American College of Radiology ACR Appropriateness Criteria[®] Screening, Locoregional Assessment, and Surveillance of Pancreatic Ductal Adenocarcinoma

Variant 1:

Adult. High-risk screening for pancreatic ductal adenocarcinoma.

Procedure	Appropriateness Category	Relative Radiation Level	
MRI abdomen without and with IV contrast	Usually Appropriate	0	
MRI abdomen without and with IV contrast with MRCP	Usually Appropriate	0	
CT abdomen and pelvis with IV contrast	Usually Appropriate		
CT abdomen with IV contrast	Usually Appropriate	$\mathbf{\mathfrak{D}}\mathbf{\mathfrak{D}}\mathbf{\mathfrak{D}}$	
CT abdomen with IV contrast multiphase	Usually Appropriate		
MRI abdomen without IV contrast	May Be Appropriate	0	
MRI abdomen without IV contrast with MRCP	May Be Appropriate	0	
US abdomen transabdominal	Usually Not Appropriate	0	
MRI abdomen without and with hepatobiliary contrast	Usually Not Appropriate	0	
CT abdomen and pelvis without IV contrast	Usually Not Appropriate		
CT abdomen without IV contrast	Usually Not Appropriate	€€€	
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€	
CT abdomen without and with IV contrast	Usually Not Appropriate		
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate		

Variant 2: Adult. Clinically suspected pancreatic ductal adenocarcinoma. Abdominal symptomatology. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	0
MRI abdomen without and with IV contrast with MRCP	Usually Appropriate	0
CT abdomen and pelvis with IV contrast	Usually Appropriate	€€€
CT abdomen with IV contrast multiphase	Usually Appropriate	���€
MRI abdomen without and with hepatobiliary contrast	May Be Appropriate	0
MRI abdomen without IV contrast	May Be Appropriate	0
MRI abdomen without IV contrast with MRCP	May Be Appropriate	0
US abdomen transabdominal	Usually Not Appropriate	0
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	€€€
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	����

Variant 3:

Adult. Pancreatic ductal adenocarcinoma. Locoregional disease staging or pretreatment planning or posttreatment evaluation related to neoadjuvant therapy or surgical planning.

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	0
MRI abdomen without and with IV contrast with MRCP	Usually Appropriate	0
CT abdomen with IV contrast multiphase	Usually Appropriate	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$
MRI abdomen without and with hepatobiliary contrast	May Be Appropriate	0
CT abdomen and pelvis with IV contrast	May Be Appropriate	€€€
CT abdomen and pelvis without and with IV contrast	May Be Appropriate	€€€
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$
US abdomen transabdominal	Usually Not Appropriate	0
MRI abdomen without IV contrast	Usually Not Appropriate	0
MRI abdomen without IV contrast with MRCP	Usually Not Appropriate	0
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	***

Variant 4:

Adult. Pancreatic ductal adenocarcinoma. Distant metastatic evaluation. Initial staging or postprocedure surveillance for metastatic disease.

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with hepatobiliary contrast	Usually Appropriate	0
MRI abdomen without and with IV contrast	Usually Appropriate	0
CT abdomen and pelvis with IV contrast	Usually Appropriate	♥♥♥
CT abdomen with IV contrast	Usually Appropriate	€€
CT chest abdomen pelvis with IV contrast	Usually Appropriate	♦€€€
MRI abdomen without IV contrast	May Be Appropriate	0
CT abdomen with IV contrast multiphase	May Be Appropriate (Disagreement)	♥♥♥♥
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	♥♥♥♥
US abdomen transabdominal	Usually Not Appropriate	0
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	���
CT abdomen without IV contrast	Usually Not Appropriate	€€€
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT abdomen without and with IV contrast	Usually Not Appropriate	◈◈♥♥
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	♦€€₽

SCREENING, LOCOREGIONAL ASSESSMENT, AND SURVEILLANCE OF PANCREATIC DUCTAL ADENOCARCINOMA

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Summary of Literature Review

Introduction/Background

Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal form of cancer, accounting for a small percentage of cancer diagnoses but a disproportionately high number of cancer-related deaths. The disease is often diagnosed at an advanced stage, resulting in a dismal 5-year survival rate of just 13% [1]. In 2010, the National Comprehensive Cancer Network (NCCN) introduced guidelines based on multidetector CT findings to classify localized PDAC into resectable, borderline resectable, and unresectable categories [2,3]. Resectable PDAC refers to tumors that are deemed suitable for surgical resection with clear margins. In this category, the tumor has not invaded major blood vessels or distant organs beyond what can be safely removed. Borderline resectable and initially unresectable PDAC indicates tumors that have some involvement or encasement of nearby blood vessels, such as the superior mesenteric artery or portal vein. These tumors require neoadjuvant therapy (chemotherapy with or without radiation therapy) to facilitate successful resection by downstaging the tumor [4,5]. Unresectable PDAC refers to tumors that have extensive involvement of nearby blood vessels or distant metastases. Treatment options may include palliative measures, such as chemotherapy, radiation therapy, or targeted therapies, to manage symptoms and slow disease progression [3]. Chemotherapy is commonly used in different stages of PDAC treatment. It can be given before surgery (neoadjuvant chemotherapy) to shrink the tumor and improve resectability [6,7]. After surgery, adjuvant chemotherapy may be recommended to reduce the risk of cancer recurrence. In advanced or metastatic cases, chemotherapy is the primary treatment to slow down disease progression and manage symptoms. Radiation therapy may be used in combination with chemotherapy (chemoradiation) as part of the treatment plan for locally advanced PDAC or for palliative purposes. Radiation therapy can help shrink tumors, relieve pain, and improve overall outcomes. The classification of PDAC into these categories is crucial in determining the appropriate treatment approach and setting realistic expectations for patient outcomes.

Imaging also plays a crucial role in the postoperative management of patients who have undergone PDAC resection. It helps detect and evaluate various complications that can arise, including pancreatic fistula, hepatobiliary/anastomotic leaks, abscesses, tumor recurrence, and strictures [8]. Vascular complications like pseudoaneurysm formation, thrombosis, and hemorrhagic or ischemic events may also be assessed by multiple imaging modalities [9]. Postoperative surveillance for assessment of tumor recurrence, both local and metastatic, is also important and is typically achieved through a comprehensive evaluation of imaging studies along with clinical assessment by a multidisciplinary team of healthcare professionals experienced in managing pancreatic cancer.

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

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• There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

• There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Adult. High-risk screening for pancreatic ductal adenocarcinoma.

The goal of screening for PDAC in high-risk patients is to detect tumors amenable to margin negative resection and to identify precancerous lesions, such as IPMNs [10]. Although the available data on PDAC screening outcomes is limited, there is a growing understanding that conducting screening in high-risk groups, particularly individuals with a genetic predisposition or family history of the disease, holds significant potential for both benefiting patients and being cost-effective. Genetic susceptibility plays a significant role in approximately 10% of all PDACs, involving specific germline mutations such as BRCA1 and BRCA2, ATM, PALB2, CDKN2A (associated with familial atypical multiple mole melanoma syndrome), MLH1, MSH2, MSH6, PMS2 (associated with Lynch syndrome), STK11 (associated with Peutz-Jeghers syndrome), and PRSS1 (associated with hereditary pancreatitis) [11]. Familial PDAC is defined as having at least 2 first-degree relatives affected by pancreatic cancer. It is widely agreed upon that screening for high-risk individuals should commence at the 50 years of age or 10 years earlier than the initial age at which familial onset was observed [12]. Screening for PDAC primarily relies on imaging techniques since there is no reliable biomarker available [13]. Microscopic lesions called pancreatic intraepithelial neoplasia (PanIN) serve as the main precursors for PDAC, but they are not easily detectable through imaging. However, the presence of small cysts in the pancreas on MRI can serve as secondary imaging markers, indicating the likelihood of PanIN being present. The primary objective of imaging is to identify early-stage PDAC (T1N0M0) or detect precancerous cystic lesions such as intraductal papillary mucinous neoplasms (IPMN) and mucinous cystic neoplasms. Most PDACs found within these high-risk groups under active screening are resectable and have an 85% 3-year survival after resection [11,14-16].

Multiple studies have shown the benefit in monitoring pancreatic cystic lesions by imaging to detect early PDAC [17-20] and to resect high risk precancerous tumors.

At this time, patients with chronic pancreatitis, including autoimmune and hereditary pancreatitis, are not recommended to undergo screening for PDAC due to the confounding imaging findings seen with chronic inflammation [16].

CT Abdomen and Pelvis With IV Contrast

Multiple studies suggest that contrast-enhanced CT may be able to detect suspicious findings before the final PDAC diagnosis. One such study by Higashi et al [21] reports that unsuspected pancreatic cancer was most commonly detected radiographically as a small solid lesion on contrast-enhanced CT. Another study suggests that within the 3 to 6 months prior to diagnosis, a contrast-enhanced CT may be 86% sensitive in the identification of findings suspicious for PDAC [22]. In addition, Toshima et al [23] report that focal suspicious pancreatic abnormalities may be detected at least 1 year prior to a diagnostic CT.

There is lack of data regarding the inclusion of pelvic imaging into high-risk screening for PDAC. Inclusion of the pelvis may be helpful if the patient has additional genetic predisposition for tumors that present within the pelvis.

CT Abdomen and Pelvis Without and With IV Contrast

The addition of precontrast imaging prior to contrast administration may only be clinically helpful in the specific setting of chronic pancreatitis to assess the pattern of calcifications since chronic pancreatitis tends to exhibit diffuse and intraductal calcifications whereas PDAC and other pancreatic lesions tend have more focal calcifications [24].

There is lack of data regarding the inclusion of pelvic imaging into high-risk screening for PDAC. Inclusion of the pelvis may be helpful if the patient has additional genetic predisposition for tumors that present within the pelvis.

CT Abdomen and Pelvis Without IV Contrast

Although no formal study evaluating the performance of noncontrast CT has been performed in the high-risk PDAC screening population, many early findings of PDAC require or are better detected with the use of intravenous (IV) contrast [21-23].

There is lack of data regarding the inclusion of pelvic imaging into high-risk screening for PDAC. Inclusion of the pelvis may be helpful if the patient has additional genetic predisposition for tumors that present within the pelvis.

CT Abdomen With IV Contrast

A study by Higashi et al [21] reports that a small solid lesion on contrast-enhanced prediagnostic CT was the most common radiologic feature suggestive of preclinical PDAC with a median size of 7.5 mm. Singh et al [22] find that a standard CT may be 86% sensitive during the 3 to 6 months before the formal diagnosis of PDAC when evaluating for a mass lesion, main duct dilation or narrowing/cutoff, common bile duct cutoff, extrapancreatic soft tissue, and vascular involvement. A study by Toshima et al [23] suggests that focal pancreatic abnormalities may be found at least 1 year prior to a diagnostic CT with the most common findings being focal parenchymal atrophy, focal faint parenchymal enhancement, and focal main duct changes.

CT Abdomen With IV Contrast Multiphase

CT has the advantage over other imaging modalities by way of its superior spatial resolution [10]. Pancreatic protocol CT, consisting of pancreatic and portal venous phases, has been shown to be 90% sensitive and 99% specific for detecting solid pancreatic neoplasms [10,25]. However, its sensitivity decreases to 77% for lesions <2 cm [10]. A study comparing screening modalities shows that EUS detected pancreatic abnormalities in 42% of subjects, MRI in 35%, and CT in 11% where the mean detected lesion size was 0.55 cm [10]. The Pancreatic Cancer Early Detection (PRECEDE) Consortium, an international multispecialty group of pancreatic specialists, suggests that pancreatic protocol CT may serve as an alternative to MRI/MR cholangiopancreatography (MRCP) for screening high-risk patients [14]. The addition of a delayed or equilibrium phase to the typical CT pancreatic and portal venous phases may improve sensitivity for small PDAC and detection of liver lesions and provide prognostic information [26-28]. Fukukura et al [26] have found that the additional of a delayed phase to the pancreatic and portal venous phases increases the sensitivity for small lesions, especially those that are isoenhancing to the pancrease on the pancreatic phase and subsequently hyperenhancing on the delayed phase.

CT Abdomen Without and With IV Contrast

Many reports consider a precontrast phase as only helpful in the specific scenario of chronic pancreatitis to assess the pattern of calcifications and their possible displacement by a lesion [24,25].

CT Abdomen Without IV Contrast

Although no formal study evaluating the performance of noncontrast CT has been performed in the high-risk PDAC screening population, many early findings of PDAC require or are better detected with the use of IV contrast [21-23].

FDG-PET/CT Skull Base to Mid-Thigh

Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT has not been incorporated into screening of PDAC [10].

MRI Abdomen Without and With Hepatobiliary Contrast

No study has been performed to evaluate PDAC detection using hepatobiliary contrast instead of conventional extracellular gadolinium-based contrast. The advantage of hepatobiliary contrast agents lies in increased sensitivity for the detection of liver metastases, which for those undergoing PDAC screening, may be of less importance [29].

MRI Abdomen Without and With IV Contrast

MR signal intensity differences between malignancy and normal pancreatic parenchyma, especially on the diffusion-weighted imaging (DWI) and precontrast T1-weighted sequences, can be helpful in the detection of PDAC [10]. Dynamic postcontrast sequences can be helpful to identify early, subtle findings of PDAC, which may be less apparent on noncontrast examinations [14].

MRI Abdomen Without and With IV Contrast With MRCP

A meta-analysis regarding screening for PDAC in those with high risk reports no significant differences in detection between the screening modalities of EUS or MRI [13]. A study comparing screening modalities shows that EUS detected pancreatic abnormalities in 42% of subjects, MRI in 35%, and CT in 11% where the mean detected lesion size was 0.55 cm [10]. The PRECEDE Consortium, recommends screening MRI/MRCP to be performed with a minimum of axial and coronal T2-weighted sequences, 2-D and 3-D T2-weighted MRCP sequences, axial in and out of phase T1-weighted gradient echo sequences, and 3-D fat-suppressed T1-weighted images acquired before and after IV contrast administration [14]. Precontrast MRI can exhibit signal intensity differences that can often differentiate between malignancy and normal pancreatic parenchyma, and MRCP sequences improve evaluation of pancreatic duct changes associated with PDAC [10]. Cystic lesions, such IPMN, may be better assessed by MRCP

sequences, as well [30]. Dynamic postcontrast sequences are recommended for the screening population since early, subtle findings of PDAC may be less apparent on noncontrast examinations [14].

MRI Abdomen Without IV Contrast

For PDAC screening, some studies suggest that contrast administration may be unnecessary [10,31,32]. Abbreviated MRI/MRCP examinations ranging from protocols omitting the postcontrast sequences to those consisting of only T2-weighted dedicated MRCP sequences have not been shown to have a significant difference in the detection of worrisome pancreatic findings or to have significant impact on patient management although the studies were not specifically focused on the high risk screening population [14].

MRI Abdomen Without IV Contrast With MRCP

For the purpose of screening, many centers still perform contrast-enhanced sequences, although some studies suggest that contrast may be unnecessary [10,31,32]. MRI can often differentiate between malignancy and normal pancreatic parenchyma via signal intensity differences with MRCP sequences allowing improved evaluation of the pancreatic duct [10]. MRCP is also helpful in visualizing cystic lesions, such as IPMN [30]. On the other hand, the use of MRCP sequences, alone, for PDAC screening has been found to be lower in sensitivity for PDAC detection than when used in combination with DWI, especially for lesions located distant from the main pancreatic duct [30]. DWI MRI has been shown useful for its increased sensitivity for PDAC, the ability to detect early-stage lesions and the possibility to provide prognostic information, especially as part of a noncontrast MRI protocol [30,33-36]. Diffusion restriction and other MR characteristics found in IPMNs may represent additional high-risk findings for malignancy and predictors of invasiveness [34,37,38].

US Abdomen Transabdominal

Ultrasound (US) has not been incorporated into the screening of PDAC due to its inability to image the entire gland [10].

Variant 2: Adult. Clinically suspected pancreatic ductal adenocarcinoma. Abdominal symptomatology. Initial imaging.

Patients with pancreatic adenocarcinoma usually present with vague, nonspecific symptoms late in the disease process, making curative surgical resection no longer possible [39]. Although carbohydrate antigen 19-9 has high sensitivity and specificity in symptomatic patients, common false-positives limit its usefulness in the diagnosis of pancreatic cancer [40]. Thus, imaging is central to the early detection and diagnosis of pancreatic lesions while the patient may still be eligible for curative surgical resection. Imaging is able to also identify patients who may not benefit from surgical resection or who may benefit from neoadjuvant therapies prior to possible resection, thus, maximizing patient outcomes while minimizing morbidity.

CT Abdomen and Pelvis With IV Contrast

Studies have shown that CT is able to suggest early suspicious pancreatic changes, even 12 to 18 months prior to the diagnosis of PDAC, likely providing survival benefit [21-23]. Higashi et al [21] have examined incidental pancreatic adenocarcinomas and report that the presence of a pancreatic solid lesion on contrast-enhanced CT was the most common radiologic feature suggesting PDAC with a median size of 7.5 mm. A study by Singh et al [22] finds contrast-enhanced CT to be 86% sensitive in detecting findings suspicious for PDAC within the 3 to 6 months prior to the establishment of a PDAC diagnosis. The suspicious findings outlined by Singh et al [22] include hypodense lesion, main duct dilation or narrowing/cutoff, common bile duct cutoff, extrapancreatic soft tissue, and vascular involvement. Another study corroborates that focal suspicious pancreatic abnormalities may be detected at least 1 year prior to a diagnostic CT establishing the diagnosis of PDAC [23].

Given the rarity of pelvic metastases in patients with PDAC, routine pelvic CT may be only considered for patients with other known distant metastases [41].

CT Abdomen and Pelvis Without and With IV Contrast

Including a precontrast phase prior to contrast administration is not routinely performed, but may be helpful for calcification assessment in the setting of chronic pancreatitis [24,25].

CT Abdomen and Pelvis Without IV Contrast

Many early findings of PDAC require or are better detected with the use of IV contrast [21-23].

CT Abdomen With IV Contrast Multiphase

A multi-institutional survey regarding practice patterns of PDAC imaging reveals that almost 93% of respondents perform dynamic multiphase pancreatic protocol CT for evaluation of patients with initial suspicion or staging of PDAC given current NCCN guidelines [9,42]. Multiphase CT findings have been shown to help identify PDAC and to enable differentiation from other pancreatic malignancies.

FDG-PET/CT Skull Base to Mid-Thigh

Despite FDG-PET/CT performance, a multi-institutional survey regarding practice patterns of PDAC imaging reveals PET/CT as not being routinely used for diagnosis or staging of PDAC, and the NCCN guidelines suggest that PET/CT should not be used as a substitute for high-quality multiphase pancreas CT [9].

A systematic review corroborates PET's superior sensitivity of 92% for the diagnosis of PDAC compared to CT (87%) and MRI (69%). The review; however, also reports that the specificity for PDAC is 65% for PET, 96% for CT, and 93% for MRI [43]. FDG-PET's low specificity for PDAC is likely due to the increased FDG avidity of inflammatory processes and other malignancies. This low specificity has been shown to improve with FDG-PET/CT to help differentiate benign pancreatic pathology from malignancy with several studies suggesting similar or superior diagnostic accuracy for PDAC when compared to contrast-enhanced CT and MRI [43,44]. The use of maximum standardized uptake value (SUV_{max}) has also been shown to be helpful in differentiating benign from malignant lesions and offer prognostic information [44-46].

MRI Abdomen Without and With Hepatobiliary Contrast

No studies have been performed to compare the use of hepatobiliary contrast agents to conventional extracellular gadolinium-based contrast agents in the evaluation PDAC detection. Hepatobiliary contrast agents are most useful in the detection of liver metastases, which for those without an established PDAC diagnosis, may be of less importance. Some studies have shown that MRI may be able to differentiate PDAC from other pancreatic malignancies, as well [47-49].

MRI Abdomen Without and With IV Contrast

Precontrast sequences, specifically, the DWI and precontrast T1-weighted sequences, can be helpful in PDAC detection since malignant lesions and normal parenchyma often exhibit signal intensity differences [10]. Early and subtle PDAC findings may also be detected on dynamic postcontrast sequences which are often complementary to the precontrast sequences [14].

MRI Abdomen Without and With IV Contrast With MRCP

According to a multi-institutional survey regarding practice patterns of PDAC imaging, MRI with or without MRCP is not typically used if there is only a clinical suspicion of PDAC [9]. This is despite the superior contrast resolution allowing for better detection of small pancreas tumors, improved characterization of liver lesions when compared to CT, and MRI's ability to differentiate PDAC from other pathologies [9,50,51]. Precontrast and dynamic postcontrast sequences both can help detect subtle suspicious findings, and postcontrast subtraction images may help to identify small enhancing mural nodules within cystic lesions or lesions at a focal ductal cutoff [10,14]. MRCP sequences improve the evaluation of PDAC's pancreatic duct changes, as well as cystic lesions, such as IPMN [30].

MRI Abdomen Without IV Contrast

Abbreviated MRI/MRCP examinations include multiple types of protocols with some omitting the postcontrast sequences and others consisting of only T2-weighted dedicated MRCP sequences. Studies have not shown a significant difference in the detection of worrisome pancreatic findings or a significant impact on patient management despite the many studies that suggest the advantages of postcontrast imaging in the detection of pancreatic abnormalities [14]. One reason may be due to signal intensity differences often observed between normal and malignant lesions within the pancreas. In addition, DWI MRI has been shown useful for its increased sensitivity for PDAC and the ability to detect early-stage lesions and possibly to provide prognostic information [30,33-36].

MRI Abdomen Without IV Contrast With MRCP

Precontrast sequences and MRCP sequences are complementary with the precontrast sequences used to evaluate for signal differences that may suggest a pancreatic lesion and the MRCP sequences used to better evaluate the pancreatic duct and cystic lesions [10,30]. The use of MRCP sequences alone, has been found to be lower in sensitivity for PDAC detection, especially for lesions located away from the main pancreatic duct [30]. DWI MRI is helpful for its increased sensitivity for PDAC and the ability to detect early-stage lesions, especially as part of a noncontrast MRI protocol [30,33-36].

US Abdomen Transabdominal

There is no relevant literature for the use of US in the diagnosis of PDAC due to its inability to image the entire gland [10]. Some reports have described contrast-enhanced US's high sensitivity for PDAC but more data are needed [52].

Variant 3: Adult. Pancreatic ductal adenocarcinoma. Locoregional disease staging or pretreatment planning or posttreatment evaluation related to neoadjuvant therapy or surgical planning.

Improved patient survival and potential cure for pancreatic adenocarcinoma are dependent on complete surgical resection with the possible addition of adjuvant or neoadjuvant therapies [39]. Patients with incomplete and margin-positive resections have much poorer survival rates and may not benefit from surgical resection. Thus, patients without distant metastases must undergo accurate assessment of locoregional disease by imaging to allow for improved decision-making for treatment recommendations to maximize survival benefit and minimize morbidity. Patients with borderline resectable disease or locally advanced pancreatic adenocarcinoma typically receive neoadjuvant therapy in the form of systemic chemotherapy with or without radiation therapy. Imaging after neoadjuvant therapy is used to assess therapeutic response, especially in regard to tumor size and disease involvement of locoregional critical structures, in order to assess the possibility for an R0 resection [53].

CT Abdomen and Pelvis With IV Contrast

Evaluation for resectability of pancreatic cancer requires detailed assessment of the regional arterial and venous structures. Possible locoregional vascular invasion by pancreatic cancer is better evaluated by multiphase contrast-enhanced CT rather than a single-phase contrast-enhanced study. Given the rarity of pelvic metastases in patients with PDAC, routine pelvic CT may be only considered for patients with distant metastases [41]; however, the standard practice is to obtain a pelvic CT to better assess for possible peritoneal, nodal, and bone metastases.

CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature for the addition of a noncontrast phase to a contrast-enhanced CT for the purpose of evaluating resectability.

CT Abdomen and Pelvis Without IV Contrast

PDAC staging requires the use of IV contrast, especially to assess for the presence of vascular invasion and liver metastases.

CT Abdomen With IV Contrast Multiphase

A multi-institutional survey regarding practice patterns of PDAC imaging reveals that almost 93% of respondents perform dynamic multiphase pancreatic protocol CT for evaluation of patients with initial suspicion or staging of PDAC given current NCCN guidelines [9,42]. Multiphase CT has been shown to have high accuracy rates for tumor stage, vascular invasion, perineural invasion, and liver metastases, but limited evaluation in accuracy for nodal invasion [54-56]. For example, Kim et al [54] report CT to be only 55% to 59.5% accurate for nodal metastases, but 77.5% to 82.9% accurate for tumor stage and 92% to 94% accurate for vascular invasion with a 0.66 to 0.733 area under the curve for perineural invasion. In addition to diagnostic assessment, many CT findings, CT perfusion, texture analysis, and radiomics may provide prognostic information [21,26,27,57-67]. Borhani et al [66] and Kim et al [68] have found various CT-based features which may predict the effectiveness of chemotherapy on the patient's PDAC. Numerous reports suggest that multiphase CT accurately depicts local disease in the pretreatment staging scenario [21,26,27,57-65,69]; however, many studies have shown CT to exhibit lower specificity after neoadjuvant therapy, often due to overestimation of vascular invasion and tumor size, resulting in decreased predictability for an R0 resection [6,7,70,71]. This may be due to CT and MRI's inability to distinguish tumor from fibrosis [53]. Studies by Park et al [72] and Jeon et al [73] suggest that the preoperative CT findings of tumor size <3 cm, decreased tumor-arterial contact compared to initial staging, and decreased abutment to the portal vein may be predictive of resectability.

FDG-PET/CT Skull Base to Mid-Thigh

Although the use of SUV_{max} may be helpful in differentiating benign from malignant lesions, offer prognostic information, and predict response to neoadjuvant therapy [44-46,74], a multi-institutional survey regarding practice patterns of PDAC imaging reveals PET/CT as not being routinely used for PDAC diagnosis, staging, or evaluation for resectability [9]. The NCCN guidelines suggest that PET/CT should not be used as a substitute for high-quality multiphase pancreas CT, but as an adjunct to CT or MRI [9,42].

Most studies of PET regarding PDAC staging examine the evaluation of locoregional nodal disease and distant metastasis [43]. Comparison studies between PET with CT and MRI for distant metastasis reveal conflicting results with many studies describing the superiority of PET or PET/CT in detecting distant disease and other studies suggesting that CT outperforms PET [41, 42]. A meta-analysis has found FDG-PET/CT to have sensitivities of 91% for PDAC diagnosis, 64% for PDAC nodal disease, and 67% for liver metastases from PDAC, suggesting that FDG-PET/CT may offer diagnostic and predictive benefits for PDAC but may not be beneficial as a first-line staging modality [75]. FDG-PET/CT has been shown to be helpful in patients with a CA19.9 >150 to 200 U/mL for metastatic disease evaluation and prognostication with a relationship between SUVmax and survival [76-78]. One study suggests that PET/CT may be most cost-effective for patients who are thought to have resectable disease [79].

A multi-institutional survey regarding practice patterns of PDAC imaging reveals that after neoadjuvant therapy for patients with borderline or locally advanced FDG-PET/CT is not typically used to reevaluate lesion resectability [9]. Given current NCCN guidelines, FDG-PET/CT has little role in the evaluation of PDAC after neoadjuvant therapy [9,42].

MRI Abdomen Without and With Hepatobiliary Contrast

MRI has superior contrast resolution allowing for better detection of small pancreas tumors and improved characterization of liver lesions when compared to CT, especially smaller liver lesions <1 cm [9,50,51]. Hepatobiliary contrast-enhanced MR may also be more accurate in depicting small liver metastases [9,42].

MRI Abdomen Without and With IV Contrast

A multi-institutional survey regarding practice patterns of PDAC imaging reveals MRI with or without MRCP is not typically used for staging of PDAC or to evaluate lesion resectability after neoadjuvant therapy [9]. Even though MRI has been shown to have equal sensitivity in local staging compared to CT, MRI is often used as an adjunct if CT findings are indeterminate or the patient is unable to undergo multiphase contrast-enhanced CT [10]. Kim et al [51] have shown that when MR with and without IV contrast is used in addition to a staging CT for PDAC, treatment modifications, including resectability status, occurred in 14.4% (31 of 216 patients) of patients. DWI MRI has been shown useful for its increased sensitivity for PDAC, the ability to detect early-stage lesions, and possibly to provide prognostic information [30,33-36,80]. DWI MRI may also help predict R0 resectability, and another study shows MR to have a 100% sensitivity in differentiating stage I/II or III/IV [81,82]. MR enhancement pattern of PDAC has been shown to provide prognostic information [83].

MRI Abdomen Without and With IV Contrast With MRCP

There is no relevant literature for the addition of MRCP sequences to an MRI abdomen without and with IV contrast for the purpose of PDAC staging before and after neoadjuvant therapy.

MRI has the added benefit of improved evaluation of the pancreatic duct with MRCP sequences [24,32,84-87].

MRI Abdomen Without IV Contrast

PDAC staging requires the use of IV contrast, especially to assess for the presence of vascular invasion and liver metastases.

MRI Abdomen Without IV Contrast With MRCP

PDAC staging requires the use of IV contrast, especially to assess for the presence of vascular invasion and liver metastases.

US Abdomen Transabdominal

There is a lack of evidence for the use of US in the initial staging of PDAC.

Variant 4: Adult. Pancreatic ductal adenocarcinoma. Distant metastatic evaluation. Initial staging or postprocedure surveillance for metastatic disease.

Identifying metastatic disease at initial presentation is critical to avoid potentially morbid operations, reliably present prognostic information, and offer adequate systemic treatment options. At this time, imaging is the primary method of pancreatic adenocarcinoma staging. According to the 2024 NCCN guidelines, chest CT may be used to evaluate for possible lung metastases from PDAC which have been reported to occur in 3.5%-16% of patients [88,89].

In addition, because recurrences after pancreatic adenocarcinoma resection occur in 80% to 85% of patients, routine follow-up imaging is used for early detection of recurrent disease. Early liver metastasis is common and associated with a poor prognosis [90]. Early detection is thought to be optimal since the disease is at its smallest and thought

to be most susceptible to treatment, suggesting that early detection may help to prolong overall survival in resected PDACs [91].

CT Abdomen and Pelvis With IV Contrast

A multi-institutional survey regarding practice patterns of PDAC imaging reveals that after definitive surgery for PDAC, 46.5% of respondents use single portal venous phase CT, 34.9% use multiphase pancreatic protocol CT, 7% use multiphase dual-energy CT, and 7% use MRI with MRCP to survey for recurrence [9]. Since the primary goal of postsurgical PDAC surveillance is to identify liver metastases and recurrence in the resection bed, a single-phase CT is adequate for surveillance [9]. CT has been shown to have high accuracy rates for liver metastases and is able to distinguish portal encasement from benign portal stenosis as a marker of local recurrence [54,56,92,93]. CT texture analysis may also predict likelihood for liver metastases [94]. The 2024 NCCN guidelines suggest that scan coverage may include the pelvis according to institutional preferences.

CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature for the addition of a noncontrast phase to a contrast-enhanced CT for the purpose of follow-up imaging after resection.

CT Abdomen and Pelvis Without IV Contrast

Follow-up imaging after PDAC resection requires the use of IV contrast, especially to assess for the presence of resection bed recurrence and metastases.

CT Abdomen With IV Contrast

Single-phase CT is deemed adequate for surveillance after resection [9]. CT has high accuracy rates for detecting liver metastases and for distinguishing benign portal vein stenosis from portal vein encasement by recurrence [54,56,92]. CT texture analysis may also predict likelihood for liver metastases [94].

CT Abdomen With IV Contrast Multiphase

Since CT is accurate in detecting liver metastases and resection bed recurrence, single-phase CT is sufficient for surveillance [9,54,56,92]. CT texture analysis may also predict likelihood for liver metastases [94].

CT Abdomen Without and With IV Contrast

There is no relevant literature for the addition of a noncontrast phase to a contrast-enhanced CT for the purpose of follow-up imaging after resection.

CT Abdomen Without IV Contrast

Follow-up imaging after PDAC resection requires the use of IV contrast, especially to assess for the presence of resection bed recurrence and metastases.

CT Chest Abdomen Pelvis With IV Contrast

The 2024 NCCN guidelines suggest that scan coverage may include the chest and pelvis according to institutional preferences. Lung metastases from PDAC have been reported to occur in 3.5% to 16% of patients [88,89].

CT Chest Abdomen Pelvis Without And With IV Contrast

There is no relevant literature for the addition of a noncontrast phase to a contrast-enhanced CT for the purpose of follow-up imaging after resection.

CT Chest Abdomen Pelvis Without IV Contrast

Follow-up imaging after PDAC resection requires the use of IV contrast, especially to assess for the presence of resection bed recurrence and metastases.

FDG-PET/CT Skull Base to Mid-Thigh

Although PET/CT has been shown to have a high diagnostic accuracy in PDAC restaging, this modality is usually used when recurrence is suspected and CT or MRI shows a lack of or equivocal findings [43,44,95]. PET/CT has been shown to have a high sensitivity of 96% in detecting recurrence at the operative site and to detect recurrence earlier than CT alone [43,44,96]. In addition, metastatic lymph nodes may be distinguished from reactive lymph nodes by PET. FDG avidity in the operative bed 3 months after surgery suggests resection site recurrence rather than postoperative change [43]. CT and MRI remain superior to PET/CT in detecting liver metastases [96].

MRI Abdomen Without and With Hepatobiliary Contrast

The primary goal of postsurgical PDAC surveillance is to identify liver metastases and recurrence in the resection bed, and MRI has been shown to be more sensitive than CT for liver metastases, especially smaller lesions <1 cm.

Hepatobiliary contrast-enhanced MRI may also be more accurate in depicting small liver metastases than with conventional gadolinium-based contrast agents [9,42]. Although MRCP images may be included in the examination, no data exists to determine whether MRCP improves the detection of pancreatic recurrence after resection.

MRI Abdomen Without and With IV Contrast

Because MRI has been shown to be more sensitive than CT for liver metastases, MRI abdomen without and with IV contrast may be effective in the surveillance of PDAC after resection [9,42]. In addition, MRI may be used to characterize liver lesions found by single-phase CT.

MRI Abdomen Without IV Contrast

There is no relevant literature for the use of MRI abdomen without IV contrast for the purpose of follow-up imaging after resection.

US Abdomen Transabdominal

There is no relevant literature for the use of US in this scenario.

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- Variants 1 and 2: For patients at high risk for PDAC and for patients whose clinical presentation raises the possibility of PDAC, CT abdomen with IV contrast multiphase, MRI abdomen without and with IV contrast, MRI abdomen without and with IV contrast with MRCP, CT abdomen with IV contrast, and CT abdomen and pelvis with IV contrast are appropriate screening and initial imaging modalities. These 5 procedures are equivalent alternative studies for screening (ie, only 1 procedure will be ordered to provide the clinical information to effectively manage the patient's care). MRI abdomen without IV contrast and MRI abdomen without IV contrast with MRCP may be appropriate. MRI abdomen without and with hepatobiliary contrast may be appropriate with the additional value of screening for possible liver metastases.
- Variant 3: Locoregional disease assessment to evaluate neoadjuvant therapy response and for surgical planning is most appropriately assessed with CT abdomen with IV contrast multiphase, MRI abdomen without and with IV contrast, and MRI abdomen without and with IV contrast with MRCP. These 3 procedures are equivalent alternative studies for screening (ie, only 1 procedure will be ordered to provide the clinical information to effectively manage the patient's care). Additional imaging examinations may be appropriate if distant metastases are suspected at the time of assessment/reassessment by performing CT abdomen and pelvis with IV contrast, CT abdomen and pelvis without and with IV contrast, FDG-PET/CT skull base to mid-thigh, or MRI abdomen without and with hepatobiliary contrast.
- Variant 4: Disease staging after confirmed diagnosis of pancreatic ductal adenocarcinoma and postprocedure surveillance for metastatic disease after resection of the primary tumor are most appropriately performed with CT chest, abdomen, and pelvis with IV contrast. Since early detection of recurrence after resection and early detection of liver metastases are thought to be optimal, postprocedure surveillance for recurrence and metastatic disease is also appropriately performed by CT abdomen and pelvis with IV contrast, CT abdomen with IV contrast, CT abdomen without and with IV contrast, MRI abdomen without and with hepatobiliary contrast and MRI abdomen without and with IV contrast. These 5 procedures are equivalent alternative studies for surveillance (ie, only 1 procedure will be ordered to provide the clinical information to effectively manage the patient's care). FDG-PET/CT skull base to mid-thigh may also be appropriate to evaluate for distant metastases.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <u>https://acsearch.acr.org/list</u>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, click <u>here.</u>

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health [97].

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Appropriateness Category Names and Definitions

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria[®] Radiation Dose Assessment Introduction document [98].

Relative Radiation Level Designations			
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range	
0	0 mSv	0 mSv	
۲	<0.1 mSv	<0.03 mSv	
*	0.1-1 mSv	0.03-0.3 mSv	
\$\$ \$	1-10 mSv	0.3-3 mSv	
\$\$\$\$	10-30 mSv	3-10 mSv	
$\mathbf{\hat{\mathbf{C}}}\mathbf{\hat{\mathbf{C}}}\mathbf{\hat{\mathbf{C}}}\mathbf{\hat{\mathbf{C}}}$	30-100 mSv	10-30 mSv	

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination.