm. However, its sensitivity to detect early chronic pancreatitis is poor. Unenhanced CT has negative attenuation value of pancreatic tissue replaced by the fat, therefore can reliably diagnose diffuse fatty change involving the pancreas.[8] MDCT is also the noninvasive modality of choice for characterizing pancreatic cystic lesions more accurately.[9]

MDCT perfusion study is an evolving and promising technique having various applications. Perfusion CT involves dynamic scanning after administration of iodinated contrast material, followed by mathematical modeling to study contrast material kinetics in the tissue. The CT perfusion data set derived from kinetic model allows assessment of physiological parameters such as tumor and normal pancreatic blood flow (BF), blood volume (BV), mean transit time (MTT) and permeability–surface area product (PS). The normal pancreas displays symmetrical BF, BV, MTT and PS. Comparing with normal value, CT perfusion imaging helps in diagnosing various pancreatic diseases (e.g. necrotizing acute pancreatitis, mass

forming chronic pancreatitis) and angiogenesis in different pancreatic neoplasms (e.g. pancreatic and ampullary adenocarcinoma, cystadenoma, endocrine tumors, solid pseudopapillary neoplasm and pancreatic metastasis).[10-13] It aids in differential diagnosis of pancreatic tumors by detecting change in their perfusion pattern.[14] It may help in early detection of small (<2 cm size) pancreatic adenocarcinomas, when these masses are still resectable, thereby improving the prognosis of the patients.[15] It has a crucial role in efficient management in the field of oncology as it provides physiological information about tumor neo-angiogenesis. New blood vessel growth is critical for tumor growth and metastasis, and newer generation oncologic treatment regimens target the neo-angiogenesis and the growth factors that stimulate neo-angiogenesis.[16] Perfusion CT can be used to predict tumor response to concurrent chemotherapy and radiotherapy (CCRT).[17]

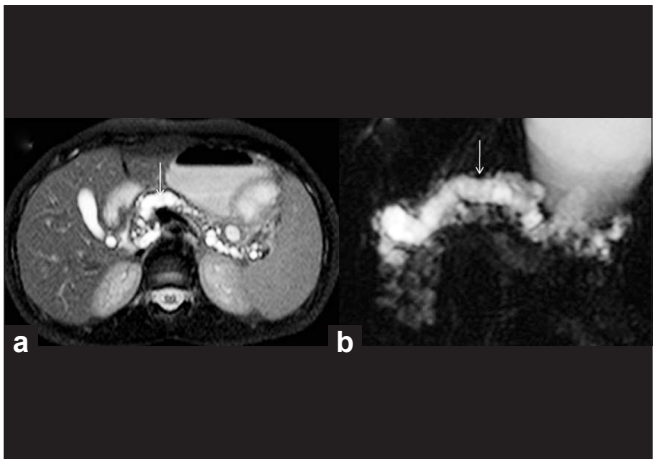

Figure 5: Chronic pancreatitis. Axial fat suppression T2-weighted MR image (a) and MRCP (b) shows atrophic pancreas with gross dilatation of main pancreatic duct and side branches (thin white arrow)

Dynamic contrast-enhanced CT is the mainstay of imaging in suspected pancreatic injury, but is frequently normal in the acute phase. Repeat CT is indicated after 24–48 hours if there are persistent unexplained symptoms or elevated amylase.[18]

Although CT remains the most effective imaging modality for evaluation of the pancreas, magnetic resonance imaging (MRI) is increasingly used for further identification and characterization of pancreatic diseases. Technical innovation in MRI, such as use of phased-array coils, allows improved spatial resolution and faster T1- and T2-weighted sequences for imaging the entire upper abdomen in a single breathhold and providing cross-sectional images of pancreatic parenchyma analogous to CT images. The use of fat saturation pulses and dynamic studies following gadolinium injection increases the sensitivity of MR in detecting pancreatic lesions. MR angiography (MRA) is useful in noninvasive evaluation of splanchnic blood vessels. Half-Fourier T2-weighted pulse sequences for magnetic resonance cholangiopancreaticography (MRCP) allow pancreatic duct and side branch delineation [Figure 5] and detection of anatomic variants such as pancreatic divisum. Administration of secretin further improves the conspicuity of the ductal system, allows monitoring of pancreatic flow dynamics, helps in evaluation of pancreatic exocrine function, and planning surgery or therapeutic endoscopic and follow-up study after therapy. Although MRI is accurate in local staging of the pancreatic malignancies owing to high soft tissue contrast resolution (for assessment of peripancreatic fat infiltration), for evaluation of vascular encasement, peritoneal deposits and lymph nodal involvement, it has limitations as compared to CT. However, for identifying the liver metastases, MRI has high sensitivity and specificity when compared to CT. The use of liver-specific contrast agents further improves the diagnostic value of MRI for detecting liver metastases. Thus, MRI in combination with secretin-enhanced MRCP and MRA is useful in the diagnosis and management of pancreatic malignancies.[19,20] Focal fatty replacement of the pancreas may appear as hypodense mass on contrast-enhanced CT and thus mimic an ill-defined neoplasm. MRI establishes the correct diagnosis of focal fatty replacement of pancreas using dual-echo (in-phase and opposed phase) chemical shift imaging and avoids invasive diagnostic procedures and surgery.[21] Diffusion-weighted MRI helps to differentiate the subtypes of pancreatic endocrine neoplasms on the basis of tumor cellularity and/or extracellular fibrosis that may account for various apparent diffusion coefficient (ADC) values in these tumors.[22] MRI is as sensitive as CT for the depiction of necrosis and peripancreatic fluid collection in the case of acute pancreatitis [Figure 6], but is less sensitive than CT for detection of calcifications associated with chronic pancreatitis. However, fat-suppressed T1-weighted MRI is more sensitive for the detection of early chronic pancreatitis, prior to the development of calcifications. MRI is also useful in differentiating pancreatic pseudocysts [Figure 7] from pancreatic cystic neoplasms [Figures 8–11]. Presence of internal dependant debris is a highly specific MR finding for diagnosing pseudopancreatic cyst.[23] Magnetic resonance spectroscopy (MRS) is a promising clinical tool for oncologic management of patients. MRS can differentiate chronic focal pancreatitis from pancreatic cancer. In proton MRS, chronic focal pancreatitis shows less lipid than pancreatic carcinoma due to difference in fibrous tissue content in the two conditions.[24] MRI also has an important role in the pancreatic transplantation. Standard MRI, MRCP (secretin-induced MRCP) and MRA demonstrate the pancreatic

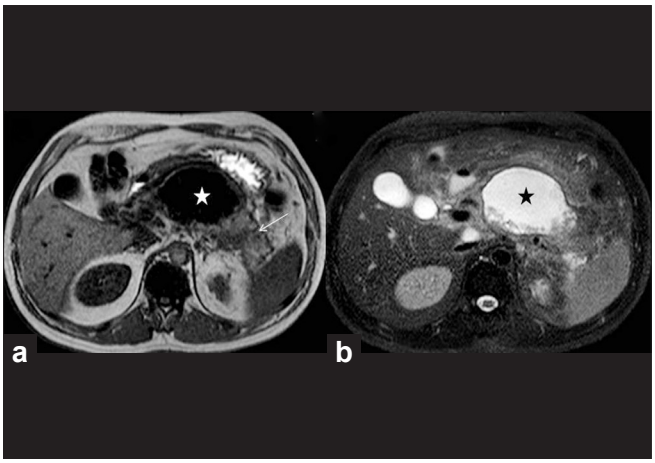

Figure 6: Acute necrotizing pancreatitis. Axial T1W (a) and spectrally selective inversion recovery (SPIR; fat-suppressed T2W) (b) MR images through upper abdomen show severe acute necrotizing pancreatitis. The body of pancreas is replaced by a large cystic appearing lesion (asterisk) showing internal debris in the dependant portion of the cyst. Extensive peripancreatic inflammatory changes are also present, best appreciated on SPAIR image. Pancreatic tissue in the tail region shows heterogeneous signal intensity (thin white arrow) consistent with intraparenchymal inflammatory change

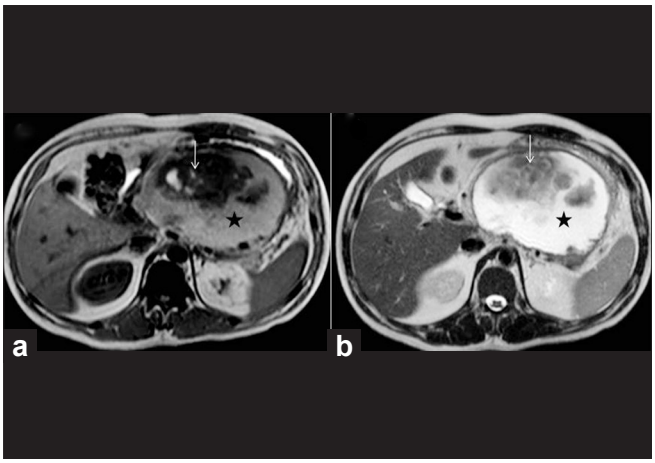

Figure 7: Pancreatic pseudocyst in a 50-year-old male who presented after an episode of pancreatitis. Axial T1W (a) and T2W (b) MR images of abdomen show a large, walled-off cystic lesion localized to lesser sac (asterisk). The lesion shows internal debris along with hemorrhage (arrow). Presence of internal debris is a highly specific MR finding for diagnosing pseudopancreatic cyst

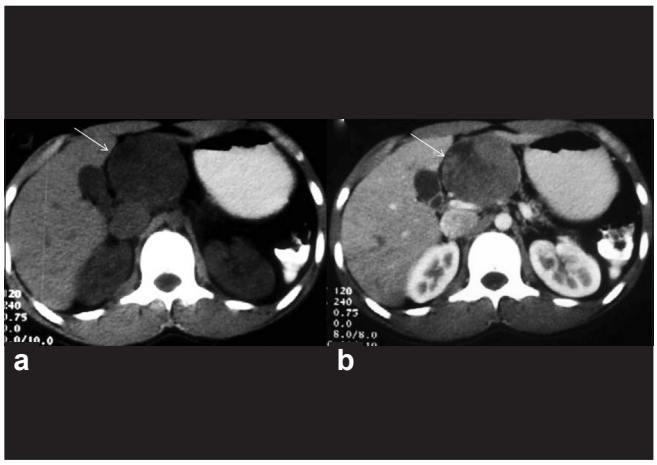

Figure 8: Solid and Papillary Epithelial Neoplasm in a 35-year-old female who presented with epigastric pain. Axial non-contrast (a) and contrast-enhanced (b) CT abdomen shows a mixed solid and cystic mass in the pancreatic head (arrow). The diagnosis of SPEN was confirmed after surgery on histopathologic examination

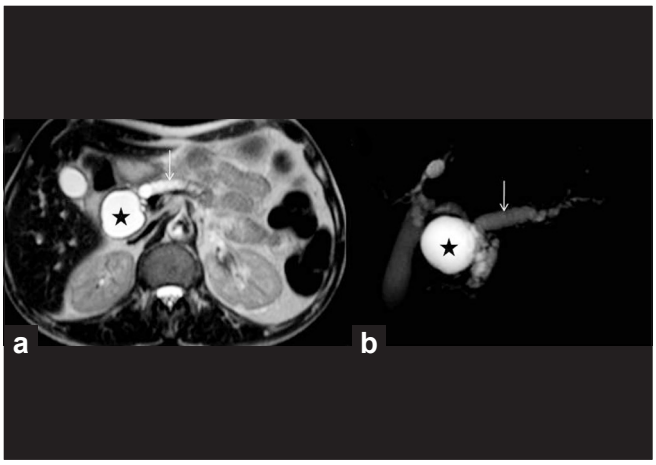

Figure 9: Branch duct type Intraductal Papillary Mucinous Tumor (IPMT) in a 55-year-old male who presented with vague abdominal pain. Axial T2-weighted MR image (a) of upper abdomen shows a well-defined, thin-walled cystic lesion in the pancreatic head (asterisk). Associated dilatation of main pancreatic duct is also evident (thin white arrow), which appears inseparable from the cystic mass lesion on MRCP image (b). ERCP revealed communication between the cystic mass and the dilated proximal pancreatic duct. The diagnosis of IPMT was confirmed on histopathologic examination of the resected tumor

anatomy well before and after transplantation. Serial contrast-enhanced MRI may demonstrate diminished perfusion in case of graft rejection, and the vascular complications are assessed by MRA.[25]

Although high-resolution MDCT with 3D image reconstruction remains the prime imaging modality for diagnosing and staging pancreatic cancers, endoscopic ultrasound (EUS) can be a valuable adjunct to MDCT for diagnostic evaluation of patients with suspected pancreatic tumors. EUS with fine needle aspiration cytology (EUS-FNA) is a highly accurate method for preoperative staging of pancreatic cancer, as it has the ability to obtain the tissue confirmation and permit accurate nodal staging without relying on lymph node size.[26] The intraoperative ultrasound (IOUS) and laparoscopic ultrasound (LUS) are highly sensitive methods to assess tumor resectability during surgery as they permit accurate assessment of location and number of lesions, locoregional tumor extension, vascular

involvement and lymph nodal or liver metastases.[27] EUS, particularly the intraductal endoscopic ultrasonography (IDUS), accurately localizes the pancreatic endocrine tumors, especially those which are too small to be characterized by CT or MRI. EUS with color Doppler further improves the detection of small pancreatic endocrine tumors and adenocarcinomas. Endocrine tumors, being hypervascular, demonstrate abundant color Doppler signal having pulsatile and/or continuous waveform pattern, while majority of adenocarcinomas demonstrate low vascularity.[28] Contrast-enhanced EUS using microbubbles has also shown to improve the detection and characterization of pancreatic lesions and liver metastasis.[29] EUS-FNA for cytology and cyst fluid analysis aids in the differential diagnosis of cystic lesions of pancreas that are indeterminate at cross-sectional imaging.[30] Finally, EUS may also be used therapeutically in image-guided drainage such as gastrocystostomy in pancreatic pseudocyst and celiac plexus neurolysis for pain control in patients of pancreatic cancer or pancreatitis.[31] Ultrasound elastography, a new technique, evaluates the relative stiffness of the tissues. EUS real-time elastography distinguishes normal pancreas from the abnormal pancreas affected by inflammatory or focal disease. However, it cannot differentiate chronic pancreatitis from malignant tumor because of their similar fibrous architecture. This technique is also useful to select lymph nodes suitable for biopsy as it can differentiate between benign and malignant lymph node involvement.[32]

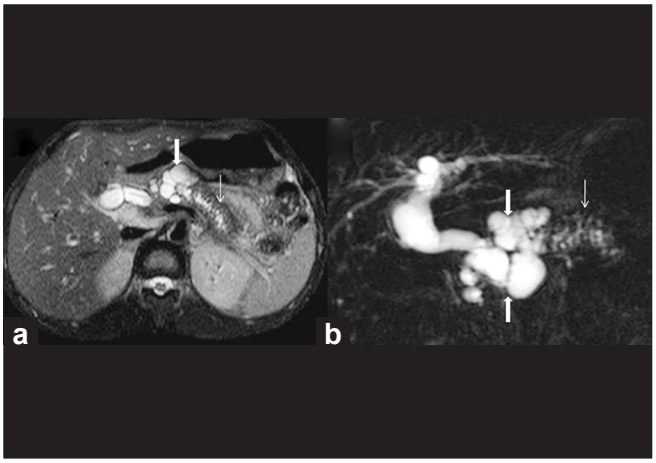

Figure 10: Mucinous cystadenocarcinoma in a 42-year-old female who presented with recurrent upper abdominal pain. Axial T2-weighted MR (a) and MRCP (b) images of abdomen show multilocular macrocystic lesion (thick white arrow) involving pancreatic head. Note fine internal septations within the lesion and associated dilatation of MPD and side branches (thin white arrow). The diagnosis of mucinous cystadenocarcinoma was confirmed after surgery and histopathologic examination

Radionuclide imaging (RNI) aids in improving the diagnosis and staging of the pancreatic tumors, identifying and localizing disseminated disease, differentiating post-treatment recurrent and residual disease from fibrosis, and planning and monitoring response to the therapy. Detection of pancreatic cancer at early stage improves the long-term survival of the patient. The diagnosis of early stage pancreatic cancer (small in size, free of peripancreatic extension and without lymph nodal/liver metastases) is often difficult with the structural imaging techniques. [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG-PET) scanning has been found to be more accurate than other imaging modalities for diagnosing early pancreatic cancer. The sensitivity of PET is superior to CT in detecting lesions less than 2 cm in diameter, but CT scanning is superior to PET for diagnosing cancers larger than 4 cm in diameter because of lower metabolic

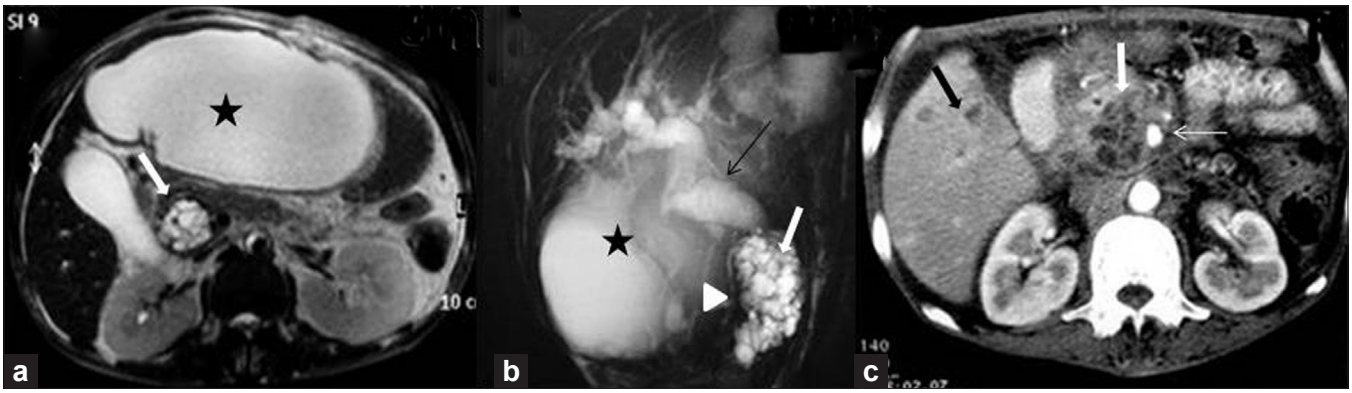

Figure 11: Serous cystadenocarcinoma in a 72-year-old male who presented with jaundice and recurrent abdominal pain. T2-weighted MRI (a) and MRCP (b) show multilocular microcystic lesion involving pancreatic head (thick white arrow). The lesion shows very thin internal septations. Large pseudocyst (asterisk), dilated common bile duct/intrahepatic biliary radicles (CBD/IHBR) (thin black arrow) and normal MPD (white arrow head) are well seen on MRCP. Cystogastrostomy and choledochoduodenostomy were performed to drain the pseudocyst and relieve the jaundice. Three months later, follow-up CECT abdomen (c) revealed increase in size of tumor (thick white arrow), multiple liver metastases (thick black arrow) and encasement of superior mesenteric vessels (thin white arrow) by the cystic mass. The diagnosis of serous cystadenocarcinoma made on imaging was confirmed after surgery and histopathologic examination

rates in larger tumors.[33] The sensitivity of FDG-PET for detecting lymph node metastasis in patients with pancreatic cancer and differentiating pancreatic cancer from chronic pancreatitis is more than that of CT or MRI.[34] FDG-PET can also alter the management of pancreatic cancer by revealing unsuspected metastases to liver, lung and bone, thereby avoiding the mortality and morbidity associated with unnecessary surgical intervention.[35] FDG-PET has the advantage of differentiating residual and recurrent tumor from postoperative inflammation or fibrosis.[36] It is also useful in the follow-up of patients undergoing chemoradiation therapy or surgical resection.[37] FDG-PET is less sensitive for detecting pancreatic endocrine tumors, particularly those which are non-functional and have small size at presentation. However, two PET radiopharmaceutical agents such as C-11 labeled 5-hydroxytryptophan (5-HPT) and L-Dopa are known to detect endocrine pancreatic tumors.[38] FDG-PET has been found to be more accurate than CT in characterizing cystic pancreatic lesions as malignant.[39] The main drawback of PET is its relative low spatial resolution which limits its role in detecting direct invasion of adjacent structures or encasement of blood vessels; these factors are important in planning surgery. [111]In-octreotide single-photon emission computed tomography (SPECT) has also shown to improve the localization of pancreatic endocrine tumors. It has been established that the anatomical–functional image fusion techniques such as hybrid PET/CT and SPECT/CT improve the localization and characterization of pancreatic endocrine tumors and therefore alter the treatment plan.[40]

Optical coherence tomography (OCT) is a new optical imaging modality introduced in 1991. It uses infrared light to produce high-resolution, cross-sectional, subsurface imaging of the microstructure. It has a promising role in evaluating pancreaticobiliary ductal system, as it can recognize different patterns of the duct wall structure in neoplastic and non-neoplastic conditions. OCT has high diagnostic accuracy, better than brush cytology, for distinguishing neoplastic from a non-neoplastic MPD stricture.[41]

Thus, we conclude that MDCT, MRI, EUS and RNI are excellent modalities for both detection and characterization of pancreatic lesions. Structural imaging techniques such as CT and MR provide superior information regarding local tumor invasion and surgical resectability, whereas FDG-PET offers a noninvasive and accurate method for detection of early pancreatic cancer, unsuspected metastases, differentiation between benign and malignant pancreatic lesions (such as inflammatory or scar tissue from recurrent or residual tumor), and evaluation of pancreatic masses with equivocal CT/MRI diagnosis. EUS-guided aspiration and biopsy is useful in cases that are indeterminate at cross-sectional imaging. OCT has emerged as a new technique that differentiates between neoplastic and non-neoplastic pancreatic duct stricture.

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