Imaging of Pancreatic Adenocarcinoma: Update on Staging/ Resectability

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KEYWORDS

• Pancreatic cancer • Staging • Resectability • Imaging • Treatment • Pancreatic adenocarcinoma

Pancreatic cancer remains one of the most challenging tumors to treat. The tumor is seated deep in the retroperitoneum and typically infiltrates a network of crucial arteries, veins, and nerves that supply or drain the liver, spleen, stomach, pancreas, and large and small bowel. Most patients present with metastatic disease that obviates potentially curative surgical intervention. Through the close cooperation of a variety of specialists, including oncologists, radiation oncologists, and surgeons, there has been an ongoing effort to improve treatment regimens and surgical techniques to maximize tumor control while minimizing potentially devastating effects. As a consequence, the criteria for resectable disease have been evolving, increasing the demands for accurate staging.

Imaging has simultaneously assumed a crucial role in helping to stratify patients to stage-appropriate therapies and clinical trials, which has also highlighted the need for consistency in radiology reporting.

This article reviews recent surgical advances and general treatment approaches that have led to a change in the understanding of resectable disease and staging, the current criteria for staging, current classifications of resectable disease, imaging techniques, imaging, and imaging criteria for staging. It also includes a brief discussion of current efforts to standardize radiology reporting for this disease.

RECENT ADVANCES LEADING TO CHANGES IN STAGING

The only option for cure remains multimodality treatment strategies that include surgical resection. For the 15% to 20% of patients who can undergo surgery, the overall survival rate is approximately 15% to 27%,[1–3] which has led to the push to develop techniques and therapies to increase the percentage of patients who can undergo surgery. These techniques include venous interposition

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grafts, hepatic arterial interposition grafts, and the use of chemotherapy and/or radiation before surgery (neoadjuvant). Knowledge of vascular anatomy is important to understand these procedures and is described in **Fig. 1**.

VENOUS RESECTION AND RECONSTRUCTION

Venous resection with reconstruction is typically performed to allow removal of tumor involving sections of the superior mesenteric vein, portal vein, and/or splenoportal confluence in a manner to reconstitute flow. This approach can include a variety of techniques (**Figs. 2** and **3**) such as saphenous venous patches, interposition grafts (such as with the internal jugular vein), primary anastomosis (if there remains sufficient length of native venous structures following resection), as well as splenic vein ligation when necessary.[4] Key to this procedure is that the 2 venous ends

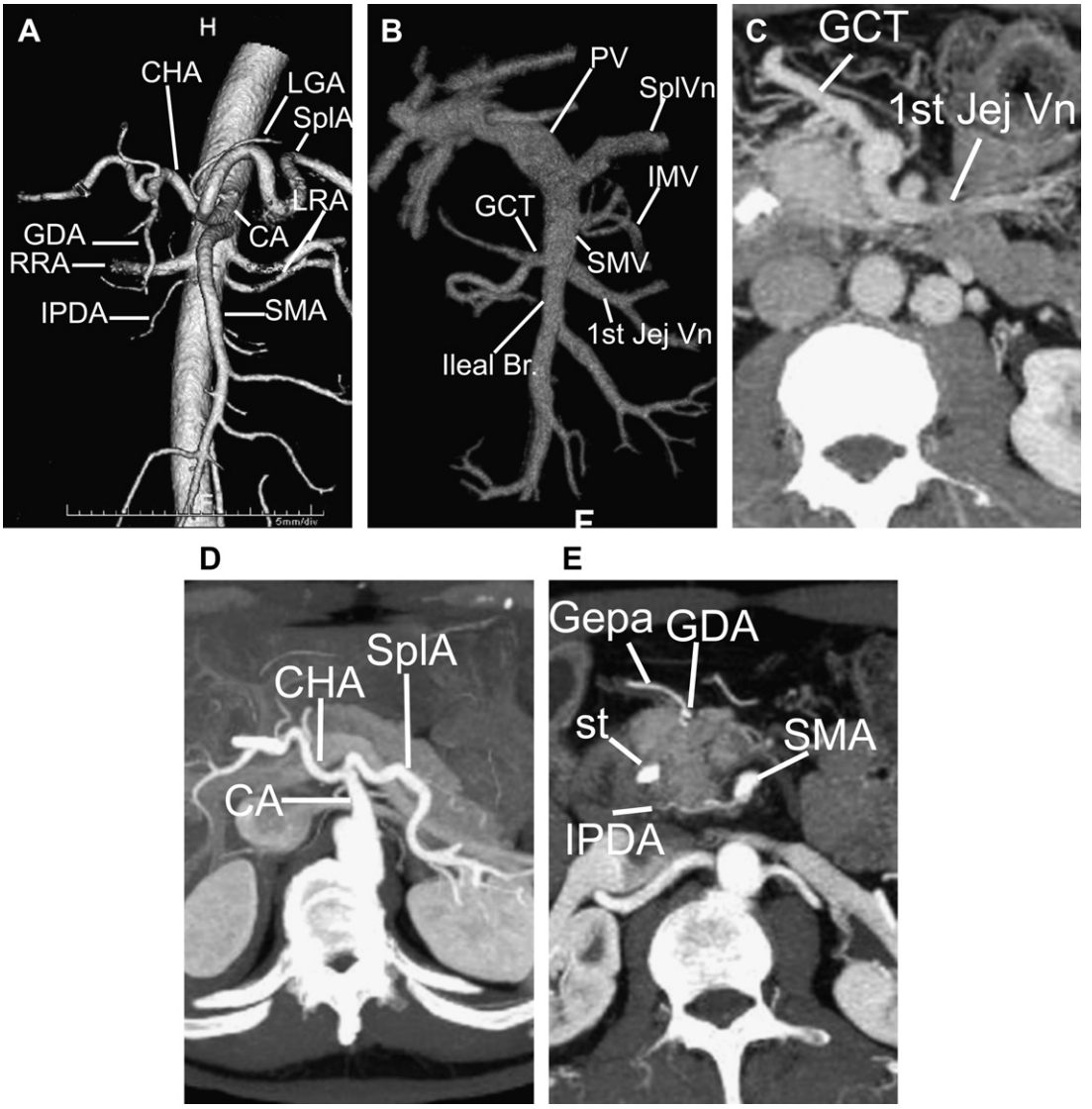

Fig. 1. Regional arterial and venous anatomy of the pancreas. Volume-rendered coronal image segmented to show (*A*) arterial anatomy and (*B*) venous anatomy. Axial 15-mm maximum-intensity projection (MIP) images show (*C*) the gastrocolic trunk (GCT) and first jejunal vein (1st Jej Vn), (*D*) celiac axis (CA), common hepatic artery (CHA) and splenic artery (Spl A), and (*E*) superior mesenteric artery (SMA), inferior pancreaticoduodenal artery (IPDA) proceeding posterior to pancreatic head, gastroduodenal artery (GDA) forming the right anterior boundary, and the right gastroepiploic artery (Gepa) originating from the gastroduodenal artery. Stent (st) is noted. Ileal Br., ileal branch of the SMV; IMV, inferior mesenteric vein; LGA, left gastric artery; LRA, left renal artery; PV, portal vein; RRA, right renal artery; SMV, superior mesenteric vein; SplVn, splenic vein.

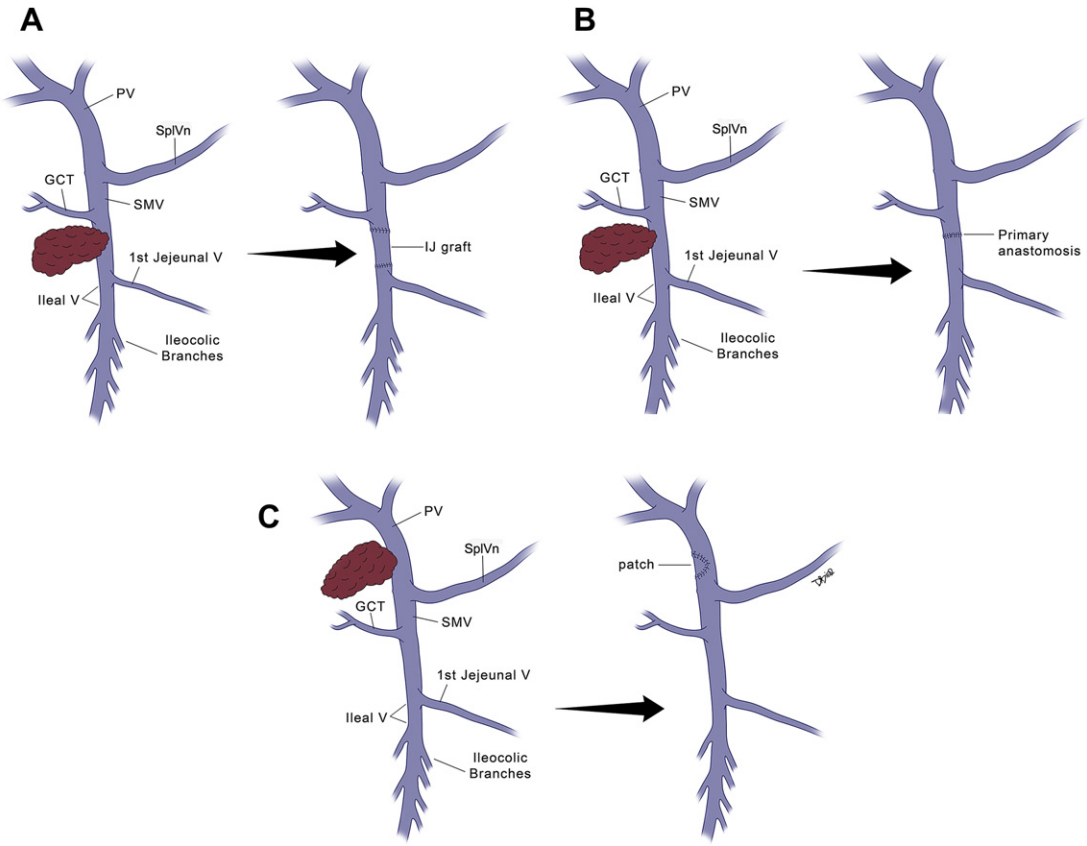

Fig. 2. Summary of basic types of venous reconstruction including (*A*) interposition internal jugular venous graft for when a segment of vein is resected, (*B*) primary anastomosis for short-segment resection, and (*C*) placement of a patch, for minimal venous involvement.

to be joined have only a single lumen. It is currently not possible to anastomose a single lumen (ie, patent portal vein) to multiple lumens (ie, ileocolic branches, **Fig. 4**). Although it is possible to do venous reconstruction in situations of venous involvement, including even short-segment occlusion, extension of tumor into branches such as the ileocolic branches precludes graft placement, even if the vessels involved are not occluded. Involvement of the jejunal vein has been considered

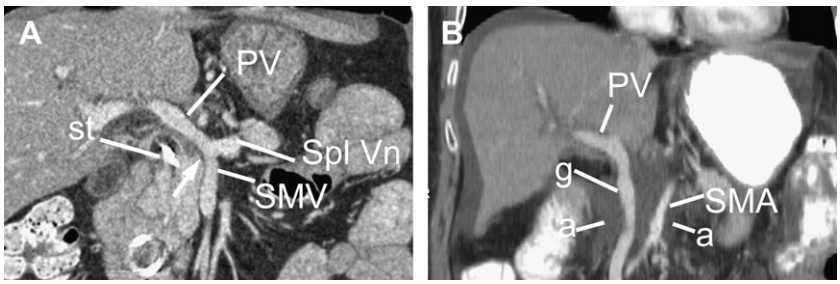

Fig. 3. A 62-year-old woman with pancreatic head/neck ductal adenocarcinoma. Coronal raysum reconstruction, portal venous phase of the baseline pancreatic CT study shows (*A*) tumor (*white arrow*) abutting the SMV. Portal vein (PV), splenic vein (Spl Vn) and stent (st) are also noted. (*B*) Postoperative coronal raysum shows the internal jugular graft (g), restoring continuity of flow back to the PV. Also noted is the SMA, and the presence of ascites (a) that resolved on subsequent scans.

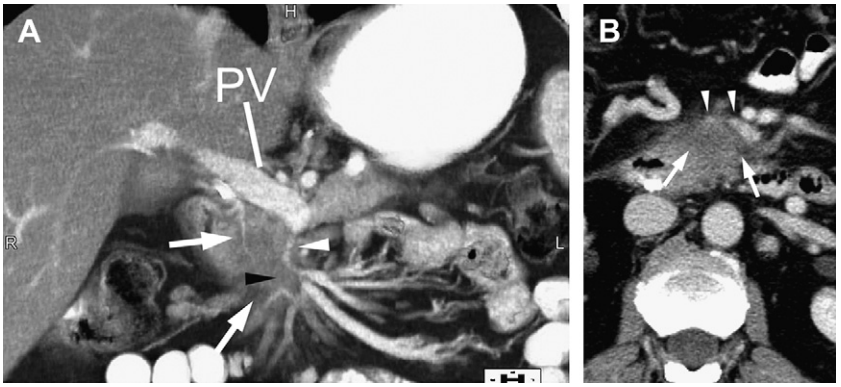

Fig. 4. A 49-year-old man with pancreatic head cancer with tumor (*white arrows*) shown (*A*) on coronal volume-rendered image to markedly narrow the SMV (*white arrowhead*) and inferiorly to occlude it focally (*black arrowhead*) and on the axial image (*B*) to infiltrate the ileocolic branches (*white arrowheads*).

at some, but not all, institutions to be a contraindication to resection.[5,6] It has been noted that reconstruction of the ileal branch of the superior mesenteric vein is preferred to reconstruction of the jejunal branch, given the latter's thin wall, as well as its posterior location.[6]

Tseng and colleagues,[4] in a study of 141 patients at our institution who underwent vascular resection (mostly venous reconstructions), showed similar survival between those who underwent resection with reconstruction (23.4 months) compared with those who underwent resection without reconstruction (26.5 months, $P = .177$). The American Hepato-Pancreatico-Biliary Association and Society of Surgical Oncology published a consensus statement in 2009 concluding that pancreaticoduodenectomy with vein resection and reconstruction is a viable option for treatment of some pancreatic adenocarcinomas.[7] Christians and colleagues[6] reported on the operation's safety, and also noted that detailed knowledge of the anatomy of the root of the mesentery is needed to optimize success.

HEPATIC ARTERY SEGMENTAL RESECTION AND/OR RECONSTRUCTION

Given that 60% of pancreatic cancers occur in the pancreatic head,[8] it is common for them to involve the gastroduodenal artery. The common hepatic artery is therefore a common site for involvement secondary to cephalad growth along the gastroduodenal artery. Another concern is for involvement of accessory or replaced right hepatic arteries, or even common hepatic arteries, originating from the superior mesenteric artery (SMA) because these vessels typically course in close proximity to the posterior pancreatic head and, therefore, are at high risk for involvement by pancreatic head tumors.[9,10] Tseng and colleagues[4] also reported on 17 hepatic arterial segmental resections with or without reconstructions. They performed a primary anastomosis for short-segment involvement of the common and/or proper hepatic arteries if the common/hepatic artery was sufficiently redundant, or interposed a reversed saphenous vein graft if it was not (**Figs. 5** and **6**). Replaced and/or accessory right hepatic arteries inseparable from tumor were resected without reconstruction when such resection was feasible. Because of the small number of patients involved, it was not possible to calculate survival statistics for this group of patients.

APPROACHES TO CHEMOTHERAPY AND/OR RADIATION THERAPY

Because survival of patients status post resection with surgery alone has been limited (median survival 11–20 months), and includes high local recurrence rates (up to 60%),[11] supplemental approaches using chemotherapy and radiation therapy have been used. These approaches are typically in 1 of 2 groups: adjuvant (postoperative) or neoadjuvant (preoperative) therapy.

ADJUVANT (POSTOPERATIVE) THERAPY

This approach treats possible residual tumor with chemotherapy or chemotherapy and radiation therapy. The European Organization for Research and Treatment of Cancer evaluated 218 patients with periampullary tumors who were randomized to either observation or treatment with radiation and 5-fluorouracil (5FU).[12] The median survival for the treated group was 17.1 months versus 12.6 for those who were observed, but the difference was not statistically significant. A subsequent long-term follow-up study of these patients also

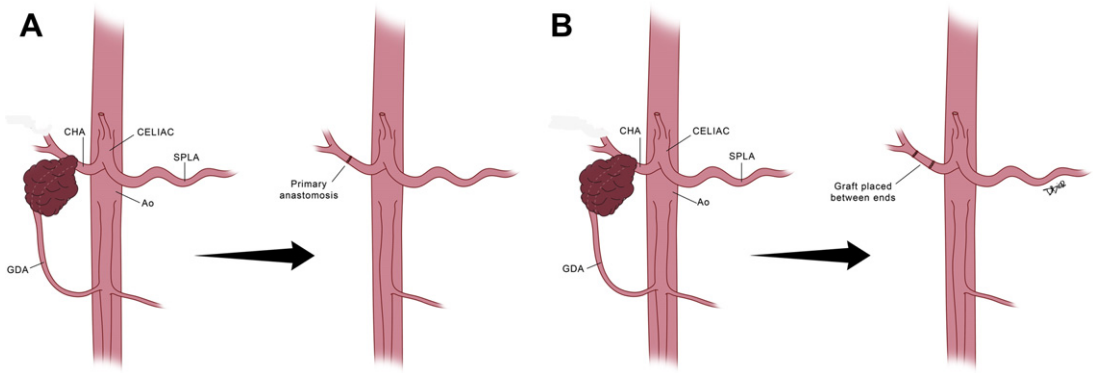

Fig. 5. Types of CHA reconstructions. Pancreatic head tumors typically ascend the gastroduodenal artery (GDA) to involve the CHA. If tumor involvement is minimal (*A*), then a primary anastomosis of the existing CHA ends can be done. However, if the involved CHA segment is longer (*B*), then a vascular graft is needed. For an anastomosis to be possible, tumor must not involve the proximal 1 cm of the common hepatic artery as it originates from the celiac trunk.

showed no statistically significant difference in survival.[13] The European Study Group for Pancreatic Cancer (ESPAC-1) trial subsequently stratified 541 patients to multiple categories including postoperative chemotherapy alone, postoperative chemoradiation, postoperative chemoradiation plus subsequent additional chemotherapy, and postoperative observation alone. That study showed a statistically significant improvement in survival from chemotherapy versus no chemotherapy (19.7 months vs 14 months, $P = .0005$) but not for chemoradiation,[14] A follow-up analysis showed a slight decrease in survival for those undergoing chemoradiation (15.9 months) compared with those without chemoradiation (17.9 months, $P = .05$).[15] Another study, the Radiation Therapy Oncology Group trial 97-04, showed a trend to increased overall survival for gemcitabine-based chemotherapy followed by 5FU chemoradiation, although results were not statistically significant (both arms in this study had

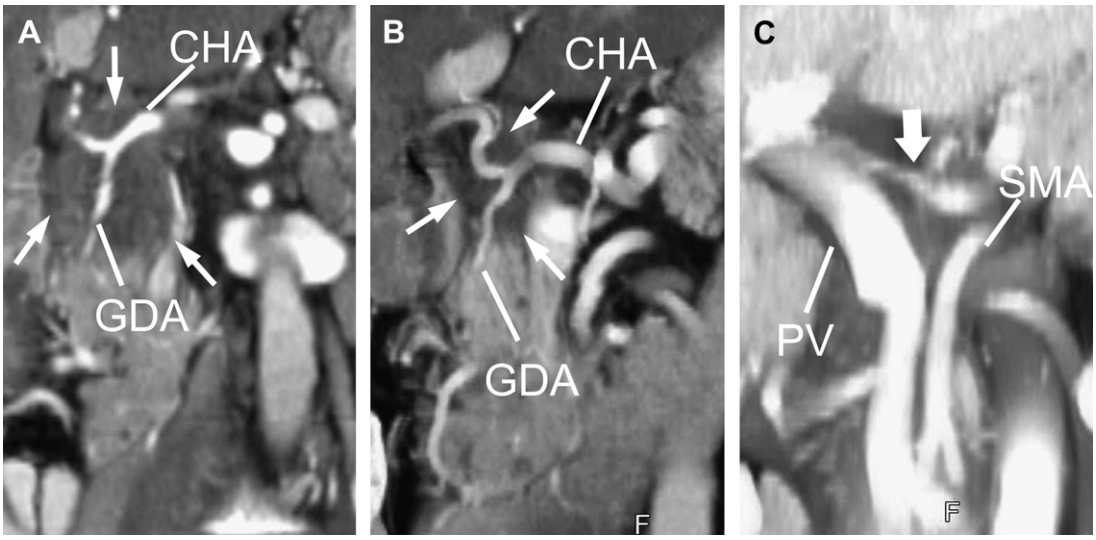

Fig. 6. (*A*) Pancreatic head tumor (*white arrows*) seen at baseline coronal raysum reconstruction to encase (involve more than 180°) the gastroduodenal artery (GDA) and the common hepatic (CHA). The patient then underwent preoperative chemotherapy and radiation therapy. (*B*) Coronal raysum reconstruction from follow-up scan shows the primary mass to have decreased (*white arrows*) but to still encase the gastroduodenal and common hepatic arteries. The patient underwent surgery, which showed no viable tumor involving the CHA. Arterial graft was placed and is shown with an arrow on the postoperative MIP image (*C*). The lower quality of postoperative reconstructions is because of thicker axial source images.

chemoradiation).[16] Further studies are underway to clarify the roles of chemotherapy and radiation therapy in the adjuvant setting. Guidelines from the National Comprehensive Cancer Network (NCCN) support the use of postoperative chemotherapy or chemoradiation therapy.[11] One of the limitations noted for the adjuvant approach has been that up to 33% cannot undergo adjuvant therapy, or it is delayed, because of illness.[12,17,18] It has been advocated that restaging imaging evaluations be performed immediately before starting adjuvant therapy to exclude residual tumor or early progression.[11]

PREOPERATIVE THERAPY

Preoperative therapy was developed as an alternative approach to adjuvant therapy for the following reasons. Preoperative therapy avoids the problem of postoperative morbidity delaying or excluding patients from undergoing adjuvant therapy. Preoperative therapy treats presumed micrometastases likely present at the time of presentation given that most patients who undergo potentially curative resection still die of recurrent pancreatic cancer. Preoperative therapy also provides a time interval before surgery in which indeterminate lesions that may be metastases can be better characterized by imaging follow-up (**Fig. 7**). It has also been suggested that patients who develop overt metastases during this period of intense preoperative therapy likely have an aggressive tumor biology and therefore would have done poorly even if they had proceeded directly to surgery. Potentially needless surgery may therefore be avoided. In addition, preoperative chemoradiation may allow for tumor downstaging (**Fig. 8**) and, in single-institution studies, has been shown to result in lower rates of surgical margin positivity.[19–23] Studies at our institution have shown median survival of up to 34 months for those who undergo preoperative therapy and surgery, but survival for those who did not proceed to surgery has been only 7 to 11 months.[24,25] Up to 30% of patients who undergo neoadjuvant therapy do not undergo surgery because of development of metastases; in contrast, isolated locoregional progression in the preoperative phase has been rare (ie, loss of a window of opportunity for surgical resection).[24,26] To our knowledge, there have been no prospective trials comparing preoperative therapy followed by surgery with upfront surgery followed by adjuvant treatment.

STAGING OF PANCREATIC CANCER: AMERICAN JOINT COMMITTEE ON CANCER GUIDELINES

The most commonly used staging system is that from the American Joint Committee on Cancer (AJCC).[27] This system assesses the status of the primary tumor (T), lymph nodes (N), and metastases (M). Stages are defined based on TNM grades.

The T status can be summarized as follows (**Fig. 9**): the T0, TX, and Tis classifications refer to lack of evidence for a primary tumor, inability to evaluate the primary tumor, or carcinoma in situ, respectively. T1 tumors are those less than

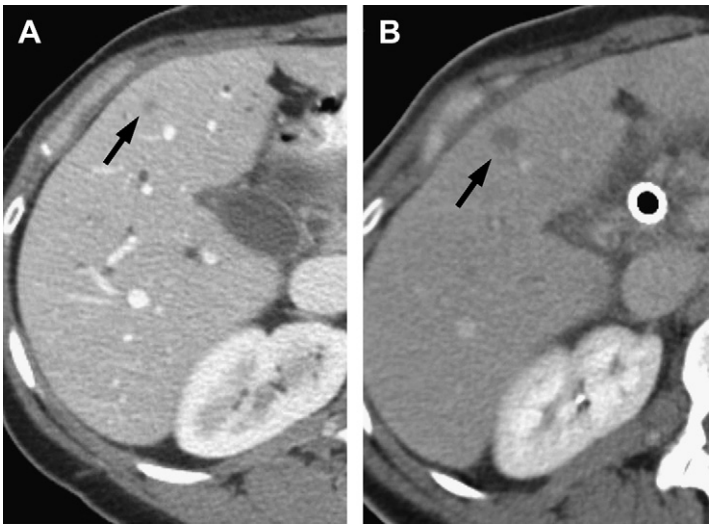

Fig. 7. A 39-year-old woman with pancreatic cancer, noted on (*A*) baseline axial images to have indeterminate liver lesion (*black arrow*), too small to characterize. Patient was therefore considered borderline for resectability, and underwent preoperative chemotherapy and radiation therapy. Follow-up axial portal venous phase imaging (*B*) shows lesion (*black arrow*) to have increased in size, consistent with a liver metastasis.

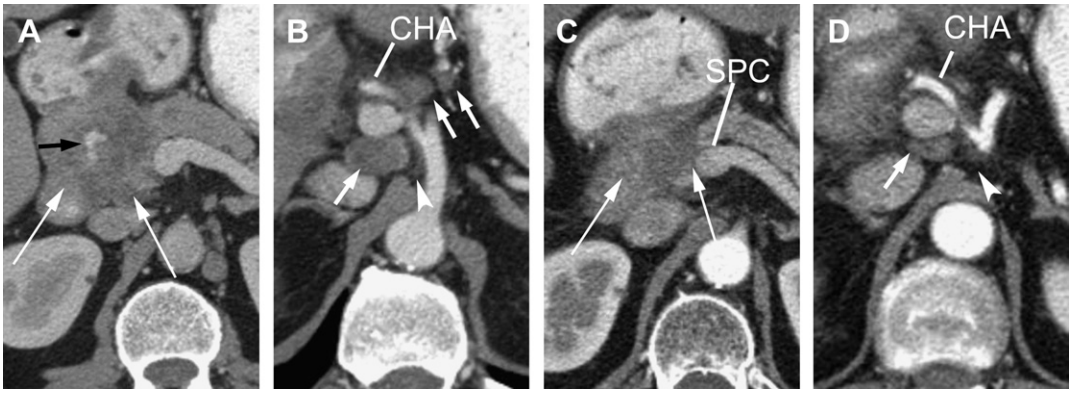

Fig. 8. A 61-year-old man with cancer of the pancreatic head. Baseline portal venous phase imaging (*A*) shows tumor (*long white arrows*) measuring nearly 5 cm, with central ulceration (*black arrow*) opacifying with gastrointestinal contrast from communication with duodenum. More superiorly obtained axial image (*B*) shows adenopathy (*white arrows*) near the CHA and in the portacaval region. Soft tissue stranding (*white arrowhead*) is seen to abut (meaning $\leq$180° of involvement) the celiac trunk. Follow-up imaging after chemoradiation (*C*) shows that tumor (*long white arrows*) has decreased, but still abuts the splenoportal confluence (SPC). On a more superiorly obtained image (*D*) adenopathy (*white arrow*) has decreased or resolved. Soft tissue stranding (*white arrowhead*) near the celiac trunk is similar or slightly increased. Patient went on to surgery, with successful tumor resection, only 1% viable tumor, and no positive regional lymph nodes for cancer.

or equal to 2 cm and bounded by the pancreas. T2 tumors are larger than 2 cm but still bounded by pancreas. T3 tumors are those that extend beyond the pancreas, but do not involve the celiac or superior mesenteric arteries. T4 tumors involve either the celiac or the superior mesenteric arteries and, in most institutions, represent unresectable tumor. With the advent of vascular resections and reconstructions, there has been a shift in staging to emphasize arterial involvement, and references to venous involvement for the T grades have been eliminated.[28] The N term can be summarized as follows: NX (unable to evaluate nodal status), N0 (no metastases to regional nodes), and N1 (presence of metastases to regional nodes). The M term is either M0 (no metastases) or M1 (distant metastases are present).

Staging can be summarized as follows (**Fig. 10**): the presence of any metastases classifies a patient as stage IV. The presence of T4 disease (celiac or SMA involvement) without metastases renders any patient as stage III. Stage IIA is T3 disease in the absence of nodal or distant metastases, and stage IIB is T1 to T3 disease in the setting of regional

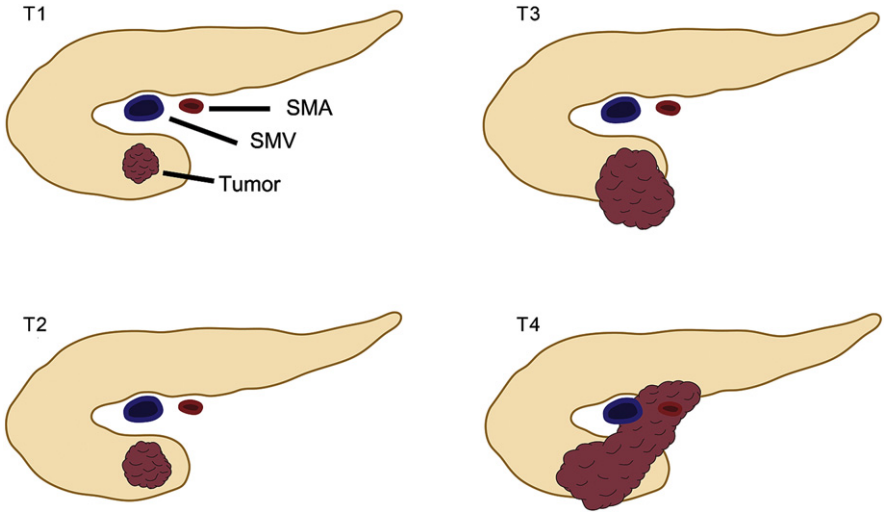

Fig. 9. T1 (<2-cm tumor, bounded by pancreas), T2 (tumor $\geq$2 cm, but bounded by pancreas), T3 (tumor extending beyond pancreas but not involving the celiac or superior mesenteric arteries), and T4 disease (tumor involving the celiac or superior mesenteric arteries). SMV, superior mesenteric vein; SMA, superior mesenteric artery.

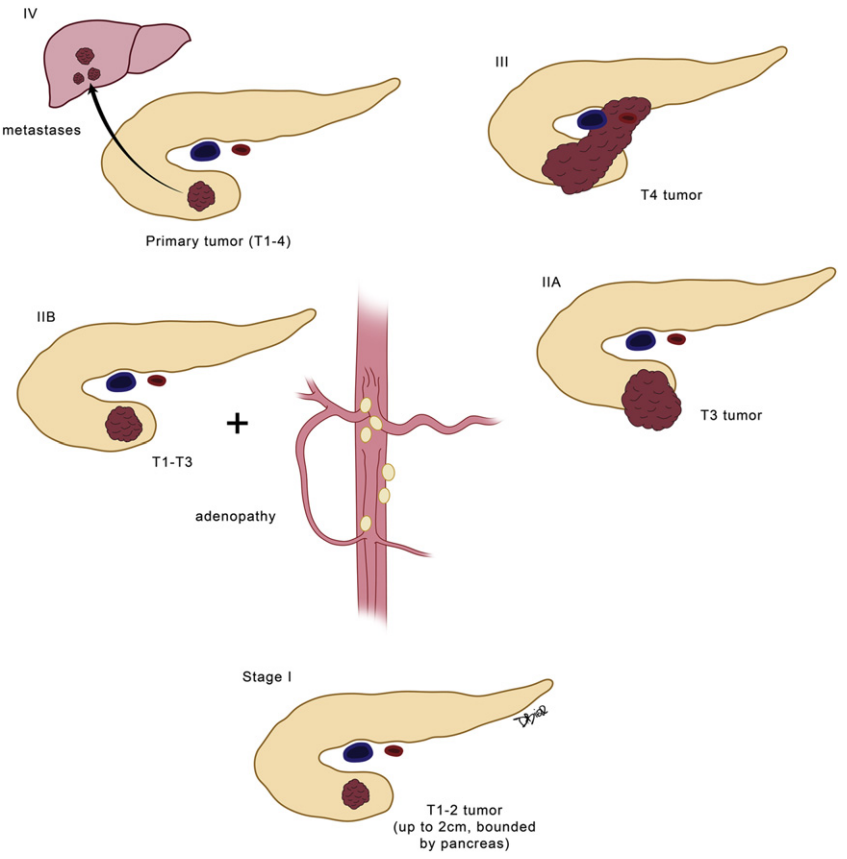

Fig. 10. Current staging of pancreatic cancer. Stage IV disease is the presence of distant metastases. Stage III disease is any other disease in which tumor involves the celiac or superior mesenteric arteries. Stage IIB disease is any other disease with adenopathy, and T1 to T3. Stage IIA is T3 disease (extending beyond the pancreas but without superior mesenteric or celiac artery involvement) without adenopathy or distant metastases. Stage I disease is any other disease (no metastases, no adenopathy) with primary tumor confined to the pancreas (T1–T2).

nodal metastases but not distant metastases. Stage I disease is T1 or T2 disease without nodal or distant metastases.[28]

CLASSIFICATION OF RESECTABLE, BORDERLINE, AND UNRESECTABLE DISEASE

Although the AJCC criteria provide classifications for staging, other efforts have been made to group patients for purposes of clinical management. Recently published pancreatic adenocarcinoma oncology guidelines by the NCCN describe grouping patients based on radiographic criteria into those with clearly resectable disease, borderline resectable disease, or clearly unresectable disease,[29,30] which supports other publications using such groupings.[7,19,31,32]

Clearly resectable disease (AJCC stages I and II) is defined as no overt metastatic disease, no overt adenopathy, and, importantly, no evidence of any tumor contact with vasculature (**Fig. 11**) other than perhaps the gastroduodenal artery in the case of pancreatic head tumors (this vessel is resected as part of a Whipple procedure). This classification means that an intact, uninvolved, so-called clean fat plane surrounds vessels such as the SMA, the celiac trunk, and the common hepatic artery. For other vessels that are in contact with the pancreas, such as the superior mesenteric vein, vessels only have contact with clearly normal pancreatic parenchyma or fat and show no deformity or narrowing that is thought to be secondary to tumor involvement.

Clearly unresectable disease (stages III and IV) is represented by clearly identifiable distant metastases (stage IV), overt adenopathy outside the surgical field, or tumor encasement (>180° of circumferential involvement, **Fig. 12**) of such arteries (**Fig. 13**) as the SMA, celiac trunk, or origin

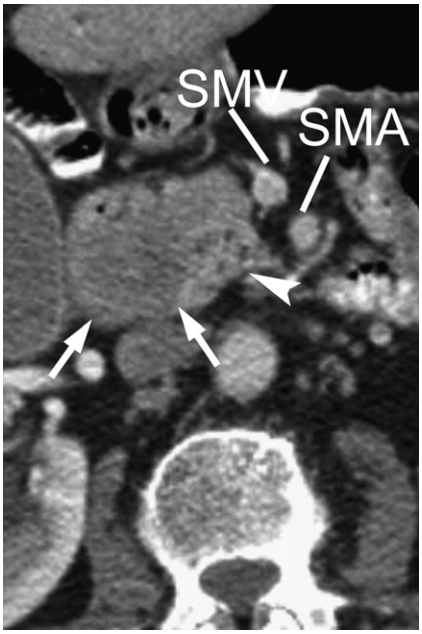

Fig. 11. A 52-year-old woman with pancreatic ductal adenocarcinoma of the pancreatic head (*white arrows*) involving the duodenum, which is effaced. Tumor is resectable, because the SMV and SMA are separated from the tumor by either an intact fat plane or normal-appearing pancreatic parenchyma (*white arrowhead*).

of the common hepatic artery (which would preclude placement of an arterial jump graft).

The more difficult group to classify, given the evolution of treatment techniques (surgery, radiation therapy, and chemotherapy), is that of borderline or marginal resectable disease. According to the current NCCN definitions, borderline resectable patients have no distant metastases, venous involvement that is at most short-segment occlusion with suitable vessel above and below the point of obstruction for resection and reconstruction (**Fig. 14**), superior mesenteric and celiac arterial involvement limited to abutment (no >180° of the circumference of involvement) of these vessels (**Fig. 15**), and common hepatic artery involvement limited to at most short-segment encasement (up to 360 involvement) with sparing of the origin from the celiac of sufficient length to allow for placement of an arterial bypass graft (see **Fig. 6**).[30] These terms are similar to those outlined by our institution for borderline resectable patients in the article by Varadhachary and colleagues,[19] although in the NCCN guidelines any degree of venous abutment is considered borderline disease. More recently, our institution defined these patients as having anatomically borderline disease (type A), and added 2 other categories, B and C.[11] Type B borderline resectable patients are those with possible extrapancreatic disease, namely computed tomography (CT) findings suspicious but not definite for metastatic disease (see **Fig. 7**) and/or N1 disease confirmed by prereferral laparotomy or endoscopic ultrasound (EUS) with fine-needle aspiration (FNA). Type C patients are those with preexisting comorbidities (including those with potentially prohibitive comorbidities thought not to have been sufficiently evaluated) or reversible degradation of performance status (even if marginal performance status).[11]

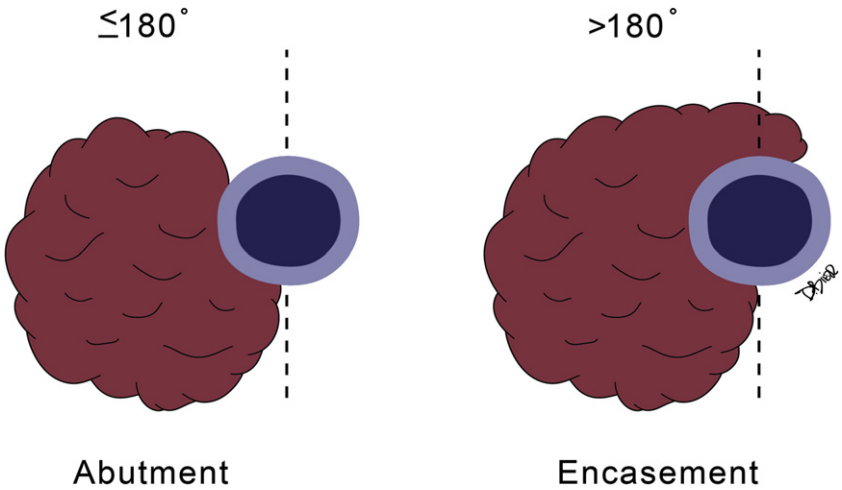

Fig. 12. The terms abutment (defined as ≤180° of tumor involvement of a vessel's circumference) and encasement (>180° of tumor involvement of a vessel's circumference). Either the terms abutment/encasement or degrees of circumferential involvement should be used to describe vascular involvement to facilitate communication with specialties outside radiology.

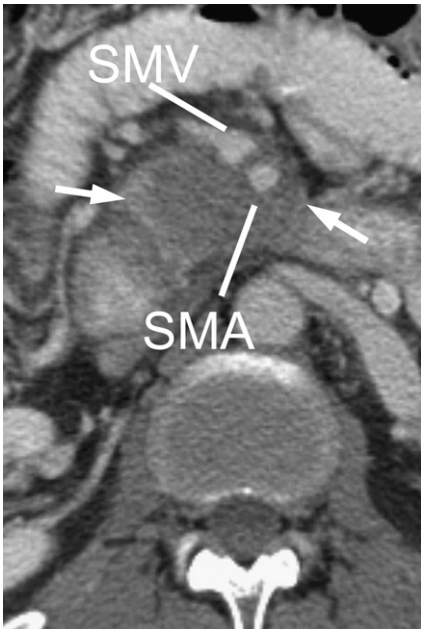

Fig. 13. A 66-year-old man with unresectable (stage III) cancer of the pancreatic head. Axial portal venous phase images show tumor (*white arrows*) encasing greater than 180° of circumferential involvement of the SMV, with 360° of circumferential involvement of the SMA.

IMAGING: TECHNIQUE

The characteristics used to define resectable, borderline resectable, and unresectable disease are based on the use of cross-sectional imaging and require the use of imaging techniques that optimize the visualization of tumor, its relationship to adjacent anatomic structures and its possible spread to nodes outside the surgical field, and distant sites such as the liver, peritoneum, lung, and bone.[11,19,30] The NCCN guidelines recommend pancreas-specific CT or MR imaging.[30]

Before discussing techniques, it is important to consider the timing for using specific imaging techniques. In our experience, the work-up for patients with abdominal pain and/or jaundice usually began with transabdominal ultrasound to evaluate the possibility of cholecystitis or simply the presence of gallstones. If ultrasound showed extrahepatic biliary dilatation, patients then typically underwent endoscopic retrograde cholangiopancreatography (ERCP) for diagnostic work-up and for treatment. However, the subsequent immediate placement of a biliary stent often eliminated visualization of the point of biliary obstruction, eliminating a useful diagnostic imaging feature for subsequent imaging with CT, MR imaging, or EUS (and for guiding biopsy for subtle lesions). More importantly, ERCP, brushings, and/or biopsy procedures can all cause postprocedure pancreatitis (**Fig. 16**), which can markedly limit the ability to visualize the tumor and the interface between tumor and vessel, limiting subsequent biopsy attempts and preventing accurate staging, and delaying or precluding enrollment in clinical trials. For this reason, at our institution, patients who present with suspicion of pancreatic cancer undergo cross-sectional imaging for staging (CT or MR imaging) before any intervention.

CT

Multidetector-row CT (MDCT) is probably the most widely used cross-sectional modality for the staging of pancreatic cancer. Thin-section (3 mm

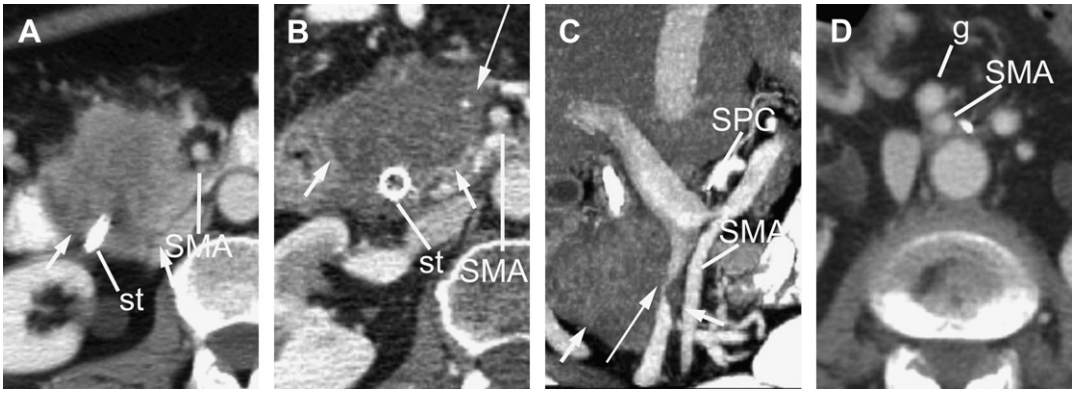

Fig. 14. Borderline venous occlusion in a 60-year-old woman. Baseline axial portal venous phase image (*A*) shows pancreatic head mass (*white arrows*) that occludes the SMV. Only the SMA is visualized. Stent (st) is present. Following a course of chemoradiation, follow-up study (*B*) axial image and (*C*) coronal reconstruction image show new minimal patency of the SMV (*long white arrow*). SMA and SPC are noted. Postoperative (*D*) axial image shows graft (g) that was successfully placed. SMA is noted.

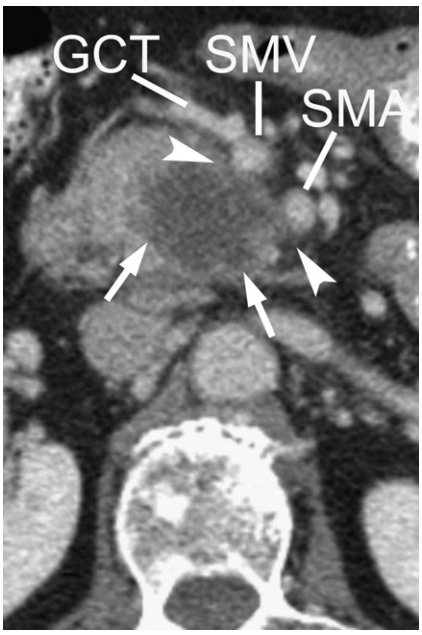

Fig. 15. A 76-year-old woman with borderline stage II to III pancreatic ductal adenocarcinoma of the pancreatic head. Axial portal venous phase imaging shows tumor (*white arrows*) with abutment (here <180° of circumferential involvement) of the SMA and SMV (*white arrowheads*). Gastrocolic trunk (GCT) is also noted.

or thinner), biphasic technique is crucial to identify the primary tumor, determine its local extent, as well as to identify distant metastases. Usually, injection rates of 3 to 5 mL/s are used with a sufficient volume of contrast for a 30-second injection duration.[33–35] The first postcontrast phase of imaging is obtained during the phase of peak pancreatic parenchymal enhancement to maximize the conspicuity of the tumor (**Fig. 17**). This phase is approximately 40 to 50 seconds after the start of contrast injection.[36] The later portal venous phase, which maximizes enhancement of the liver parenchyma (approximately 60–70 seconds after injection), is useful for identification of liver metastases and also results in excellent opacification of the mesenteric, splenic, and portal veins, which is useful for evaluation for tumor involvement of these structures.[36] We typically reconstruct axial images to 2 slice thicknesses, 2.5 mm for primary review, and 0.625 to 1.25 mm (depending on the MDCT platform) to allow for postprocessing. For example, we create coronal and sagittal 2.5-mm thick contiguous multiplanar reconstructions (see **Fig. 17**), but these thinner axial images are also useful for creating curved planar reformations, maximum-intensity projection (MIP), minimum-intensity projection, as well as volume-rendered and segmented volume rendered images.

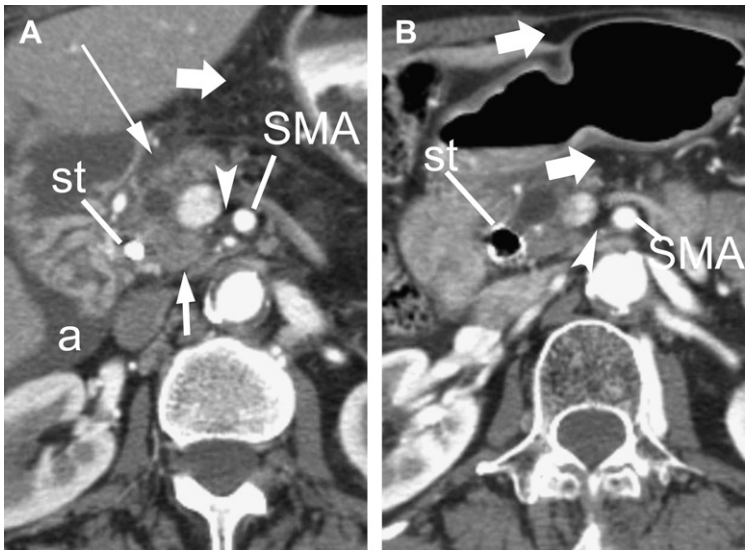

Fig. 16. A 72-year-old woman with biopsy-proven stage I pancreatic adenocarcinoma. Baseline axial CT image at our institution (*A*) shows stent (st) placed by outside institution. Large white arrow shows edematous changes in mesenteric fat, ascites (a), and fluid near the pancreatic head (*long white arrow*) consistent with post–stent placement pancreatitis. In this setting, it is not clear whether stranding (*white arrowhead*) near the SMA represents tumor or inflammation. Tumor (*medium white arrow*) involves the pancreatic head and uncinate process. (*B*) Posttreatment scan shows resolution of pancreatitis, with resolution of ascites, and fat (*big white arrows*) anterior and posterior to the stomach no longer appearing edematous. Fat interface (*white arrowhead*) near SMA now appears intact with previously seen stranding having resolved. Plastic stent was replaced with a metallic stent (st).

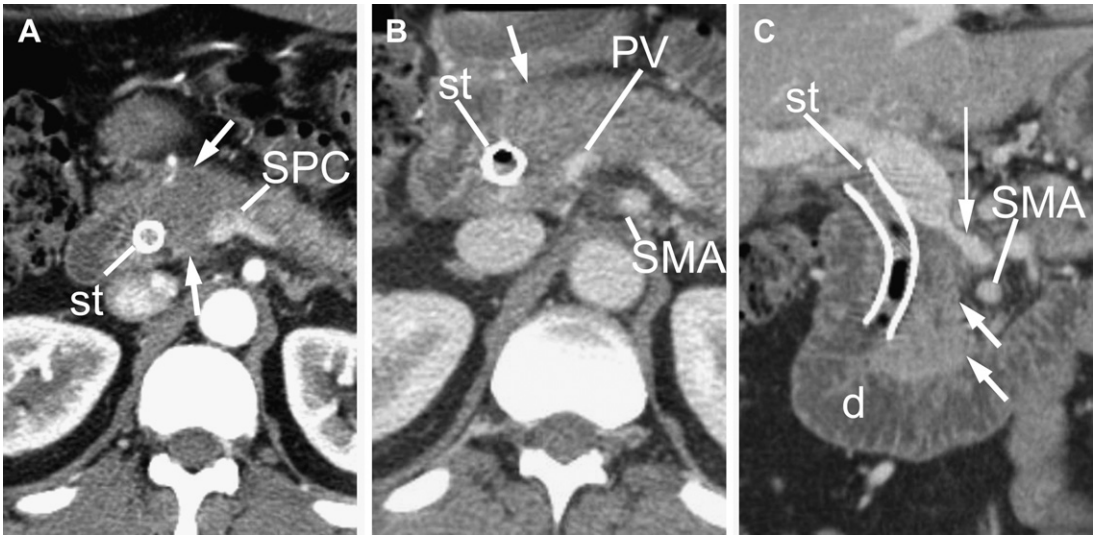

Fig. 17. A 53-year-old man with stage II-III borderline pancreatic head ductal adenocarcinoma on baseline multiphasic examination. (*A*) Axial pancreatic parenchymal phase image shows tumor (*white arrows*) abutting the SPC and surrounding stent (st). (*B*) On portal venous phase image, tumor (*white arrow*) is less conspicuous. Tumor narrows the well-opacified portal vein (PV) superior to the SPC. Nonspecific stranding abuts the right border of the SMA. Coronal reconstruction of the portal venous phase (*C*) shows that the tumor (*white arrows*) causes marked narrowing of the portal vein (*long white arrow*). d, duodenum.

Pancreatic adenocarcinoma has a typically hypodense appearance on the pancreatic parenchymal phase (see **Fig. 17**) but can be isodense, and either remains hypodense on the portal venous phase or may become isodense. Axial images and coronal and sagittal reformations are useful for providing a comprehensive review of the celiac, superior mesenteric, common hepatic, and splenic arteries as well as the main portal, splenic, and superior mesenteric veins and their major branches (gastrocolic trunk, first jejunal vein, and ileocolic tributaries).

MR IMAGING

MR imaging offers the advantage of multiple sequences that can provide information regarding the primary tumor, its local extent, vascular involvement, and distant metastases. Multiple recent technical developments include platforms with higher field strength, increasingly powerful multichannel coils, new contrast agents, and new sequences. An example of a typical imaging examination (**Figs. 18** and **19**) includes T2-weighted fat-suppressed, T1-weighted, in and out of phase, diffusion-weighted, and T1-weighted dynamically obtained postcontrast multiplanar imaging (such as three-dimensional [3D] gradient recalled echo volumes obtained with parallel imaging). Dynamically obtained images can be obtained as single breath holds at 20, 60, 120, and 180 seconds after the start of contrast injection.[37,38] Such sequences as Fast Imaging Employing Steady-State Acquisition (FIESTA; GE Medical Systems, Milwaukee, WI) with fat suppression (see **Fig. 19**) can help to differentiate fat, vessels, tumor, and uninvolved pancreas. Images are most commonly obtained directly in the axial plane. However, other planes can be obtained directly. Coronal-plane FIESTA images are useful for evaluating the relationship of tumor to vessels, particularly the origin of the celiac and superior mesenteric arteries in cross section, and to visualize the extent of common hepatic artery involvement.

Pancreatic adenocarcinoma has a variable appearance on MR imaging depending on the sequence being examined. On dynamic images, its appearance is similar to that on contrast-enhanced CT, being hypointense to adjacent pancreatic parenchyma, but at times also appearing isointense, in which case identification of primary tumor can be difficult. A recent article suggested that MR imaging may be able to visualize up to 79% of tumors that appear isodense to normal pancreatic parenchyma on multiphasic CT studies.[39]

EUS

Using a combination of radial and curvilinear arrays, EUS has developed a significant role in the ability to image lesions and provide tissue

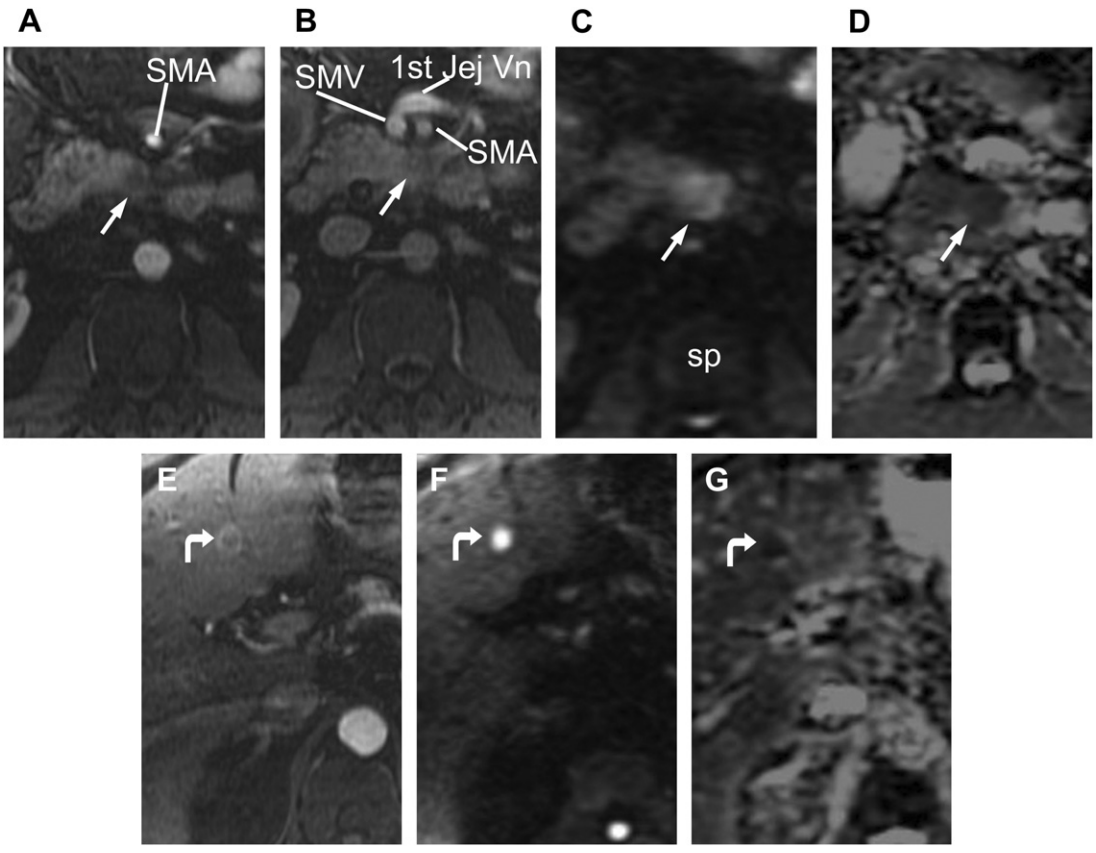

Fig. 18. MR imaging of a 56-year-old man with history of stage IV pancreatic cancer. Pancreatic tumor (*white arrow*) appears hypointense on (*A*) pancreatic parenchymal phase and (*B*) portal venous phase. Venous structures such as the SMV and first jejunal vein (1st Jej Vn) are well opacified on the portal venous phase, optimizing evaluation for venous involvement. On diffusion weighted imaging (*C*), tumor appears bright, and on apparent diffusion coefficient (ADC) map (*D*), tumor appears dark, indicating restricted water movement. Liver metastasis (*curved white arrow*) on dynamic three-dimensional (3D) spoiled gradient echo late arterial phase (*E*) shows ring enhancement; on (*F*) diffusion weighted imaging appears bright and shows low signal on ADC (*G*) consistent with restricted water movement, supporting that this is a metastasis.

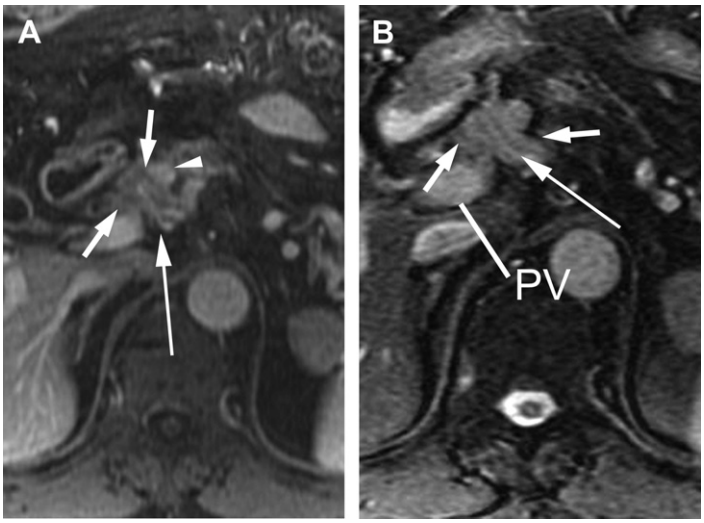

Fig. 19. A 61-year-old man with stage IIA to B pancreatic cancer. Portal venous phase 3D spoiled gradient T1-weighted fat-suppressed image (*A*) shows tumor (*white arrows*) abutting enlarged common hepatic artery node (*white arrowhead*) and encasing the CHA (*long white arrow*). (*B*) Fat-suppressed Fast Imaging Employing Steady-State Acquisition (FIESTA) image similarly shows CHA encasement.

diagnoses via EUS-guided FNA for pancreatic cancer through real-time imaging without the need for administration of a contrast agent.[40,41] Future directions include the possibility of contrast enhancement, as well as potentially the use of elastography.[42] This ability to visualize and obtain tissue specimens in real time is also useful for the evaluation of suspicious lymph nodes. However, the role of EUS for staging is likely more limited than CT or MR imaging, given its limited view of abdominal anatomy (discussed later).

POSITRON EMISSION TOMOGRAPHY/CT

Positron emission tomography (PET)/CT is usually performed without intravenous contrast, and therefore has had a limited role in the local staging of pancreatic cancer given its poor depiction of tumor and its relationship to adjacent vasculature. However, a study comparing PET, unenhanced PET/CT, and intravenous contrast-enhanced PET/CT showed, as expected, improved accuracy for intravenous contrast-enhanced PET/CT (88% vs 76% for unenhanced PET/CT) for staging, and was suggested as a possible single technique for the staging of pancreatic cancer.[43] The role of unenhanced PET/CT has primarily been to detect metastatic disease and has been useful especially for unexpected sites because it is a whole-body imaging modality (**Figs. 20** and **21**).[44]

IMAGING AND STAGING

Local Staging

Staging on cross-sectional imaging currently involves determining in cross section the degrees of circumferential involvement of regional arteries and veins (see **Figs. 11–13** and **15**) by tumor and narrowing/occlusion of veins (see **Fig. 14**). As described originally by Lu and colleagues[45] in 1997, using a threshold of greater than 180° of circumferential vessel involvement as indicating unresectable disease on contrast-enhanced CT imaging yielded a sensitivity of 84% and specificity of 98% for unresectable disease, which maximized the sending of all those with resectable disease to surgery, at the expense of undercalling unresectable disease. This was in the setting of older staging criteria in which venous involvement meant unresectable disease, and likely did not include the use of preoperative therapy.[45] Determining the accuracy of CT and MR imaging for staging has currently become more complex given the variability of therapy and surgical approaches between institutions. As noted previously, institutions vary in their use of neoadjuvant and/or adjuvant therapy. Nevertheless, more recent staging studies have shown sensitivities for unresectable disease between 52% and 91%, and specificities of 92% to 100%, but there were likely differences between institutions in what was considered surgically resectable disease.[46–50] In addition, in these

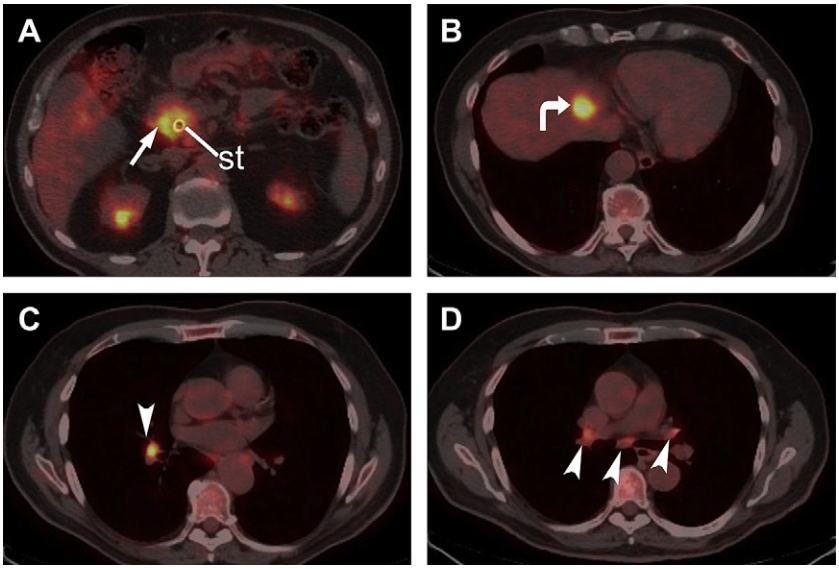

Fig. 20. A 78-year-old man with biopsy-proven stage IV pancreatic cancer. Axial fused images from PET/CT study shows (*A*) fluorodeoxyglucose (FDG) avid pancreatic head mass (*white arrow*) surrounding stent (st), (*B*) liver metastasis (*curved white arrow*), (*C*) right hilar nodal metastasis (*curved white arrowhead*), and (*D*) other, slightly less FDG avid, hilar and mediastinal nodes (*curved white arrowheads*).

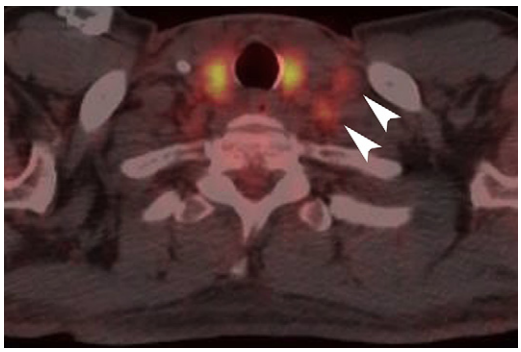

Fig. 21. A 59-year-old man with stage IV pancreatic adenocarcinoma. Axial fused PET/CT image shows FDG-avid left supraclavicular adenopathy (*curved white arrowheads*) consistent with metastatic disease.

studies, small-volume metastases to the liver or peritoneum were as common, or more common, than vascular invasion as causes for patients being identified as unresectable at surgery who were identified as resectable on cross-sectional imaging. A study that compared different generations of MDCT equipment in the same institution did not show a significant difference in performance between generations.[48] Another question is that of MR versus CT for staging. MR offers inherently better soft tissue contrast (see **Figs. 18** and **19**), whereas CT offers higher spatial resolution and the ability to freeze bowel motion. Although it is difficult to compare 2 modalities that are evolving so rapidly, several studies have shown comparable performance between MR and CT for local staging.[46,51] It is therefore probably best to use the strengths of a given institution (CT vs MR imaging) in terms of equipment, experience, and skill when choosing which modality to use for determining local staging.

Another confounding factor is that of preoperative chemoradiation (**Fig. 22**). To date, it is not possible to distinguish on imaging between nonviable tumor and remaining viable tumor following therapy. Another issue is that of posttreatment changes. Radiation therapy can cause changes around vessels that we have found to primarily manifest as soft tissue stranding. We have found baseline studies useful for identifying the extent of tumor before radiation therapy; in our experience, patients undergoing preoperative therapy who develop, or show stable, minimal stranding without significant soft tissue thickening adjacent to vessels should not be prevented from undergoing surgery.[49] Overall, we found the accuracy of determining vascular involvement to be similar to that reported in the absence of preoperative therapy.[49]

The role of EUS for local staging and determining vascular invasion is not clear, because results have been mixed. A study by Dewitt and colleagues of 120 patients showed EUS to be superior to CT for tumor staging (67% vs 41%), but equivalent for nodal staging (44% vs 47%), and similar or slightly inferior to CT for judging

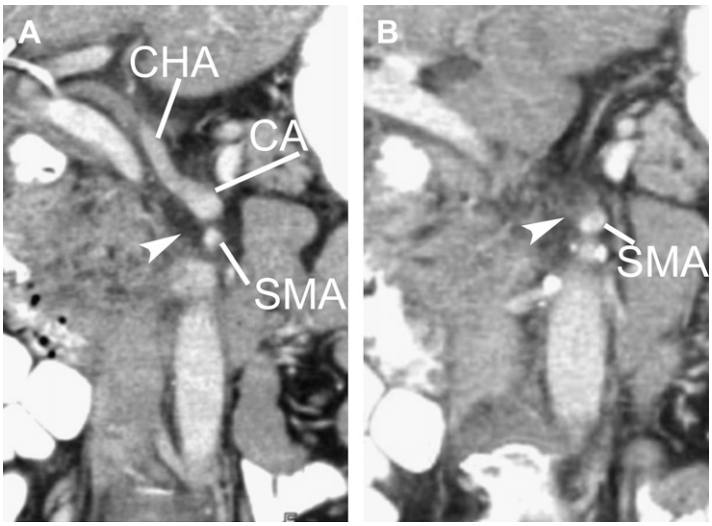

Fig. 22. A 53-year-old woman with borderline stage II to III pancreatic cancer, with imaging before, and following, chemoradiation. (*A*) Coronal gray scale reformation shows, at presentation, subtle stranding (*white arrowhead*) near the SMA origin. CA, celiac axis. (*B*) Follow-up coronal reconstruction at the same level following chemoradiation, before surgery. Soft tissue thickening has become more prominent (*white arrowhead*) but does not have the appearance of definite solid tissue. The patient underwent surgery, with negative resection margin on microscopy, and no positive regional lymph nodes.

resectability (88 vs 92%). However, in another study, the EUS feature of loss of the integrity of the echoplane surrounding a vessel indicated tumor adherence to vasculature in only 29% of cases, and in none was there histologic evidence of invasion.[52] A prospective blinded study of 62 patients evaluating accuracy of locoregional staging using surgical confirmation compared EUS, MR imaging, and CT and showed accuracies of 62%, 68%, and 74% respectively.[53] In the same study, CT had an accuracy of 83% for vascular invasion versus 75% for EUS. These investigators concluded that EUS may be best used as a potentially confirmatory test following CT for resectable tumors.[53] A systematic review of the literature by Dewitt and colleagues[54] concluded that heterogeneous study design, study quality, and differing results prevented a clear determination of whether CT or EUS was better for evaluation of patients before surgery and that well-controlled prospective studies were necessary.

Unenhanced PET/CT, as already noted, does not have a role for local staging of pancreatic cancer. However, as also already noted, when performed with intravenous contrast, it seems to perform comparably with contrast-enhanced CT. Attention to technique, including thin-section imaging and the timing of phases of image acquisition, likely remain important for accurate staging.

Nodal Disease

The accuracy for assessing nodal disease is limited regardless of the modality used. Nodal size of greater than 1 cm in the short axis has most commonly been used on MR imaging and CT as a threshold for identifying metastatic nodes, but is nonspecific. In a study using a size criterion of 1.5 cm or larger on CT as a sign of metastatic nodal disease, only 16.7% of patients with nodal involvement were identified as having nodal disease on preoperative CT.[50] Nevertheless, it is important to identify nodes outside the conventional surgical field, such as nodes to the left of the SMA (**Fig. 23**). PET/CT has been reported to have sensitivities of 46% to 71% and specificities of 63% to 100%[55–57] for nodal disease (see **Figs. 20** and **21**). PET/CT is probably useful in the setting of identifying nodes most suspicious for biopsy, but is limited for small-volume disease, and cannot differentiate between inflammatory adenopathy versus metastatic adenopathy. The limited field of visibility of EUS prevents a comprehensive evaluation of the abdomen for adenopathy, particularly for nodes outside the surgical field.[58] As with other modalities, its sensitivity is also limited because of the inability to detect nodal micrometastases. The

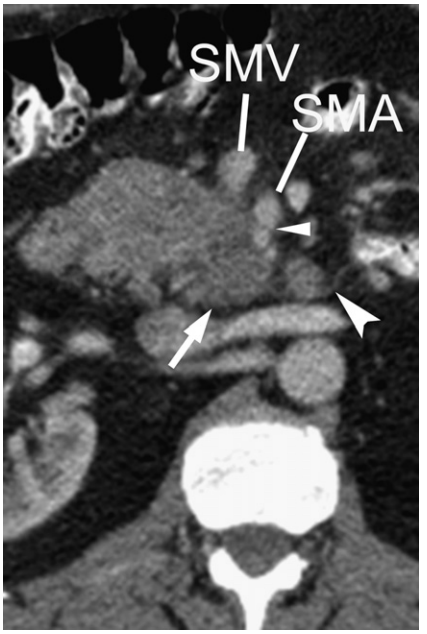

Fig. 23. A 54-year-old man with biopsy-proven borderline stage II to III pancreatic cancer and regional nodal disease. Axial image from baseline CT study shows tumor in the uncinate (*white arrow*) abutting by more than 90° the SMA, by extension along the IPDA (*white arrowhead*). To the left of the SMA is adenopathy (*curved white arrowhead*).

combination of EUS with FNA has been shown to greatly increase the specificity of diagnosis for pancreatic cancer,[59] and although information in the literature is limited, it is expected that EUS-FNA would have high specificity, and therefore usefulness, in the evaluation of suspicious lymph nodes, making it a useful problem solver when such determinations need to be made, although its ability to evaluate such nodes is again limited by the range of visualization of the abdomen by EUS, the range of safe access for FNA biopsy, and the problems of sampling error inherent with nodal micrometastases. Early work suggests that EUS paired with elastography may have promise in improving its sensitivity and specificity for nodal involvement.[60]

Metastases

Pancreatic cancer most commonly metastasizes to liver, peritoneum, lungs, and bone, although bone metastases typically occur late in the course of this disease. CT, MR imaging, and PET/CT play complementary roles in the evaluation for metastatic disease.

Liver metastases are most commonly assessed by either CT or MR imaging. Although older studies have reported CT (see **Fig. 7**; **Fig. 24**) having

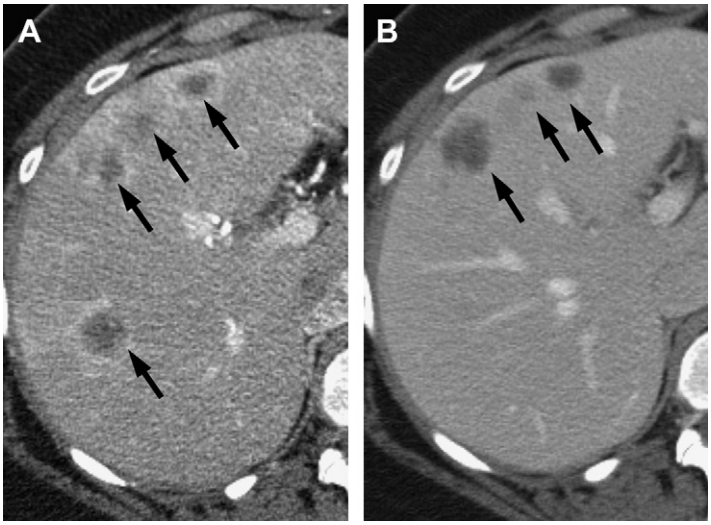

Fig. 24. A 54-year-old woman with multiple liver metastases from pancreatic cancer. (*A*) Pancreatic parenchymal phase shows multiple metastases (*black arrows*) that show peripheral hyperdense enhancement and central hypodensity. (*B*) Portal venous phase image shows only a hypodense appearance of metastases (*black arrows*).

a sensitivity of 75% to 87%,[61–63] a recent study comparing MDCT with CT arterial portography and CT-assisted hepatic arteriography showed MDCT to have a sensitivity of 48.4% and specificity of 97.9% for liver metastases.[64] Small-volume metastases to liver, particularly peritoneal implants to the liver surface, have been a difficulty for cross-sectional imaging, as is also the lack of specificity of very small lesions.[47–49] MR imaging has often served as a problem solver for liver metastases (Fig. 25), and recent developments such as diffusion-weighted imaging (Fig. 26) and the use of liver-specific contrast agents are promising. In a study of 15 patients with 62 liver metastases, comparing gadoxetic acid MR imaging (a liver-specific agent that can also be used for

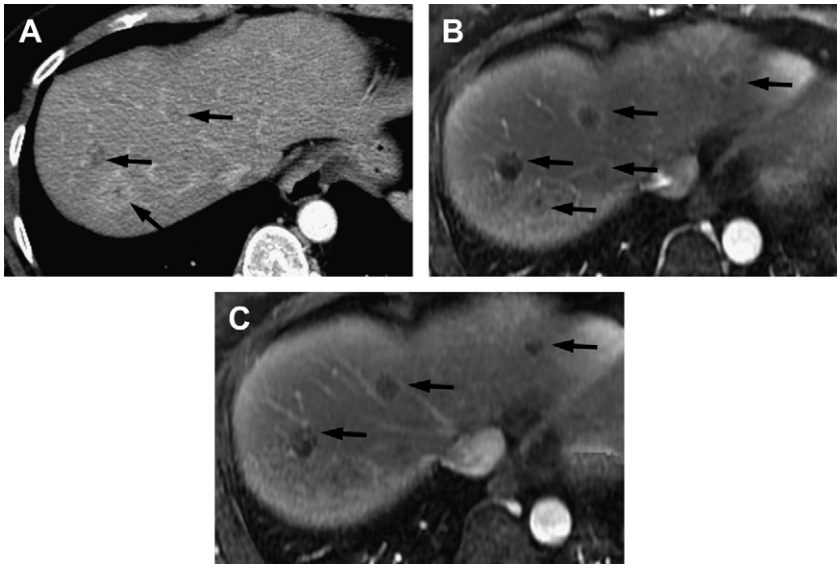

Fig. 25. A 43-year-old woman being evaluated for possible liver metastases. Contrast-enhanced portal venous phase CT image (*A*) shows lesions suspicious for metastases (*black arrows*) appearing slightly hypodense or showing unusual, slightly prominent, enhancement. Subsequent MR imaging examination (*B*) shows late arterial phase ring enhancement for several lesions with (*C*) washout on portal venous phase, appearing more prominent on the MR imaging than on CT and confirming that several of these lesions are liver metastases.

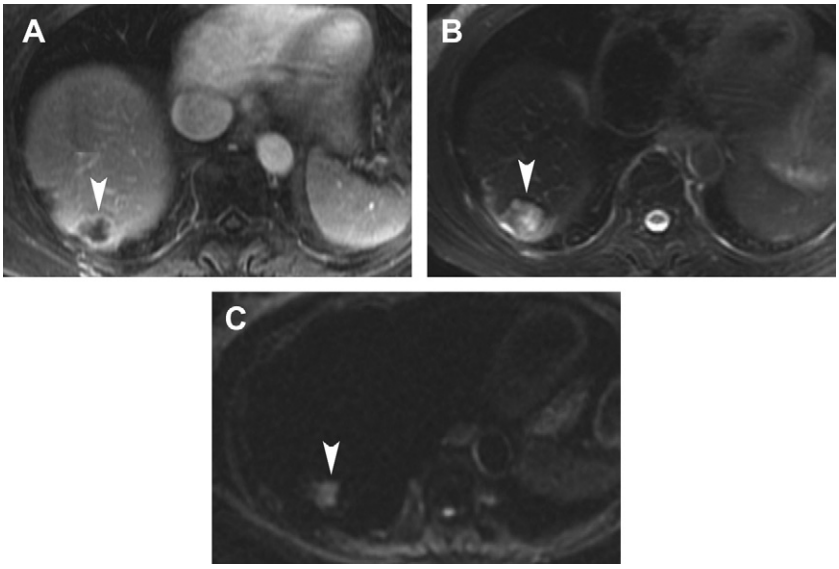

Fig. 26. A 71-year-old woman with pancreatic cancer status post Whipple procedure 2 years earlier. Lesion (*white arrowhead*) in liver on (*A*) portal venous phase shows low-intensity center and peripheral enhancement. (*B*) On fat-suppressed T2-weighted imaging, the lesion shows bright central focus likely representing necrosis. On diffusion (*C*), the lesion appears bright. Note that the rim of enhancement of liver metastases is a variable finding between patients on MR imaging.

dynamic imaging) with MDCT, MR imaging had greater sensitivity than CT (85% vs 69%).[65] MR imaging assessment of the primary tumor was thought to be similar to that of MDCT for the purposes of local staging.[65] Limited information is available on the role of PET/CT in the diagnosis of liver metastases (see **Fig. 20**). Studies that evaluated whole-body fluorodeoxyglucose (FDG) PET showed sensitivities of approximately 67% to 70%.[66–68] A more recent study comparing intravenous contrast-enhanced PET/CT, unenhanced PET/CT, and PET alone showed sensitivities for liver metastases of 82%, 46%, and 46%, respectively.[43]

Pancreatic metastases to the peritoneum are usually of small volume and have been difficult to detect by any modality (**Fig. 27**). This difficulty has led to the suggestion of using laparoscopy to screen patients for peritoneal disease. This approach has the limitation that sites identified on laparoscopy may not be identifiable on cross-sectional imaging, and therefore would not be amenable to imaging follow-up. In addition, a meta-analysis suggested that, in the setting of dual-phase thin-section CT, the use of additional exploratory laparoscopy would alter management in, at most, 4% to 15% of patients.[69]

PET/CT has been advocated as a means for identifying unexpected distant sites of metastatic disease (see **Figs. 20** and **21**) because it is a whole-body modality, as opposed to conventional MDCT and MR imaging, which are typically used in a narrow range of anatomic regions (abdomen, abdomen/pelvis, or, in the case of CT, chest, abdomen, and pelvis). A study of 103 patients in which the FDG-PET data were reviewed and compared with MDCT, the detection rate for liver metastases was less than that of CT, but better than CT for detection of remote

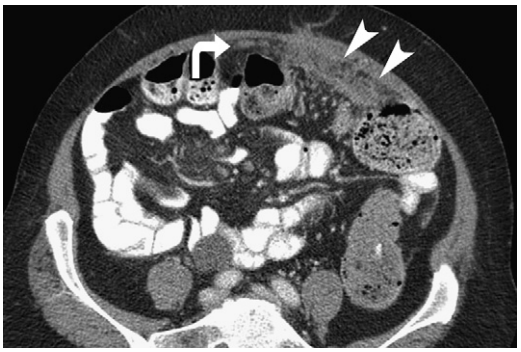

Fig. 27. Peritoneal metastases in a 46-year-old woman with pancreatic cancer. Axial contrast-enhanced portal venous phase CT image shows peritoneal disease manifesting as small nodule (*curved white arrow*) and as broad soft tissue thickening (*white arrowheads*).

lymph node and bone metastases.[70] However, the same study also noted that MDCT "indicated other noncurative factors in these patients." All patients who were not resectable could be identified as such without FDG-PET. Additional information is needed to identify whether there is added benefit for PET/CT compared with MDCT. Another consideration is the use of contrast-enhanced PET/CT, which could allow for this modality to become a single technique for whole-body staging of pancreatic cancer, providing information on the full gamut from local vascular involvement to distant liver, lung, bone, and far distant nodal metastases.[43]

REPORTING OF IMAGING FINDINGS

Following imaging and its accurate interpretation, probably the next most important issue is that findings be described in a clear, consistent manner, understandable by all physicians who are involved in a patient's care. Unclear reports can create confusion that can potentially result in patients being assigned incorrectly to treatment trials. For patients traveling between institutions, unclear reports could result in the repeating of imaging studies.

For this reason, attempts have been made to standardize reporting of imaging findings for pancreatic cancer. An article from our institution regarding multidisciplinary care of patients with pancreatic cancer proposed a template for dictation of CT findings for patients with pancreatic cancer, including descriptions of the primary tumor's size, location, relationship to vessels (using the terms abutment, $\leq 180^\circ$ of contact, and encasement, $>180^\circ$ of contact), vessel occlusion, variant vascular anatomy, a grade regarding local tumor resectability (resectable, borderline resectable, or locally advanced), and extent and location of extrapancreatic disease.[71] A template published by the Radiologic Society of North America (RSNA), and available on the Internet, similarly characterizes the primary lesion but also includes descriptive features for cystic lesions, suggested descriptors for vascular involvement (degrees of enhancement, abutment/encasement, or contiguous/noncontiguous), as well as providing additional descriptors of the adjacent parenchyma, nodes, and whether distant metastases are present.[72] It is our understanding that other organizations, such as the American Pancreatic Association (APA), are developing similar suggested reporting standards. It is our opinion that these templates serve 2 important functions: a checklist of features to be reported, and a standardized vocabulary (most importantly for vascular involvement) understood by multiple specialties.

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