



A narrative review of imaging for pancreas adenocarcinoma: staging, surgical considerations, and surveillance

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Background and Objective: Pancreas adenocarcinoma is a disease with dire prognosis. Imaging is pivotal to the diagnosis, staging, reassessment, surgical planning, and surveillance of pancreas cancer. The purpose of this paper is to provide the reader an overview of current imaging practices for pancreas adenocarcinoma.

Methods: A literature search of original papers and reviews through 2022 was performed using the PubMed database. The most current American College of Radiology Appropriateness Criteria and National Comprehensive Cancer Network guidelines on pancreas cancer imaging were also included.

Key Content and Findings: Multidisciplinary team care at a high-volume institution is instrumental to optimal patient management and outcomes. It is therefore important for all team members to be aware of imaging modality options, strengths, and challenges. Additionally, a high-level understanding of imaging findings is useful clinically. This manuscript provides a current overview of imaging modalities used in the identification and assessment of pancreas adenocarcinoma, including ultrasound, computed tomography, magnetic resonance imaging, and positron emission tomography. Imaging findings, including the expected and unexpected, are reviewed to give the novice imager a better understanding.

Conclusions: This review provides a current overview of imaging for pancreas adenocarcinoma, including strengths and weakness of various imaging modalities; therefore, providing the reader with a robust resource when considering imaging in the management of this disease.

Keywords: Pancreas cancer; pancreas adenocarcinoma; imaging; staging; surveillance

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Introduction

Background

Pancreas ductal adenocarcinoma (PDAC) is an aggressive tumor with an increasing incidence and poor prognosis, with a 5-year survival of only 11.5% (1-3). Early detection, when the tumor is surgically resectable, is the only hope for cure; however, only a minority (10–15%) present with resectable disease (2). Due to the low lifetime risk of

approximately 1.3%, and the lack of a robust screening mechanism, screening of the general population is not recommended (3).

Rationale and knowledge gap

Imaging plays a crucial role in both the diagnosis and staging of PDAC. Initial diagnosis of a lesion must not be missed on the unexpected exam, such as imaging

from the emergency room for nonspecific symptoms, as reported in 50–70% of cases in one study (4). Similarly, robust differentiation from other differential diagnoses is important in guiding management (5).

Accurate staging has major implications on treatment and prognosis (6). The goal is to prevent overstaging which would remove the possibility of surgical cure, while also not understaging and inflicting unnecessary morbidity of a surgery that offers no benefit.

Objective

This overview will delve into the imaging modality options for early detection, accurate staging, and optimal surveillance of pancreas adenocarcinoma. Staging as well as preoperative considerations will be reviewed. Lastly, expected and unexpected findings during the surveillance period will be discussed.

To our knowledge, this is the most recent review to discuss all noninvasive imaging modalities, including their distinct opportunities and challenges when imaging PDAC. Additionally, our institution has a unique opportunity to provide current state of the art imaging examples, specifically with magnetic resonance imaging (MRI), as we are one of the few institutions that has solely utilized MRI for all imaging of the pancreas for greater than 10 years. The up-to-date assessment of imaging, as well as the MR examples, are strengths to the review. A limitation is the lack of endoscopic ultrasound (EUS) discussion as we regarded the invasive EUS modality to be a separate consideration used more for pathology diagnosis rather than a primary imaging tool for staging and surveillance.

The manuscript is organized to first describe the various imaging modalities available with their respective strengths and weaknesses, and to then focus on the imaging findings during the time course of PDAC treatment. We present this article in accordance with the Narrative Review reporting checklist (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-22-1044/rc>).

Methods

A literature review was conducted via the PubMed database. Search terms included pancreas adenocarcinoma, pancreatic ductal carcinoma, imaging, endosonography, endoscopic ultrasound, ultrasound, computed tomography, magnetic resonance imaging, multi-detector computed tomography, dual-energy computed tomography, positron emission

tomography, cholangiopancreatography and contrast-enhanced. *Table 1* is provided for additional detail.

Imaging modalities: opportunities and challenges

Ultrasound

Transabdominal ultrasound (US) offers an accessible and affordable imaging modality, with lack of ionizing radiation or exposure to contrast media. However, challenges include high operator dependence, difficult imaging due to the retroperitoneal location of the pancreas, overlying bowel gas, and obesity with a limited imaging window (7,8). These hurdles limit the utility of US in staging and surveillance, with the American College of Radiology (ACR) Appropriateness Criteria listing US in the Usually Not Appropriate category (7). While the initial diagnosis may be nicely depicted as a hypoechoic mass with or without pancreatic and biliary duct dilation in the workup for jaundice or abdominal pain (*Figure 1A,1B*); once the diagnosis is suspected, the patient should then be further assessed with dedicated cross-sectional computed tomography (CT) and/or MRI (7,9).

Computed tomography

CT is the most commonly accepted modality for the diagnosis, staging, and surveillance of PDAC. CT offers accessible, reproducible imaging with high spatial resolution and well-defined protocol parameters, and it is deemed Usually Appropriate by ACR Appropriateness Criteria (7,9,10). Some drawbacks of CT include the use of ionizing radiation and exposure to iodine-based contrast agents, which can be an important consideration in patients with allergies and/or suboptimal kidney function (11).

Current National Comprehensive Cancer Network (NCCN) recommendations state that dedicated pancreas protocol CT or MRI be performed in the evaluation of PDAC even if a standard single-phase CT is already available (12). Pancreas protocol CT includes a dual phase study with negative oral contrast, helical scanning, and thin sections (*Figure 2A,2B*) (7,9). The dual phases are acquired in the pancreas parenchymal phase (40–50 seconds) and portal venous phase (65–70 seconds). The thinnest slice thickness available should be obtained in order to recreate high quality reformats and volumetric imaging.

Dual energy CT (DECT) has been investigated more

Table 1 Search strategy

Items	Specification
Date of search	10/2022 (initial), 01/2023 (revision)
Databases and other sources searched	PubMed
Search terms used	Pancreas adenocarcinoma, pancreatic ductal carcinoma, imaging, endosonography, endoscopic ultrasound, ultrasound, computed tomography, magnetic resonance imaging, multi-detector computed tomography, dual-energy computed tomography, positron emission tomography, cholangiopancreatography and contrast-enhanced
Timeframe	No limit
Inclusion and exclusion criteria	Inclusion: articles published in the English literature and including human subject. Exclusion: articles published in languages other than English and/or with nonhuman subjects
Selection process	Focus placed on original papers, reviews, and society guidelines

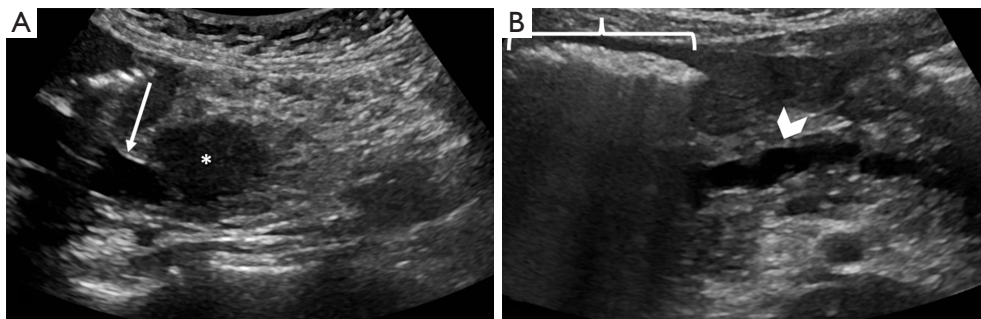


Figure 1 US of pancreas head mass. (A) US in a 46-year-old woman with right upper quadrant pain demonstrates a 3.1 cm hypoechoic mass (asterisk) causing biliary duct dilation (arrow). (B) During portions of the exam, the mass is obscured by overlying bowel gas (bracket) while a dilated pancreatic duct remains visible (chevron). US, ultrasound.

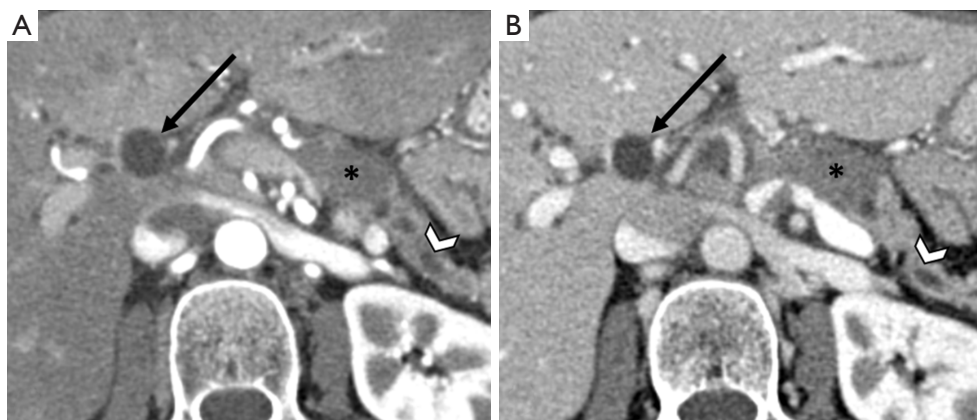


Figure 2 CT of pancreas body mass. Axial (A) arterial and (B) portal venous phase CT in a 53-year-old woman demonstrates a 4 cm hypodense pancreas body mass (asterisk) which causes pancreatic duct (chevron) and mid common bile duct dilatation (arrow). CT, computed tomography.

Table 2 Magnetic resonance imaging protocol for pancreas cancer

Sequence	Flip angle (degrees)	Repetition time (ms)	Echo time (ms)	Slice thickness (mm)	Slice gap (mm)	Field of view (mm ²)
Coronal T2 SSFSE	140	1,300	93	5	6	319×319
Axial T2 SSFSEfs	160	1,300	100	5	6	210×320
Sagittal T2 SSFSE	135	1,300	111	5	6	218×280
Axial in/out of phase	9	4.53	2.51/1.28	3	N/A	240×320
Axial DWI	90	6,600	50	6	7.2	280×399
3D MRCP	120	1,700	533	1.7	N/A	280×280
Thin axial T2 SSFSE	160	1,300	105	4	4.4	217×290
Thin coronal T2 SSFSE	160	1,300	105	4	4.4	300×300
Axial T1fs pre/post	9	3.36	1.31	3	N/A	210×320
Thin axial T1fs post	13	3.6	1.15	1.5	N/A	225×300
Coronal T1fs pre/post	9	3.2	1.17	3	N/A	318×340
Sagittal T1fs pre/post	9	3.38	1.28	2.5	N/A	224×299

SSFSE, single-shot fast-spin echo; MRCP, magnetic resonance cholangiopancreatography; DWI, diffusion weighted imaging; fs, with fat suppression.

recently with some success. DECT is acquired with two different photon energies and is used to augment contrast enhancement differences between the tumor and the adjacent normal pancreatic parenchyma (10). Metallic artifacts, such as with stents or surgical clips, can also be reduced with DECT. Iodine mapping with DECT has been found useful in improving tumor detection, assessing cystic versus solid components of masses, and evaluating response to therapy (10).

A significant challenge of CT is the decreased sensitivity in identifying liver metastases when compared to MRI (13,14). Given that the recognition of metastatic disease is paramount to the staging and management of PDAC, this is a serious consideration which will be discussed further in the staging section.

MRI

MRI is an additional tool for imaging of PDAC, with studies showing similar sensitivity and specificity for local staging when compared to CT, and increased sensitivity for liver metastases and peritoneal disease (10,15-18). MRI offers superior soft tissue contrast resolution and lack of ionizing radiation, and it is deemed Usually Appropriate by ACR Appropriateness Criteria (7). However, MRI

is less accessible, more expensive, and longer in exam duration compared to CT. MRI also exposes the patient to gadolinium-based contrast agents, which raise concern with allergies or if there are risk factors for nephrogenic systemic fibrosis (NSF). Fortunately, the NSF risk is almost negligible when using group II contrast agents (11). Implanted devices must also be interrogated for safety prior to MRI. Lastly, because MRI is not universally used, some institutions and radiologists may be unfamiliar with pancreas specific imaging techniques and/or interpretation with MRI.

Current NCCN and Society of Abdominal Radiology (SAR) pancreas protocol recommendations for MRI exist (9,10). Our institution's detailed protocol, which has been routinely updated over the last 15 years, is also available (Table 2). Images should be obtained in multiple contrast phases, with thin slice thickness, and magnetic resonance cholangiopancreatography (MRCP) (Figure 3A-3D). The authors highly recommend the use of an antiperistaltic agent to suppress bowel motion during the exam (5).

An additional advantage with MRI is the superior soft tissue contrast resolution, which is particularly useful for depicting subtle non contour deforming pancreatic masses; this is essential given that up to 15% of masses will be isodense and missed on CT (Figure 4A-4C) (6,14).

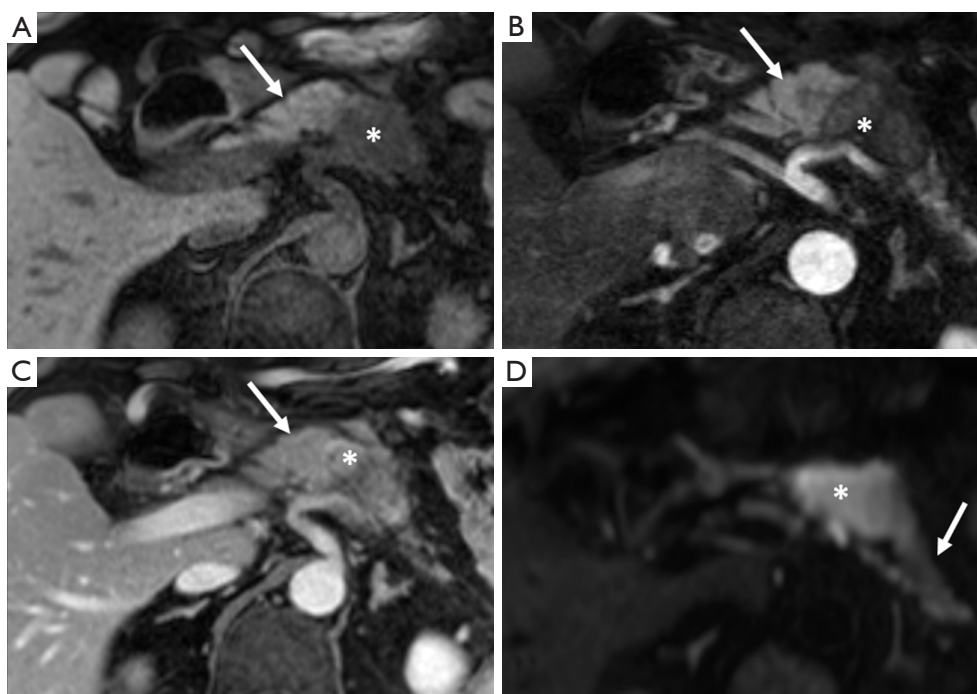


Figure 3 MRI of pancreas body mass. Axial (A) noncontrast, (B) arterial, (C) portal venous, and (D) DWI MR images in a 73-year-old man with new onset diabetes mellitus demonstrate a 4 cm pancreatic body mass (asterisks) that is T1 hypointense (A), hypoenhancing (B-C), and diffusion restricting (D) compared to the adjacent normal parenchyma (arrows). MRI, magnetic resonance imaging; DWI, diffusion weighted imaging.

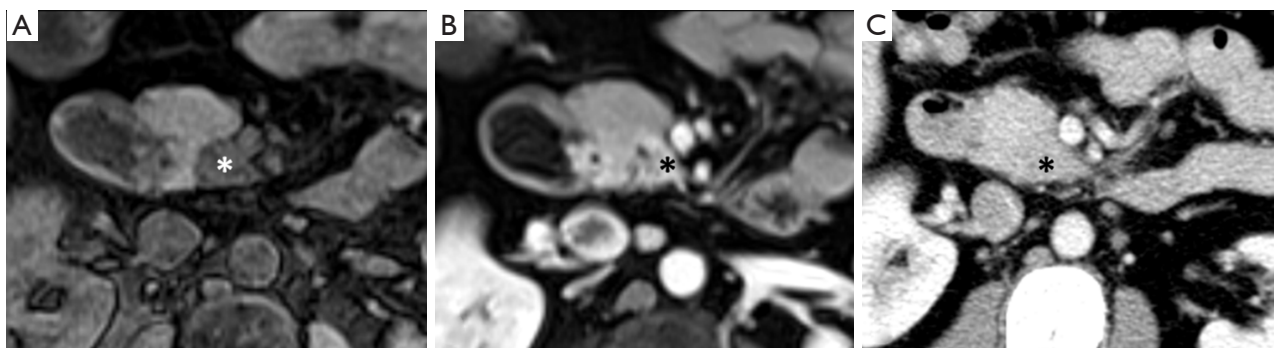


Figure 4 MRI and CT of non-contour deforming uncinate process pancreas mass. Axial (A) noncontrast and (B) arterial MR images in a 44-year-old woman reveal a non-contour deforming mass (asterisks) in the uncinate process of the pancreas, which is isodense and nearly indiscernible on (C) venous phase CT. MRI, magnetic resonance imaging; CT, computed tomography.

Positron emission tomography (PET)

Fluorodeoxyglucose PET (FDG-PET) without and/or with diagnostic CT or MRI has been studied as an option for imaging PDAC (Figure 5A-5C). The CT/MRI portion of the PET, however, is often performed variably, without

or with contrast. When the CT portion is performed with contrast, it is often a single phase only. This variability makes the assessment of FDG-PET utility in PDAC difficult, and it is currently deemed as May Be Appropriate by the ACR Appropriateness Criteria (7).

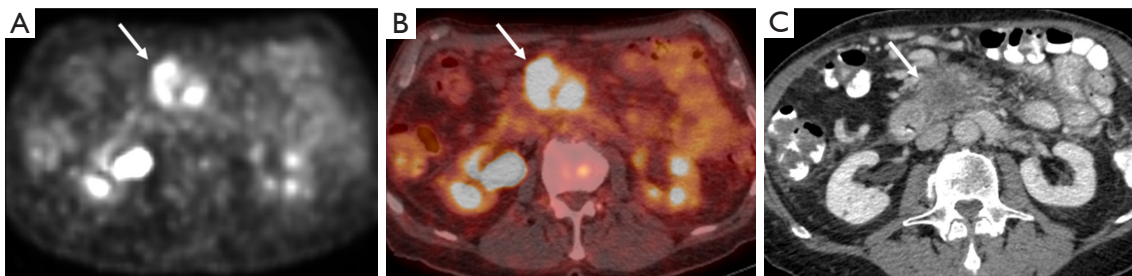


Figure 5 PET and CT of pancreas head mass. (A) Attenuation corrected PET, (B) fused imaged, and (C) corresponding venous phase CT image from exam 1 day prior demonstrate a hypermetabolic pancreas head mass (arrows) with SUV of 8.3 in a 79-year-old man. PET, positron emission tomography; CT, computed tomography; SUV, standardized uptake value.

Given that MRI and/or CT perform well for the diagnosis and local staging of PDAC, PET is often reserved as a tool for identifying distant metastases (7,19). PET-MRI, in particular, offers a potential opportunity for combining the strengths of exquisite soft tissue contrast of MRI plus the ability to identify distant disease via PET. PET-MRI machines are integrated scanners with improved registration and fusion images, and decreased radiation dose compared to PET-CT (10). This PET-MRI combination may prove advantageous in the evaluation of treatment response (using ADC and SUV measurements), assessment for recurrent disease, and identification of metastases (19). However, with PET, challenges remain in the identification of small liver and peritoneal metastases. Appreciating that these are the most common sites for metastatic PDAC, more research is needed to fully understand its role in PDAC imaging (19,20). Future studies to validate PET-MRI utility as an adjunct or replacement to current standard of care imaging will ideally be performed with prospective enrollment, consistent PET and MR scanning techniques, and with cost benefit analysis. While the authors are unaware of a prospective study focused specifically on peritoneal carcinomatosis in PDAC, Furtado *et al.* recently demonstrated improved peritoneal carcinomatosis detection using PET-MRI in various primary abdominopelvic malignancies (21).

Regardless of the modality, it is proposed that each institution follow a workflow and protocol that is optimized and familiar to ultimately provide best patient care. If possible, initial dedicated pancreas imaging should be obtained prior to any stent placement to minimize confounding inflammatory changes. Once a patient is diagnosed with this dismal disease, it is recommended that they be referred to a high-volume tertiary care center (12).

Imaging features: staging, preoperative, and surveillance

Initial staging

Imaging features of pancreas adenocarcinoma common to all modalities include a hypovascular, hypoenhancing mass with desmoplastic stroma, which manifests as an ill-defined, often infiltrative mass that is hypodense/hypointense to the adjacent pancreas parenchyma (Figures 2-4) (10,22). Larger tumor size and tumor rim enhancement on MRI have been shown to portend a poorer prognosis (23). Typical secondary findings consist of pancreatic duct dilation, biliary duct dilation, and vascular encasement (22). A classic imaging finding is that of the “double duct sign,” resulting from both biliary and pancreatic duct dilation due to an obstructing pancreatic head mass (Figure 6) (5,10). Reporting should include information on tumor size, enhancement, location, biliary and/or pancreatic duct dilatation, vessel involvement and/or variants, as well as extrapancreatic spread (lymph nodes, liver, peritoneum) (9).

The American Joint Committee on Cancer staging system is based on tumor size, lymph node involvement, and the presence or absence of metastatic disease (24). This staging system provides prognostic information and helps determine eligibility for clinical trials. In the absence of metastatic disease, tumors are then further classified by surgical status, such as with the NCCN Guidelines (12). Survival is dependent on the stage at diagnosis, with those having localized disease afforded the best five-year survival rates (1).

Metastatic disease

Metastatic disease will most commonly present in the liver



Figure 6 Double duct sign. Thick slab MRCP image from a 46-year-old woman with PDAC of the pancreatic head (asterisk) that obstructs and causes dilatation of the biliary (chevrons) and pancreatic ducts (arrows). MRCP, magnetic resonance cholangiopancreatography; PDAC, pancreas ductal adenocarcinoma.

and peritoneum, and less commonly the lungs and bones (14,20,22,25). Liver metastases will declare themselves as typically small, hypoenhancing lesions, often with perilesional or rim enhancement. MRI with diffusion weighted imaging (DWI) provides possibly the most sensitive and specific technique for the identification of even subcentimeter liver metastases, and thus has been proposed as a screening tool for all PDAC patients prior to surgery (Figure 7A-7D) (13,17,26).

Peritoneal disease may show up as stranding, distinct nodules, and/or a thickened peritoneum with or without ascites. MRI, particularly with DWI, has been shown to perform better than CT in detection of small volume peritoneal disease (6,15,27).

Lymph nodes are a limitation to all imaging modalities as larger nodes may be reactive, while smaller nodes may harbor micrometastases. Lymph nodes are characterized as enlarged when greater than 1 cm in short axis; however, this provides a sensitivity of only 14–49% with CT, MRI, or PET (14,20). It is important to note that regional lymph nodes are not considered metastatic, and regionality is

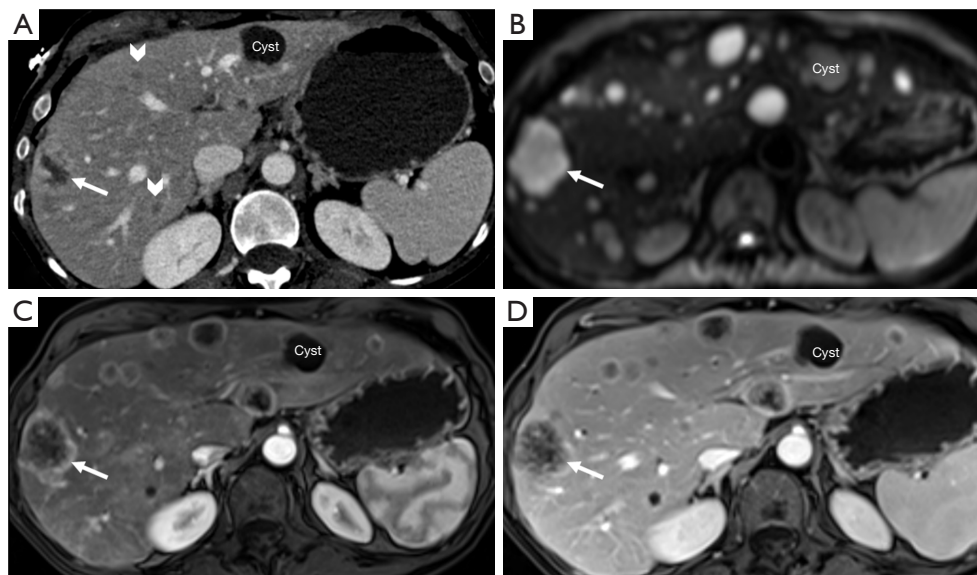


Figure 7 Liver metastases. Axial (A) venous CT, (B) DWI-MRI, (C) arterial, and (D) venous MRI images at the same level with CT and MRI obtained within 14 days of each other demonstrating numerous rim-enhancing, diffusion restricting liver metastases. Only one metastasis (arrow) and two indeterminate lesions (chevrons) are appreciated on this CT slice, while over twenty can be appreciated on the MRI slices (demonstrating the increased sensitivity of MRI). CT, computed tomography; DWI-MRI, diffusion-weighted imaging magnetic resonance imaging.

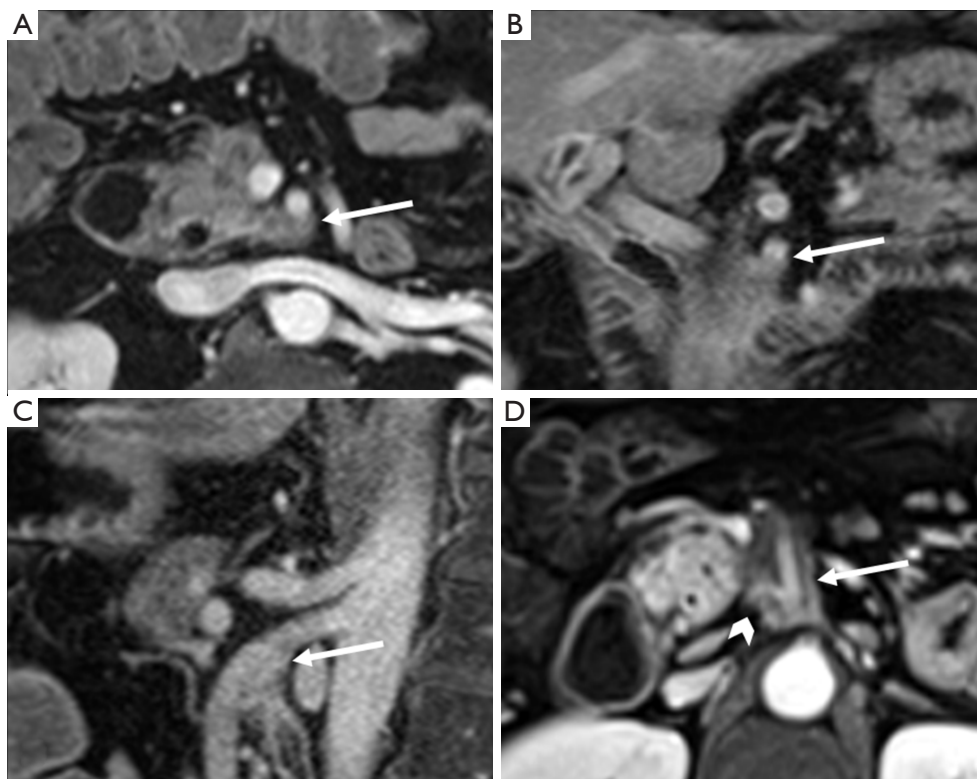


Figure 8 Vascular assessment. Postcontrast MR images in (A) axial, (B) coronal, (C) and sagittal planes in the same patient demonstrate tumor abutment (<180 degrees) with the SMA (arrows). In a separate patient, postcontrast (D) axial MR image shows tumor encasement (>180 degrees) of the SMA (arrow) and replaced right hepatic artery (chevron). MR, magnetic resonance; SMA, superior mesenteric artery.

based on location of the pancreas tumor. For example, hepatic artery lymph nodes are regional if the tumor is in the pancreatic head (compared to the pancreatic tail). However, any lymph nodes outside of the surgical field, such as infrarenal lymph nodes, are considered metastatic (9,14). These should be clearly differentiated during initial assessment for metastatic disease.

Nonmetastatic disease

Nonmetastatic disease will be further classified as resectable, borderline resectable, or locally advanced with multiple surgical classification systems available (6,12). Overall, surgical classification will be based on tumor location and vascular involvement. Unfortunately, interobserver agreement for disease classification has been found to be only moderate (28). However, the area under the receiver operating curve (AUC) for prediction of margin negative resection was high at >0.80 (28).

Tumors are classified as resectable if there is no vascular involvement, or the involved vessel can be removed with the tumor (ex. splenic artery with a pancreas tail mass). Borderline tumors demonstrate potentially resectable/reconstructible vascular involvement, while locally advanced tumors possess nonresectable/nonreconstructible vascular involvement. The exact definitions are variable among classification systems and dependent on surgeon ability, highlighting the essential need for collaborative, multidisciplinary discussion for ultimate classification and best patient care. Vessel involvement of up to 180 degrees is termed abutment, and vessel involvement >180 degrees is termed encasement (*Figure 8A-8C*) (6,9,12).

Because accurate vascular assessment is crucial to staging and surgical planning, viewing the tumor in multiple planes is essential. This can be performed with high quality multiplanar reformats on CT or multiplanar acquisition with MRI. MRI also provides the addition of several distinct

sequences, each with different tissue assessments, to prove or disprove vascular involvement. Variant vascular anatomy, such as a replaced right hepatic artery from the superior mesenteric artery (SMA), also needs to be accounted for to avoid overlooking tumor extension and/or injury in the operating room (*Figure 8D*).

Preoperative reassessment

Once the absence of metastatic disease has been established during initial assessment, it must be reconfirmed at each imaging time point prior to surgery if the patient is undergoing neoadjuvant therapy, such as with borderline and locally advanced tumors. Additional preoperative consideration includes evaluation of response to therapy and addressing of specific surgical nuances. Detailed surgical questions may vary with the surgeon, and thus multidisciplinary communication is again emphasized.

Response to therapy

Neoadjuvant therapy will allow a portion of borderline resectable and even locally advanced patients to go on to surgery with negative margin resection (R0), and similar survival rates as those patients undergoing successful upfront surgery (14). However, imaging assessment after neoadjuvant chemo- and/or chemoradiation therapy offers many challenges regardless of the modality. The treatment itself causes and/or leaves behind fibrosis that cannot be differentiated from residual tumor (6,14). It is important to assess for change in tumor size, enhancement, and diffusion properties (on MRI). Tumor-vasculature relationships must be reevaluated, with a previous study discussing regular overestimation of vessel involvement following neo-adjuvant therapy (26). Even with decreased or diminished solid tumor contact on a vessel, there is often an amorphous perivascular haziness left behind. Therefore, NCCN recommends that in the face of a favorable clinical picture (ex. improved tumor markers and symptoms), lack of progression (i.e., decreased or stable disease) on imaging may be sufficient to proceed to surgery (12,26).

Surgical questions

In general, patients with a mass in the head or uncinate process

of the pancreas [to the right of the superior mesenteric vein (SMV)] will go on to pancreaticoduodenectomy with or without pylorus preservation. Those with a tumor in the body or tail of the pancreas (to the left of the SMV) will undergo subtotal or distal pancreatectomy. Less commonly, the Applebee procedure will be provided as an option for those with a pancreatic body or tail tumor that also involves the celiac axis. Therefore, location and extent are important for surgical determination. The goal of surgery is an R0 (margin negative) resection.

Any aberrant vascular or biliary anatomy is of upmost importance to denote. First, if an anomalous vessel is not recognized, then tumor involving this vessel could be overlooked. Second, variant vessels and biliary ducts can be a source of surgical complication if unknown and thus injured or ligated.

Invasion of other organs, such as the stomach, are also important to point out for surgical planning as these may require additional procedures (ex. partial gastrectomy). And while peripancreatic perineural and duodenal invasion are resected with the specimen, they portend a poorer prognosis (29,30).

There are also areas that can be technically challenging in surgery and lend themselves to variable surgical approaches. For example, tumor extending from the head or uncinate process of the pancreas behind and to the left of the SMA can pose a hardship and should be clearly outlined prior to surgery (31).

Postsurgical surveillance

Following surgery, most patients will begin surveillance imaging in two to four months (32). Imaging prior to this time would be prompted by a clinical scenario inducing a search for a surgical complication. Early complications may include bowel injury, vascular compromise, pancreatic leak, and hepatic abscess (*Figure 9A-9C*). However, when assessing for these complications, normal, expected postoperative findings such as small fluid collections at surgical margins, must be recognized so as not to be mistaken for unexpected abnormalities (*Figure 9D-9F*). Oxidized regenerated cellulose (Surgicel) used for hemostasis during surgery can be particularly confusing to

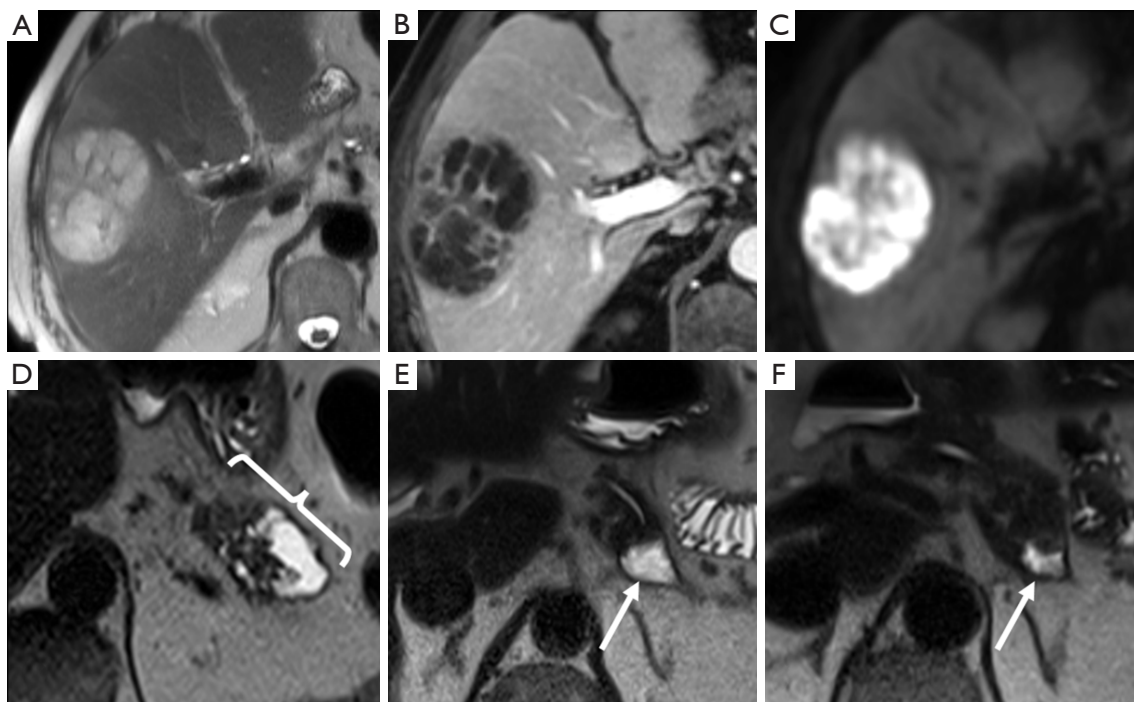


Figure 9 Unexpected and expected postoperative findings. Axial (A) T2, (B) venous, and (C) DWI MR images demonstrate a multiloculated hepatic abscess with rim and septal enhancement and diffusion restriction. In a different patient, axial T2 images (D) preoperatively demonstrates an invasive PDAC arising in IPMN (bracket), with an expected small, simple appearing, and diminishing fluid collection (arrow) at the surgical margin at (E) 3 months and (F) 12 months postoperation. DWI, diffusion-weighted imaging; MR, magnetic resonance; PDAC, pancreas ductal adenocarcinoma; IPMN, intraductal papillary mucinous neoplasm.

the unaware imager and mistaken for an abscess (25).

Surveillance imaging will continue to assess for recurrence, metastatic disease, and benign complications. Recurrent disease will most commonly present as a spiculated mass and/or ill-defined soft tissue in the surgical bed, around surgical clips, and/or along the vasculature. On initial post-operative imaging, soft tissue stranding, and post-treatment changes can be difficult to delineate from recurrence, and it is often only through serial imaging and correlation with laboratory values that will declare this as benign versus malignant (32). Stranding alone in the operative bed should not raise a high index of suspicion initially (*Figure 10A,10B*). Worsening and/or solid soft tissue should raise alarms, as should new liver or peritoneal nodules (*Figure 10C,10D*) (32). Local recurrence may also present as new venous or pancreatic anastomotic strictures,

which must be differentiated from benign strictures (25).

Conclusions

Multidisciplinary care in a high-volume institution is one of the keys to optimal management in patients carrying the dire diagnosis of pancreas adenocarcinoma. Accurate staging is vital as it will guide management and prognosis. Given that initial diagnosis will often be discovered with non-dedicated imaging, prompt dedicated multi-phase cross sectional imaging (CT or MRI) will be of utmost importance for adequate staging and subsequent surveillance. Radiologists must be aware of the expected and unexpected imaging findings following treatment. Robust imaging and interpretation are both vital to patient outcomes at all stages of PDAC management.

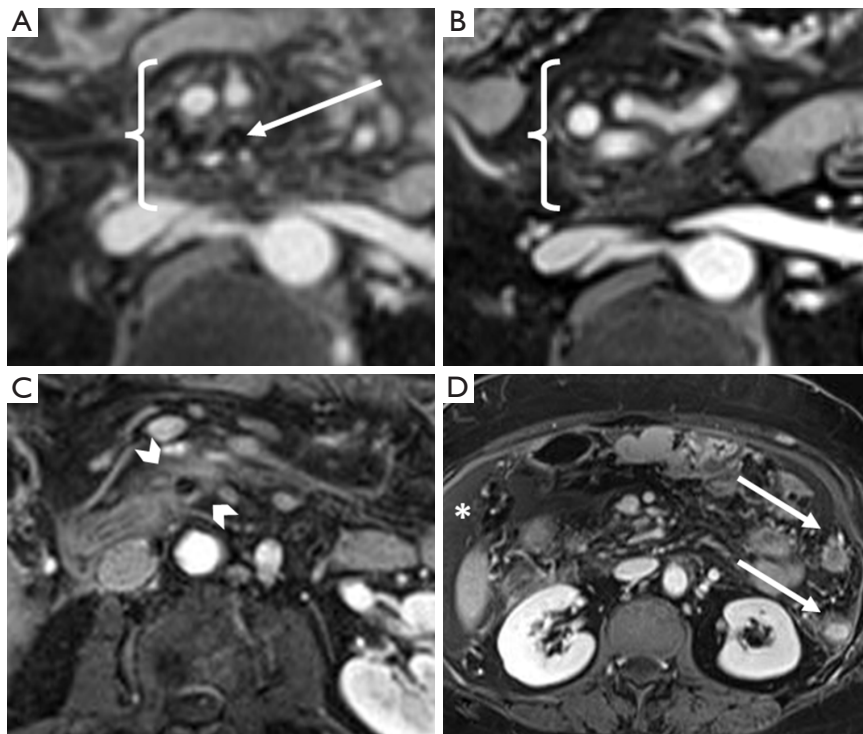


Figure 10 Surveillance imaging. Axial venous MR images at (A) 2 months and (B) 18 months postoperation reveal hazy stranding around the mesenteric vessels (bracket), which continues to improve with time (black signal voids represent surgical clips, arrow). In another patient, axial venous MR postoperative images revealed (C) solid soft tissue recurrence surrounding a surgical clip (chevrons), (D) in addition to peritoneal nodules (arrows) and ascites (asterisk). MR, magnetic resonance.

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Footnote

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