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The Role and Value of Imaging Studies in the Clinical Management Pathway of Pancreatic Ductal Adenocarcinoma (Postprint)

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Abstract

Pancreatic ductal adenocarcinoma (PDAC) is an extremely aggressive and highly malignant tumor of the digestive tract. The common issues in its diagnosis and treatment pathway mainly include: (1) screening and early detection; (2) accurate diagnosis and staging; (3) differential diagnosis; (4) follow-up and treatment evaluation, with imaging playing an important role in all these aspects. This article summarizes the role and value of various imaging modalities in the PDAC diagnosis and treatment pathway, provides an in-depth understanding of their advantages and limitations, proposes an evidence-based imaging workflow for PDAC, and elaborates on the key points of PDAC imaging diagnosis and differential diagnosis, thereby better guiding clinical decision-making and improving the prognosis of PDAC patients.

Full Text

Preamble

Journal: Medical Journal of Peking Union Medical College Hospital (ChinaXiv Cooperative Journal)
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Title: The Role and Value of Imaging Examinations in the Clinical Diagnosis and Treatment Pathway of Pancreatic Ductal Adenocarcinoma

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Abstract

Pancreatic ductal adenocarcinoma (PDAC) is a highly malignant tumor of the digestive tract. The common challenges in its diagnosis and treatment pathway include: (1) screening and early detection; (2) accurate diagnosis and staging; (3) differential diagnosis; and (4) follow-up and treatment evaluation, in all of which imaging plays a crucial role. This article summarizes the role and value of various imaging examinations in the PDAC diagnosis and treatment pathway, explains the advantages and limitations of different imaging modalities, provides an evidence-based imaging examination process, and focuses on key points in PDAC imaging diagnosis and differential diagnosis to better guide clinical decision-making and improve patient prognosis.

Keywords: pancreatic ductal adenocarcinoma; diagnosis and treatment; clinical pathway; imaging

PDAC is an extremely aggressive and highly malignant digestive tract tumor. Epidemiological data show a clear trend toward younger onset age, with an overall 5-year survival rate of only 7-8%. Data from 2015 indicate that PDAC has risen to become the third leading cause of cancer-related mortality in the United States and is projected to become the second leading cause by 2030. The common problems in the PDAC diagnosis and treatment pathway mainly include: (1) screening and early detection; (2) accurate diagnosis and staging; (3) differential diagnosis; and (4) follow-up and treatment evaluation, with imaging playing an important role throughout. Early screening can improve prognosis, and screening target selection is primarily based on family history and identifiable genetic susceptibility. However, there are inconsistencies between different studies regarding size criteria for early PDAC, with some using <2 cm and others <3 cm. Transabdominal ultrasound has limited value for early PDAC detection. This article will summarize the role and value of various imaging examinations in PDAC management, provide an evidence-based imaging workflow, and highlight recent advances in imaging technology.

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1. Screening and Early Detection

1.1 Screening

The International Cancer of the Pancreas Screening (CAPS) Consortium recommends screening for high-risk individuals starting at age 50 (or 10 years younger than the youngest affected relative). High-risk groups include: (1) first-degree relatives (FDRs) of familial pancreatic cancer (FPC) patients with at least two affected FDRs in the family; (2) Peutz-Jeghers syndrome patients; (3) carriers of CDKN2A (p16), BRCA1, BRCA2, PALB2, or Lynch syndrome gene mutations; and (4) patients with hereditary pancreatitis.

Endoscopic ultrasound (EUS) offers many advantages for screening, including better detection of small solid pancreatic lesions, lack of ionizing radiation, and

no need for contrast agents. However, EUS has limitations including significant operator dependence, being an invasive procedure, and inability to assess extra-pancreatic conditions. MRI with magnetic resonance cholangiopancreatography (MRCP) can evaluate extra-pancreatic structures and pancreatic ductal lesions, with secretin-enhanced MRCP further improving ductal lesion detection. If no lesions are found at baseline evaluation, annual MRI/MRCP is recommended; if lesions are detected, EUS monitoring is recommended.

Blinded comparative studies show equivalent lesion detection rates between EUS and MRI/MRCP. However, EUS may miss small cystic lesions that MRI can detect. MRI has higher soft tissue resolution and can non-invasively evaluate the pancreaticobiliary ductal system. Studies show MRI, particularly diffusion-weighted imaging (DWI), has higher detection rates for small pancreatic lesions than CT. A retrospective study of pancreatic tumors <2 cm found that un-enhanced MRI had the highest diagnostic accuracy (AUC = 0.930, 95% CI: 0.884-0.977), followed by DWI (AUC = 0.884, 95% CI: 0.822-0.924).

1.2 Early Detection

Despite advances in PDAC diagnosis and treatment, prognosis remains poor, partly because most tumors have local invasion and distant metastasis at diagnosis. The sensitivity for detecting small lesions (<1 cm) is still problematic. Multiple studies on spectral CT show that different energy level images and iodine material density maps can improve conspicuity of small PDAC lesions. Dual-energy CT can improve detection sensitivity, with one study showing sensitivity and specificity of 91.2% and 94.4% respectively for detecting isoattenuating PDAC.

1.3 Isoattenuating PDAC

Isoattenuating PDAC, where tumor density is similar to normal pancreatic parenchyma during enhanced scanning (density difference <15 HU), occurs in 5-17% of cases. Early diagnosis of isoattenuating tumors is critical as they are typically small but have better differentiation and prognosis. However, isoattenuating does not equal early PDAC, as less than one-third of isoattenuating tumors are early-stage. Most studies show DWI can improve detection of isoattenuating tumors. When imaging, cytology, and even biopsy results are negative, close follow-up is still required for highly suspected cases.

1.4 Indirect Signs

Indirect signs are important for PDAC diagnosis, with sensitivity and specificity ranging from low to high as follows: pancreatic duct dilation (sensitivity 78%, specificity 84%), distal pancreatic atrophy (sensitivity 82%, specificity 96%), abnormal pancreatic contour (sensitivity 92%), and common bile duct dilation (sensitivity 73%, specificity 92%). These indirect signs can be crucial when direct tumor visualization is difficult.

2. Accurate Diagnosis and Staging

2.1 T Staging

Accurate PDAC diagnosis primarily relies on high-quality multi-phase contrast-enhanced imaging. Pancreatic protocol CT with dual-phase enhancement (pancreatic parenchymal phase and portal venous phase) is the preferred method for T staging and treatment decision assessment in most guidelines. During the pancreatic parenchymal phase, the enhancement difference between lesion and pancreatic parenchyma is maximal. Multiple post-processing techniques including multiplanar reconstruction can optimally display the relationship between lesions and surrounding structures.

2.2 Resectability Evaluation

Multiple evaluation systems exist for resectability assessment, including NCCN criteria, MD Anderson Cancer Center classification, and ASCO guidelines. While there are minor differences between systems, the most widely accepted classification is borderline resectable PDAC. Most studies show CT has good sensitivity for evaluating vascular invasion and resectability. New techniques like virtual monoenergetic 70keV images can improve assessment of vascular resectability and increase prediction of negative resection margins.

3D printing technology, using computer post-processing for image analysis, can intuitively and accurately display the morphological and spatial relationships between lesions, vessels, and bile ducts. This is primarily used for pancreatic head cancer to guide individualized surgical planning, prevent anomalous vascular injury, and facilitate precise surgery for complex pancreatic head cancers, while also shortening the learning curve for young surgeons.

2.3 Lymph Node Metastasis

Lymph node metastasis outside the surgical field (retroperitoneal, jejunal mesenteric, left side of superior mesenteric artery) indicates poor prognosis and is a contraindication for surgery. These lymph nodes must be described to guide surgical lymph node biopsy. However, all imaging modalities have limited value for diagnosing lymph node involvement. CT, MRI, and PET-CT all have poor diagnostic accuracy for lymph node metastasis because normal-sized lymph nodes can have micrometastases, while enlarged nodes may be reactive. Using short-axis diameter >1 cm as the criterion for metastasis yields only 14% sensitivity. Other morphological criteria like round shape, central necrosis, and lack of fat density also cannot accurately diagnose metastatic lymph nodes.

A 2018 study of pathology-confirmed lymph nodes showed MRI with DWI could differentiate metastatic from non-metastatic nodes with high accuracy, but this technique requires validation in large-sample studies. Radiomics has shown

promise in evaluating lymph node metastasis in other tumors and may be applicable to PDAC, though studies correlating imaging findings with final pathology are still needed.

2.4 Distant Metastasis Evaluation

For patients with potentially resectable PDAC without detected liver metastases, liver-specific imaging is recommended to confirm absence of metastases. A prospective multicenter study found that routine MRI with DWI sequences detected liver metastases in 11% of patients with potentially resectable PDAC who had negative initial CT scans, with a statistically significant difference. For lesions <1 cm, CT has even lower detection rates.

PET-CT has limited value for PDAC diagnosis but can evaluate extrahepatic distant metastases, particularly bone metastasis. Whole-body diffusion-weighted imaging (WB-DWI) can provide one-stop evaluation of lymph node, bone, and peritoneal metastases without contrast injection. However, FDG uptake is reduced by high blood glucose levels, and inflammatory conditions like chronic or acute pancreatitis can show focal metabolic uptake, causing false-positive results. PET has lower resolution and can yield false-negative results.

2.5 Perineural Invasion

PDAC has a propensity for neural invasion, involving peripancreatic, retroperitoneal, and celiac plexus nerves. Perineural invasion is associated with early postoperative recurrence and worse prognosis. Imaging findings include loss of peripancreatic retroperitoneal fat or irregular soft tissue in perivascular fat. A 2007 study by Tian et al. established CT criteria for extrapancreatic neural plexus invasion, though perineural invasion is not currently included in radiologic staging. Accurate diagnosis remains challenging.

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3. Differential Diagnosis

In most cases, contrast-enhanced CT is the primary imaging method for differential diagnosis. For difficult cases, MRI can serve as a problem-solving tool due to its higher soft tissue resolution and multi-parametric imaging capabilities, which can improve diagnostic accuracy.

3.1 Mass-forming Chronic Pancreatitis

Repeated chronic pancreatitis can form focal masses causing pancreatic and bile duct obstruction, with imaging features difficult to distinguish from PDAC. Early studies show that contrast-enhanced pseudo-color maps and elastography can help differentiate mass-forming pancreatitis from PDAC. EUS-guided fine-needle aspiration can provide pathological information, but negative results cannot completely exclude PDAC, and close monitoring is still required.

3.2 Focal Autoimmune Pancreatitis

Autoimmune pancreatitis (AIP) shares many clinical features with PDAC, both commonly occurring in elderly patients with painless jaundice, new-onset diabetes, and elevated serum tumor markers. Typical imaging features include smooth, diffuse pancreatic enlargement with homogeneous delayed enhancement and capsule-like rim. Focal AIP appears as a mass that is difficult to differentiate from PDAC. MRCP shows long-segment ductal narrowing without upstream dilation, and PET-CT shows diffuse uptake in both pancreas and salivary glands. Serum IgG4 levels are elevated in 45-70% of AIP cases. EUS-guided biopsy and short-term steroid trial can help differentiate these conditions.

3.3 Solid Pseudopapillary Tumor

Solid pseudopapillary neoplasm (SPN) is a rare, low-grade malignant tumor that is difficult to differentiate from PDAC radiologically. SPNs are more common in young women, typically located in the pancreatic tail, larger in size, and may show hemorrhage and cystic degeneration—features that help distinguish them from PDAC.

3.4 Pancreatic Neuroendocrine Tumor

Pancreatic neuroendocrine tumors (PNETs) are another differential consideration. Functional PNETs can be accurately diagnosed based on typical clinical syndromes of hormone excess. Non-functional PNETs are often incidentally discovered or detected when causing mass effect. Typical imaging shows arterial phase hyperenhancement with well-defined borders, but atypical features such as non-arterial phase enhancement increase diagnostic difficulty. Radiomics has been applied to differentiate PDAC from other pancreatic solid masses with good results, though studies specifically for PDAC versus PNET differentiation are still needed.

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4. Assessment and Follow-up

4.1 Neoadjuvant Therapy Assessment

Imaging evaluation of treatment response after neoadjuvant therapy is complex, with limited research and no consensus. Studies since 2004 have shown that CT restaging underestimates treatment response. Recent studies indicate that both RECIST and Choi criteria cannot accurately assess neoadjuvant therapy response. Some scholars suggest that any reduction in tumor-vessel contact interface indicates pathological response, even if subtle.

PET-CT can monitor clinical outcomes, with decreased standardized uptake value (SUV) suggesting good chemotherapy response. However, tumor-related inflammatory reactions also cause diffusion restriction, making it difficult to

accurately determine tumor boundaries in over half of cases. Perfusion CT has been used for rectal cancer neoadjuvant therapy evaluation, but its application in pancreatic disease remains immature. Multiple quantitative functional imaging techniques including DWI and intravoxel incoherent motion (IVIM) parameters show promise but require large-sample validation.

4.2 Follow-up

Post-treatment follow-up for PDAC includes serological tests and imaging examinations to clarify diagnosis, monitor disease progression, and guide treatment. When differentiating PDAC from mass-forming pancreatitis, close follow-up is essential. Follow-up imaging includes ultrasound and contrast-enhanced CT every 2-3 months. For suspected liver or bone metastasis, liver MRI and bone scan are recommended. For advanced disease with distant metastases, follow-up should continue for at least 2-3 years.

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5. Summary and Outlook

Imaging plays a crucial role throughout the PDAC clinical pathway in early detection, accurate staging, differential diagnosis, and treatment response assessment. High-quality multi-phase contrast-enhanced CT is the preferred method for staging and resectability assessment. MRI with DWI serves as an excellent problem-solving tool for difficult cases. PET-CT has limited diagnostic value but can evaluate extrahepatic metastases. Multiple functional and quantitative imaging techniques are being applied to PDAC, though current routine imaging cannot accurately assess neoadjuvant therapy response. Radiomics and machine learning show promise for overcoming these limitations. Multidisciplinary collaborative diagnosis and treatment should integrate imaging throughout the entire patient care process.

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