

ORIGINAL ARTICLE

Does mesenteric venous imaging assessment accurately predict pathologic invasion in localized pancreatic ductal adenocarcinoma?

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Abstract

Background: Accurate prediction of mesenteric venous involvement in pancreatic ductal adenocarcinoma (PDAC) is necessary for adequate staging and treatment.

Methods: A retrospective cohort study was conducted in PDAC patients at a single institution. All patients with resected PDAC and staging CT and EUS between 2003 and 2014 were included and subdivided into “upfront resected” and “neoadjuvant chemotherapy (NAC)” groups. Independent imaging review was correlated to venous resection and venous invasion. Sensitivity, specificity, positive and negative predictive values were then calculated.

Results: A total of 109 patients underwent analysis, 60 received upfront resection, and 49 NAC. Venous resection (30%) and vein invasion (13%) was less common in patients resected upfront than those who received NAC (53% and 16%, respectively). Both CT and EUS had poor sensitivity (14–44%) but high specificity (75–95%) for detecting venous resection and vein invasion in patients resected upfront, whereas sensitivity was high (84–100%) and specificity was low (27–44%) after NAC.

Conclusions: Preoperative CT and EUS in PDAC have similar efficacy but different predictive capacity in assessing mesenteric venous involvement depending on whether patients are resected upfront or received NAC. Both modalities appear to significantly overestimate true vascular involvement and should be interpreted in the appropriate clinical context.

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Introduction

Pancreatic adenocarcinoma (PDAC) remains an aggressive disease with poor prognosis. The best chance for prolonged survival and possible cure includes multimodality therapy involving surgical resection and chemotherapy \pm radiation. Unfortunately, only 15% of patients who present with PDAC have localized disease amenable to upfront surgical resection.¹ After metastatic disease, the primary limitation to safe surgical resection involves local mesenteric vascular involvement. Multi-detector computed tomography (MDCT) and endoscopic ultrasound (EUS) are the initial modalities utilized for diagnosis, biopsy and staging of PDAC, and remain the primary means of classifying the patient as resectable, borderline resectable, or unresectable.^{2,3}

As medical and surgical treatments continue to improve, an increasing number of patients can safely be offered curative resection. Venous resection in the setting of portal-mesenteric venous involvement (PMV) is currently considered the standard of care, typically after a course of neoadjuvant chemotherapy (NAC) \pm radiation.^{3,4} Therefore, accurate assessment of vascular involvement in PDAC is critical in determining the suitability of resection, and often influences the decision to offer NAC. While radiographic regression of tumor during NAC is uncommon, it is associated with higher rates of R0 resections and thus is often recommended as first line treatment for borderline resectable and locally advanced PDAC.^{3,5}

It has been demonstrated that planned vascular resections have significantly lower rates of R1 resections compared to unplanned resections.⁶ Additionally, the degree of vascular involvement may also have prognostic value in PDAC.⁷ Therefore, it is imperative that we possess tools to accurately assess the relationship between pancreas, tumor, and vascular structures, and fully understand how preoperative treatments can affect the diagnostic accuracy of this assessment. While multiple studies have been performed in order to evaluate the accuracy of MDCT and EUS in detecting pancreatic cancer and associated resectability, very few studies have focused on the changing reliability of imaging in the context of preoperative treatment. The aim of our study was to assess and compare the diagnostic accuracy of preoperative imaging to predict need for vascular resection and presence of vascular invasion of pancreatic head adenocarcinomas with and without neoadjuvant therapy.

Methods

A retrospective cohort study was conducted among all consecutive patients undergoing pancreaticoduodenectomy (PD) for PDAC at a single high volume pancreatic surgery tertiary referral hospital between 2003 and 2014. The study was approved by the Institutional Review Board (IRB). Patients with histologically proven PDAC of the pancreatic head or uncinate process, and both high quality MDCT and EUS at our institution before surgical resection were included for analysis. Patients operated on during the study period were selected to undergo either upfront surgery or neoadjuvant chemotherapy based on institutional practices and surgeon preference/experience. The most common reason for recommendation of neoadjuvant chemotherapy in this retrospective study was vascular invasion seen on MDCT or EUS, but may also have been due to severe concomitant pancreatitis, significantly elevated CA 19-9 >2000, reduced performance status of patient, or patient/surgeon preference. No patients had preoperative radiation per institutional practice. When patients were selected for NAC, a re-staging MDCT only was performed within thirty days of planned surgical intervention. The type of NAC was heterogeneous, but most often involved either FOLFIRINOX or gemcitabine and docetaxel doublet. EUS was routinely performed only during the initial diagnostic phase of care, and was not repeated after NAC for comparison. Among those receiving NAC, only patients who proceeded to successful surgical excision were included for analysis. Additionally, any patient that was found to be metastatic or unresectable at the time of surgery, did not have a specimen for pathological examination and was excluded from analysis.

Blinded independent re-review of radiographic images was conducted by a staff body radiologist to determine and standardize the presence of vascular invasion by a single radiologist for the purposes of this study. MDCT was performed with separate arterial and venous phase contrast administration with 2.5 mm cuts through the pancreas. Any tumor involvement of

vasculature <180° was considered abutment, whereas involvement >180° was considered encasement. EUS imaging was interpreted by one of several experienced interventional endoscopists and reported via a standardized template. EUS images were not subjected to a blinded independent re-review. Any involvement of the portal vein, superior mesenteric vein, or a short segment of the hepatic artery identified pre-operatively was considered borderline resectable according to the AHPBA/SSAT/SSO consensus definition.⁸ Patients who had abutment of the celiac artery, encasement of the superior mesenteric artery or extensive involvement of the hepatic artery precluding reconstruction were considered locally advanced and unresectable.

A blinded independent re-review of pathological specimens was conducted by a gastrointestinal pathologist experienced in pancreatic malignancy. Specimens were reviewed intentionally for the presence or absence of true histological PMV by tumor. If there was no direct tumor involvement into the vessel wall, distance between tumor and vessel wall was measured. A “close margin” was defined as distance between tumor and vessel wall <1 mm. Pathological interpretation was the reference standard for this study.

Determination of need for vascular resection was ultimately made at the time of surgery by an experienced pancreatic surgeon. If the pancreatic head and uncinate process were easily freed from the surrounding vasculature, no vascular resection was performed. If the portal vein or superior mesenteric vein were involved with either obvious tumor extension or significant inflammation without the ability to rule out tumor involvement, then venous resection was performed en bloc with PD. Institutional practice was to prefer en bloc resection when there was any doubt regarding tumor invasion in order to prevent the chance of R1 resection or massive hemorrhage. Tumors that were discovered at the time of surgery with extension into the celiac, superior mesenteric, or with significant involvement of the common hepatic artery were deemed unresectable and excluded from the study. Performance of vascular resection was a secondary reference standard.

Diagnostic accuracy estimates of each index test of interest, MDCT and EUS, were calculated for three reference standards: vascular resection, vein invasion, and close margins. The presence of either vascular abutment or encasement on MDCT or EUS were considered positive results. In the cases of neoadjuvant therapy, the MDCT performed upon initial diagnosis was used for data analysis and calculations. Indeterminate results were excluded from analysis. Sensitivity and specificity were computed with accompanying exact binomial confidence intervals. Positive predictive value and negative predictive value were listed without accompanying confidence intervals or statistical comparison due to the fact that prevalence of the outcomes of interest was different in the two groups, and thus had potential to affect the positive and negative predictive values of the tests. These were listed as descriptive values only rather than inferential or intended to be generalizable. Calculations were performed

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