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Vascular involvement in periampullary tumors: MDCT, EUS, and CDU

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Abstract

In patients affected by periampullary tumors, surgical resection represents the only treatment with curative intent. Preoperative evaluation of vascular involvement is necessary to avoid surgical treatments unable of curative intent resection. The aim of our update article is to assess the performance of multidetector computed tomography (MDCT), endoscopic ultrasonography (EUS), and color Doppler ultrasonography (CDU) in the evaluation of vascular involvement of major peripancreatic vessels, in periampullary tumors, analyzing the current and past literature.

Key words: Periampullary tumors—Vascular involvement—MDCT—EUS—CDU

Periampullary neoplasia

This class of neoplasia includes different types of tumors, involving the pancreas, duodenum, Vater ampulla, and distal common bile duct. These tumors have different features, both in local invasion and in prognosis. They generally present themselves with clinical symptoms such as pain, loss of weight, and jaundice.

Pancreatic tumors

These can be divided into epithelial and nonepithelial tumors. The first group includes exocrine (99%), acinar, and endocrine tumors. The second group includes lymphomas, metastatic lesions (kidney, colorectal) and other, less frequent, lesions.

Exocrine tumors include cystic or mucinous lesions and ductal adenocarcinoma.

Cystic neoplasms represent 5% of pancreatic tumors. They are serous cyst adenoma, mucinous cyst adenoma and mucinous adenocarcinoma, and intraductal papillary mucinous tumor (IPMT) (Figs. 1 and 2). The first is considered a benign lesion, and surgical treatment is indicated only in large lesions. Surgical treatment is performed in all the other types, for potential malignancy in mucinous cyst adenoma and IPMT, for malignancy in mucinous adenocarcinoma. They all can be found in the periampullary region.

The application of diagnostic techniques such as multidetector computed tomography (MDCT) and endoscopic ultrasonography (EUS) has led to an increased incidence of cystic pancreatic lesions [1–3].

The features of pancreatic adenocarcinoma are well known [4]. This tumor causes patient's death in more than 98% of cases, and less than 20% of patients with pancreatic adenocarcinoma have resectable disease at the time of initial diagnosis [5], because of local invasion (vascular involvement) and distant metastases.

Pancreatic endocrine tumors [6] may be malignant, giving distant metastases; in the case of nonsecreting tumors, they can have even local invasion as adenocarcinoma does.

Acinar tumors are very rare (1% of pancreatic cancer), but they can give distant metastases (lung and liver) and have local invasion.

Other periampullary tumors

Duodenal and Vater papilla tumors are not so frequent [7–10], but they can present local invasion and give distant metastases, slowly than pancreatic cancer.

They arise from the ampullary region, where three different mucosae are present: duodenal, main bile duct, and main pancreatic duct mucosa.

Distal bile duct tumors arise from main bile duct mucosa, and carcinoma is the most frequent [11, 12].

Imaging techniques

Computed tomography

Computed tomography (CT) is a primary imaging modality, with a great role in diagnosis and staging of

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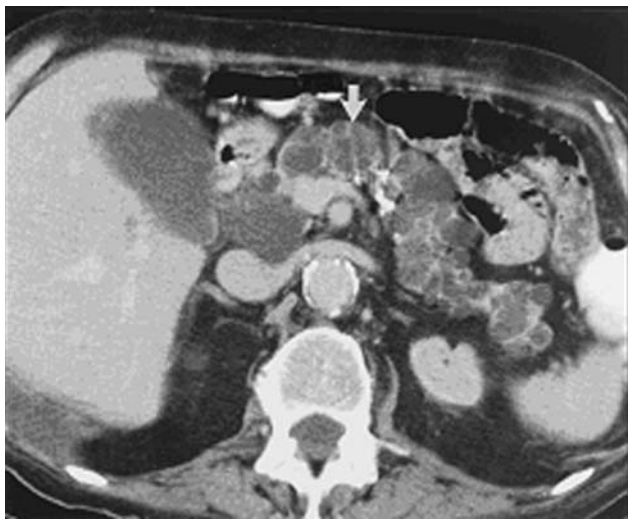


Fig. 1. IPMT involving main pancreatic duct and secondary pancreatic ducts: axial CT scan.

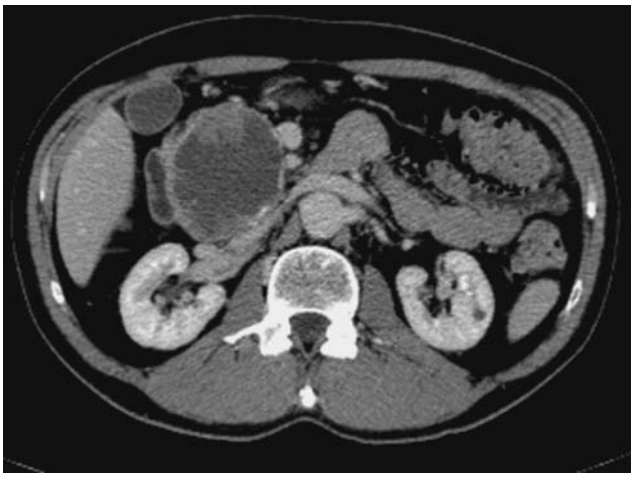


Fig. 2. Cystoadenocarcinoma: MDCT appearance. Mass on cystic lesion wall.

periampullary tumors [13]. It is even very important in preoperative evaluation, in order to avoid surgical treatment not amenable of curative intent. Technical improvement over the past years increased the diagnostic capability of this technique, improving accuracy and diagnostic confidence. The last innovation is the development of multidetector technology, converting CT from an axial modality to a three-dimensional one, with undisputed benefits. These benefits are particularly evident in the evaluation of pancreatic and periampullary tumors, in the assessment of vascular involvement, and the detection of distant metastases [14, 15].

Although MDCT is a panoramic, diffuse imaging modality, it has got some limits, such as the use of X-ray, with the consequent radiation dose, and the need of intravenous contrast medium. The use of contrast medium, in fact, excludes from MDCT study patients with acute or chronic renal insufficiency (high serum creatinine), active multiple myeloma (Bence Jones proteinuria), and severe intolerance to contrast medium. Currently, 64-detector row MDCT technology seems to increase CT potential [16].

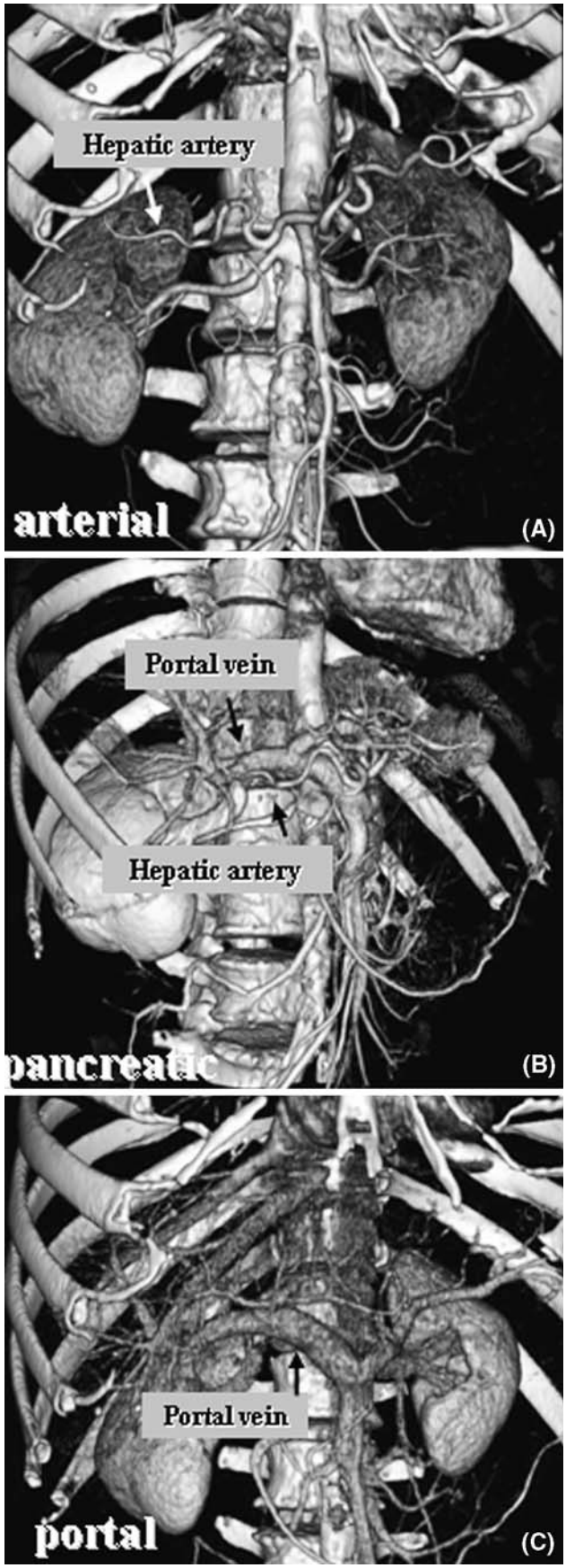
Contrast medium administration. In order to obtain a correct distinction of gastric wall and duodenum, 500–1000 mL of water is administered during the 30 min preceding the examination; 250 mL of water is administered immediately before CT scanning. The water administration is suggested because some small endocrine tumors of the duodenal wall may be seen, and even possible duodenal wall infiltration from pancreatic tumors. The possibility to increase CT diagnostic potential in pancreatic cancer by the use of hyoscyamine butylbromide, to promote distention of the duodenum and minimize artifacts due to peristalsis, was analyzed by Aschoff [17]; he demonstrated that promotion of distention of the duodenum and reduction of artifacts due to peristalsis do not improve image quality and diagnostic findings in helical CT of the pancreas.

An unenhanced scan is preformed and then contrast medium is intravenously administered. Two milliliters/kg of intravenous contrast medium is administered. A high flow rate of administration is used: from 3.5/4 mL to 8 mL/s. Schueller [18] analyzed two different high-contrast material flow rates (8 mL/s vs. 4 mL/s) and concluded that increased contrast material flow rate of 8 mL/s and individualized scan delay improved pancreatic enhancement and tumor-to-pancreas contrast.

Fenchel [19] compared two different iodine concentrations of contrast media on contrast enhancement in multislice CT of the pancreas (300 vs. 400 mg/mL of iodine concentrations) and assessed that there were no differences for tumor delineation and evaluation of infiltration of organs adjacent to the pancreas between the two iodine concentrations. The higher iodine concentration leads only to a higher arterial phase contrast enhancement of large and small arteries in MDCT of the pancreas and therefore improves the evaluation of vessels only in the arterial phase.

Acquisition technique. The pancreas and periampullary region are usually analyzed with dual or triple phase MDCT technique; dual phase consists of acquisition during pancreatic and portal phase while triple phase is acquisition during arterial (Fig. 3A), pancreatic (Fig. 3B), and portal phases (Fig. 3C). Exact timing of arterial, pancreatic, and portal phase is very different in the literature [15, 20, 21].

Even a single-phase technique in MDCT assessment of pancreatic tumors has been reported [22]. This author assessed that thin-section single-phase MDCT is an accurate technique for the diagnosis and assessment of resectability in patients with a suspected pancreatic neoplasm.



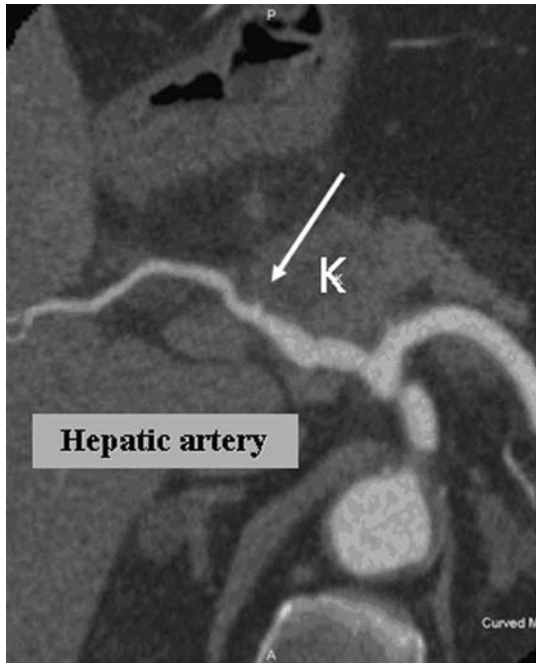


Fig. 4. MDCT 2D reconstructions: curved planar reconstruction in pancreatic head cancer. Gastroduodenal artery invasion (*arrow*), extended contact with common hepatic artery.

For pancreatic adenocarcinoma it has been well defined by Fletcher [15] that dual phase technique should be considered the best choice, with pancreatic phase at 40–50 s, and portal phase at 60–70 s after the contrast medium injection. He assessed that routine acquisition of images in the arterial phase is unnecessary for detection of pancreatic adenocarcinoma. In 2007, our group [23] concluded that, in pancreatic endocrine tumors, dual phase technique should be used, and that pancreatic phase can replace the arterial phase.

For pancreatic cystic lesions, no indications on type of acquisition are given and triple phase may be performed. For duodenal and distal bile duct tumors, triple phase may be performed.

Post-processing. Bi- and three-dimensional reconstructions are fundamental in the evaluation of the periampullary region [24] (Figs. 4 and 5A, B). By use them it is possible to get over the old assessment of CT as an axial diagnostic modality. MDCT reconstructions are usually performed on a second dedicated console.

In particular, 2D reconstruction has been proposed to evaluate pancreatic IPMT [25] because it can provide details of the main pancreatic duct as MRCP does. The

◀ Fig. 3. MDCT 3D reconstructions: volume rendering in arterial (**A**), pancreatic (**B**), and portal phase (**C**). In arterial phase, hepatic artery is seen (*arrow*). In pancreatic phase, hepatic artery and portal vein can be evaluated (*arrows*). In portal phase, only portal vein can be seen.

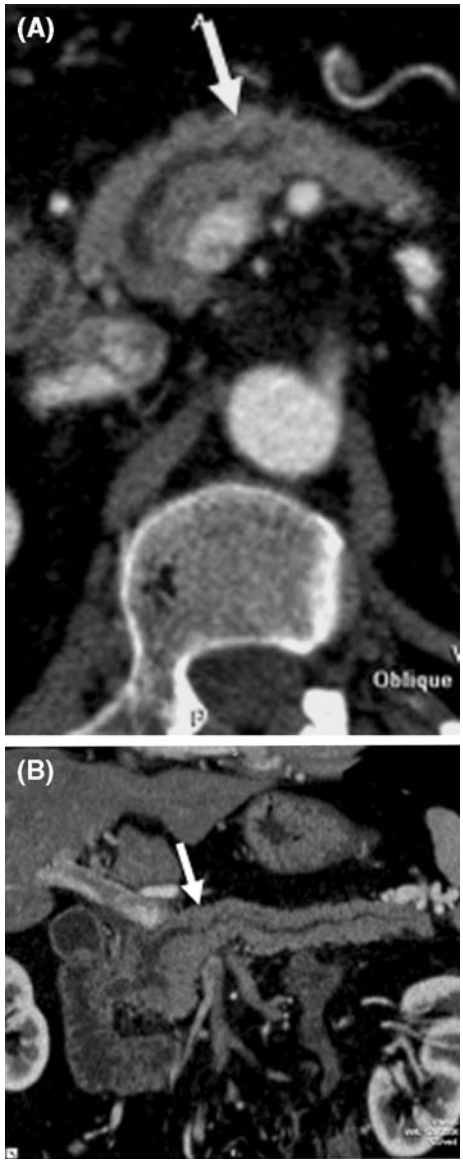


Fig. 5. MDCT: main pancreatic duct IPMT with mass (*arrow*). Axial scan (**A**) and curved planar reconstruction (**B**).

usefulness of MDCT reconstructions in the evaluation of the biliary and pancreatic duct [26], and even in the evaluation of vascular involvement [5, 27], has been reported in the following.

Endoscopic ultrasonography

EUS can be considered the best technical innovation in gastrointestinal endoscopy in the last 20 years.

This diagnostic technique puts together ultrasonographic and digestive endoscopic features, with high frequency ultrasound (5–10 MHz), in order to obtain high-resolution images of gastrointestinal tract (stomach, duodenum) and particularly of periampullary region (pancreas, main bile duct) (Fig. 6).

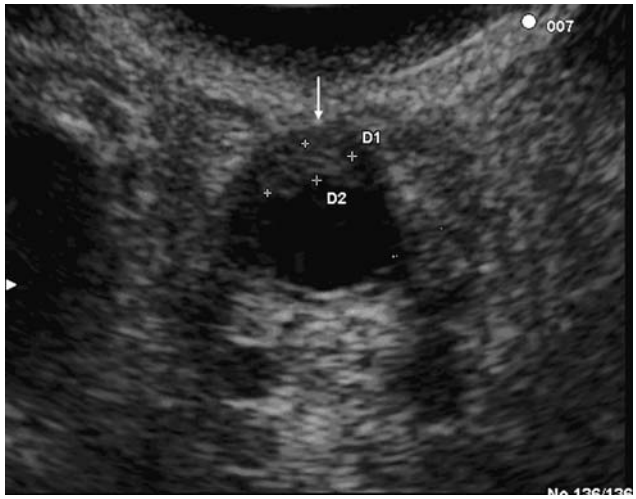


Fig. 6. EUS appearance of malignant IPMT with mass (*arrow*) in main pancreatic duct.

EUS is an invasive diagnostic technique and patients need to have conscious sedation. Moreover, it is not a panoramic and reproducible diagnostic technique, and it is expensive. Like every sonographic technique, it requires a long training time; in fact the value of EUS is directly proportional to the training, skill, and experience of the endosonographer [28].

It cannot be performed in patients who previously underwent surgical gastrectomy, with Roux-en-Y gastric bypass, because this surgical reconstruction does not consent a correct evaluation of the periampullary region, because of the impossibility to reach duodenum with endoscope. EUS performance can be affected by the presence of an endobiliary stent [29, 30].

EUS has the great advantage to permit the execution of fine needle aspiration cytology (FNAC) (Fig. 7), or histological evaluation [31]; this feature is very important especially in cystic lesion, in order to differentiate between benign, potentially malignant and malignant lesions.

EUS may even have a role in therapy, in locally advanced pancreatic and periampullary tumors, particularly in EUS-guided celiac plexus neurolysis [32].

EUS indications are summarized in Table 1 [33].

Color Doppler ultrasonography

Color Doppler ultrasonography (CDU) is a noninvasive, radiation-free, cheap diagnostic technique; it needs fasting. But it has some limits, due to patients' features (obese patients) and, as already said for EUS, it needs a long training time, its results are contingent on the radiologist's skill, and it is not panoramic and reproducible.

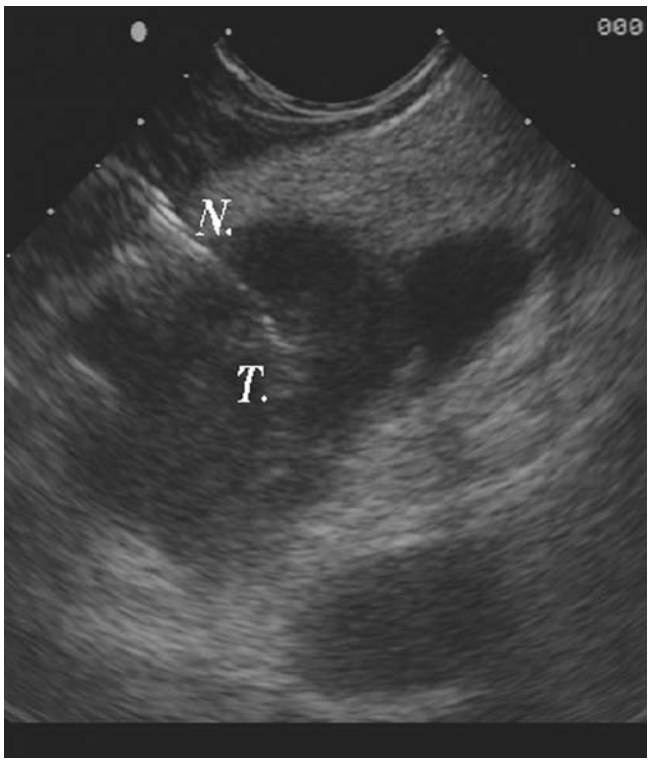


Fig. 7. FNAC under EUS guidance. Fine needle (N) in pancreatic cancer (T).

Table 1. American Society of Gastrointestinal Endoscopy recommended indications for EUS

EUS generally is indicated for
Staging tumors of the GI tract, pancreas, bile ducts, and mediastinum
Evaluating abnormalities of the GI-tract wall or adjacent structures
Tissue sampling of lesions within, or adjacent to, the wall of the GI tract
Evaluation of abnormalities of the pancreas, including masses, pseudocysts, and chronic pancreatitis
Evaluation of abnormalities of the biliary tree
Providing endoscopic therapy under US guidance

In periampullary lesions, particularly in pancreatic tumors, the role of CDU really increased in the recent years [34, 35] but it was reported since the nineties [36].

Periampullary lesions detection

In clinical practice it is clearly assumed that MDCT and EUS are diagnostic techniques with a high accuracy in detection of pancreatic [37] and periampullary tumors [29, 38]. The technological innovation in computed tomography, with multidetector rows, particularly 64-detector row MDCT technology, increased CT potentiality [26].

The use of transabdominal sonography in periampullary tumors is argued; it has relatively low sensitivity in detecting pancreatic and periampullary cancer; its sensitivity decreases a lot in small tumors (<2 cm) [29, 36, 39].

Vascular involvement

Periampullary major vessels

The major periampullary vessels analyzed in the literature are superior mesenteric vein and artery, celiac trunk, portal vein and hepatic artery.

Computed tomography

Since the 1990s, preoperative evaluation of periampullary tumors has become very important and CT criteria of vascular involvement has been reported [40, 41]. These criteria, summarized in Table 2, were defined by spiral CT, but they are valuable nowadays on MDCT.

Recently, two studies from the same group [42, 43] defined the signs of vessel invasion of pancreatic cancer.

In 2001, Lepanto performed a prospective study [44], with helical computed tomography, with CT angiography, in 69 patients affected by periampullary tumors, in order to evaluate vascular invasion and to assess the added value of CT angiography. CT angiography was analyzed on a second dedicated workstation. The accuracy of helical CT with CT angiography in identifying venous invasion was 92%; accuracy of CT images alone decreases to 69%. In arterial invasion, the accuracy of CT with CT angiography and of CT alone was 86%. Hence, CT angiography significantly increases only the ability to identify venous invasion, but it does not add any information on arterial involvement.

In 2004, for the first time, two papers described the accuracy of MDCT in the evaluation of vessel involvement in pancreatic and periampullary tumors, even by the use of post-processing.

Vargas [27] published a retrospective study performed on 22 patients who underwent surgical treatment for pancreatic adenocarcinoma by the use of an eight-rows CT scanner, using a dual-phase pancreatic protocol; images were acquired 40 s (pancreatic phase) and 70 s (portal-venous phase) after contrast medium injection. The aim of the study was to determine the negative predictive value of MDCT with curved planar reformations for detecting vascular invasion and predicting overall resectability in patients with pancreatic adenocarcinoma. Vargas concluded that, by tumor on a vessel-by-vessel basis, MDCT negative predictive value in detecting vascular invasion was 100% with no false-negative findings; an accuracy of 99% was assessed (Fig. 8).

The other study, using MDCT and post-processing, was published by House [5], to evaluate the impact of preoperative 3D-CT in determining the resectability of patients with periampullary tumors. It was a prospective study, on 95 resected patients, using a four-rows CT scanner, with dual-phase technique; images were acquired 30 s (arterial phase) and 60 s (venous phase) after contrast medium injection. With 3D-CT, accuracy

Table 2. CT criteria of vascular involvement

Grade	Raptopoulos [41]	Lu [40]	Surgical treatment
0	No vessel involvement	No vessel involvement	Resectable
1	Loss of fat plane	Circumferential involvement $<25\%$	Resectable
2	Vessel irregularity	Circumferential involvement $>$ 25–50%	Doubtful resectability
3	Vessel encasement	Circumferential involvement >50–75%	Unresectable
4	Vascular occlusion	Circumferential involvement $>75\%$	Unresectable

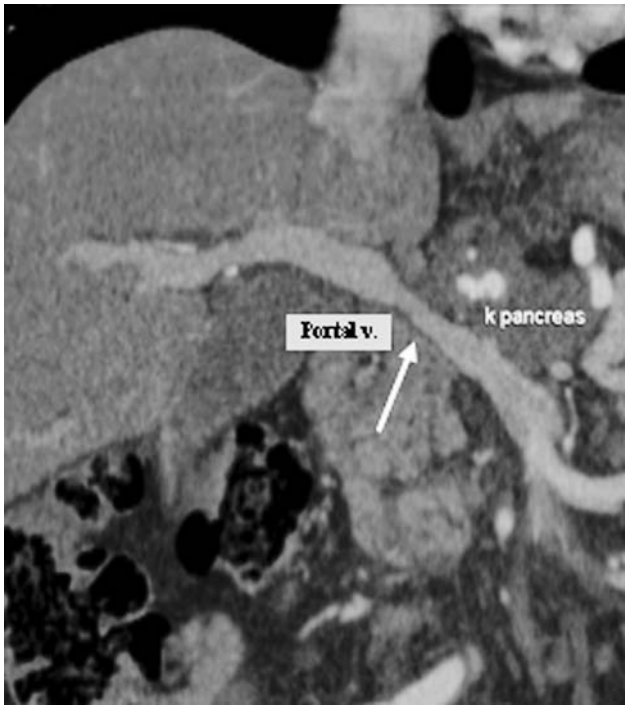


Fig. 8. MDCT 2D reconstruction: vascular invasion of superior mesenteric vein (*arrow*).

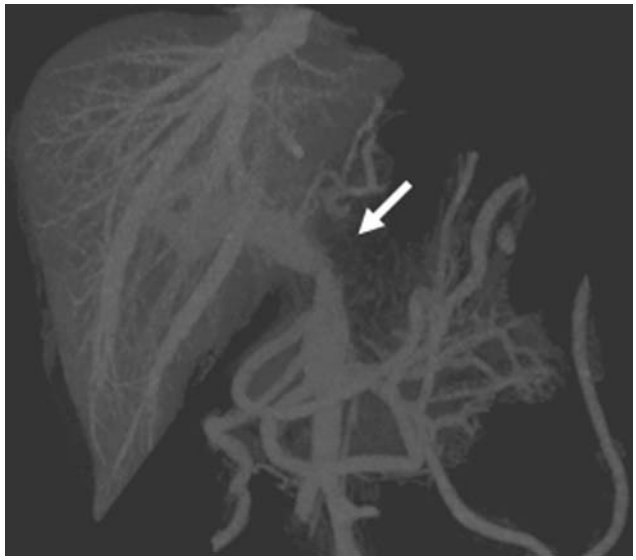


Fig. 9. MDCT: 3D reconstruction (MIP) demonstrating vascular involvement of portalmesenteric confluence (*arrow*). Presence of venous collateral arcades.

in detection of vascular involvement of the superior mesenteric vein and portal vein was 90%; for superior mesenteric artery and for celiac trunk, accuracy was 95% and 98%, respectively (Fig. 9).

Recently, Manak [45] assessed MDCT negative predictive value of 99% for detection of vascular invasion, by the use of biphasic MDCT, with bi-dimensional reconstructions, on 48 patients affected by pancreatic cancer.

From the data expressed in the literature, it is quite easy to assess that MDCT may be performed preoperatively in every patient affected by periampullary lesion.

Endoscopic ultrasonography

Vascular involvement by periampullary tumors is considered when any one of the following features is present [46]: loss of hyperechoic interface between tumor and vessel for at least 5 mm (adherence), irregular tumor and vessel interface, tumor within vessel lumen (invasion) vessel encasement, and perigastric or periduodenal collaterals with associated venous occlusion (Fig. 10). EUS has some limitations in the visualization of the superior mesenteric vein and artery [47].

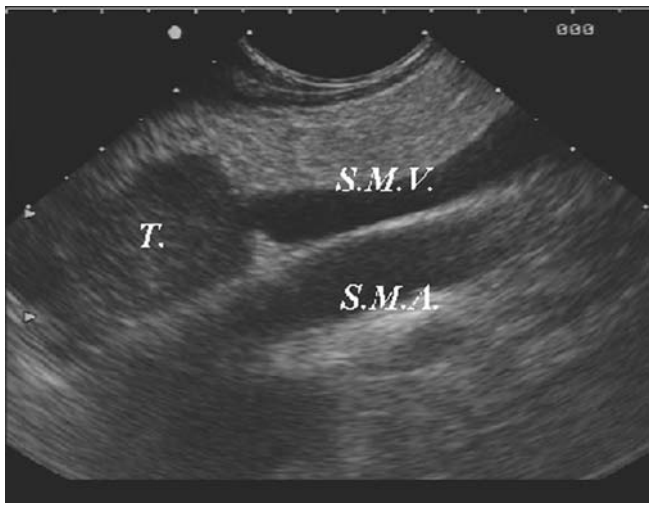


Fig. 10. EUS: vascular invasion of superior mesenteric vein (SMV) by pancreatic tumor (T). No involvement of superior mesenteric artery (SMA) is evident.

In 2002, Hunt [47] analyzed CT and EUS in the staging of pancreatic cancer. In literature, till 2002, EUS was demonstrated to be better then helical CT, both in accuracy in resectability (91% vs. 83%) and in sensitivity in the evaluation of vascular invasion (91% vs. 64%). However, he correctly said that these reports had some bias, on CT protocols and reconstruction, and because authors may be biased in favor of their own procedure.

In 2004, DeWitt [46], in a prospective study, compared EUS and quad-rows CT scanner in pancreatic cancer. He assessed that compared with multidetector CT, EUS is superior for tumor detection and staging but similar for nodal staging and resectability of preoperatively suspected nonmetastatic pancreatic cancer. In vascular involvement, on 25 patients with resectable pancreatic tumors, EUS incorrectly identified portal vein ($n = 2$) and superior mesenteric vein ($n = 1$) invasion, while MDCT incorrectly identified tumor invasion of the superior mesenteric vein ($n = 1$). In 28 patients with unresectable tumors, EUS failed to detect invasion of the superior mesenteric vein ($n = 1$) and artery ($n = 1$) and portal vein ($n = 1$) while MDCT failed to detect invasion of portal vein ($n = 2$), celiac trunk ($n = 1$) and superior mesenteric vein ($n = 1$).

DeWitt, in 2006, in a review of the literature [48], correctly said that the published literature comparing EUS and CT for preoperative assessment of pancreatic cancer is heterogeneous in study design, quality, and results. All studies have methodologic limitations that potentially affect validity. Prospective studies with state-of-the-art imaging are needed to further define the role of each test.

Color Doppler ultrasonography

The use of this diagnostic technique is not yet accepted in literature. In 1997, our group, particularly Angeli [49], assessed that color Doppler imaging is a sensitive and highly specific technique in assessing vascular involvement by pancreatic cancer when absence of contact or vascular encasement is seen. When vascular encasement is detected by color Doppler imaging, a definitive diagnosis of unresectability can be made, and further diagnostic procedures can be avoided. When sonography is used in the initial evaluation of pancreatic cancer, color Doppler imaging can improve the selection of patients for further diagnostic examinations or surgical exploration. In 61 patients affected by pancreatic tumors, he defined criteria of Doppler unresectability as a long contiguity (>2 cm), compression, encasement, or thrombosis; criteria of resectability were absence of contact or short contiguity (≤ 2 cm) between tumors and peripancreatic vessels (Fig. 11).

By the use of these criteria he assessed sensitivity of 79%, specificity of 89%, overall accuracy of 84%, positive predictive value of 89%, and negative predictive value of 79%.

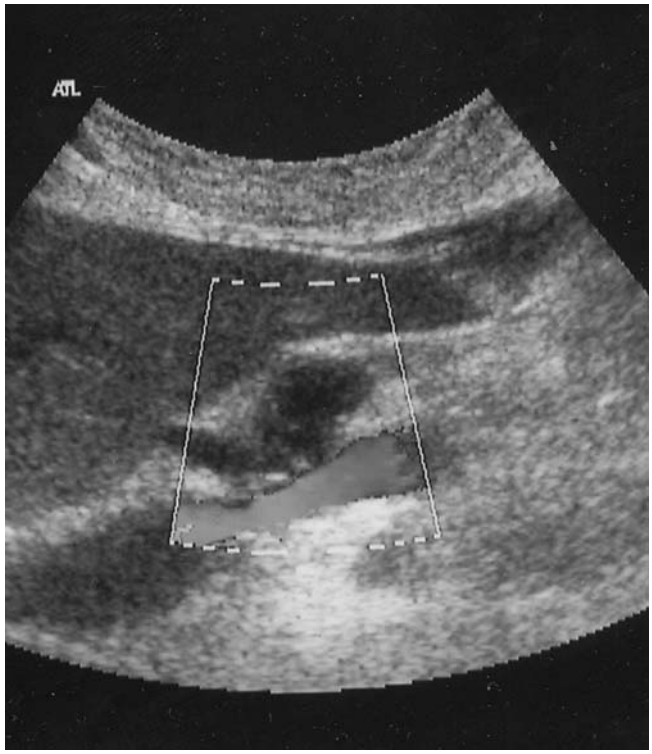


Fig. 11. CDU in pancreatic head cancer. Superior mesenteric vein compression

In a very recent study, Kern [33] analyzed the integrity of the echogenic border layer between the vein and tumor (mural demarcation) and maximum blood flow velocity (V_{max}) in the portal vein segment in contact with the tumor.

By measuring V_{max} and evaluating mural demarcation, he observed a sensitivity of 66.7% and 100% and a specificity of 98.3% and 93.9%, respectively, in predicting full thickness vein invasion, including the intima. V_{max} above 80 cm/s and lack of mural demarcation were predictors of ortal vein or superior mesenteric vein invasion.

He concluded that modern color Doppler imaging is a reliable and valid technique for evaluation of morphological and hemodynamic parameters in the portal vein segment adjacent to pancreatic adenocarcinoma. Maximal blood-flow velocity in the portal segment in contact with the tumor and absence of the echogenic vessel-parenchymal sonographic interface are parameters predictive of tumor infiltration of the portal intima.

Prediction of margin-negative resection R0 after surgical treatment

Although in a recent paper [50] there was no statistically significant difference in patient survival or recurrence based on R status, some authors have tried to predict margin-positive or margin-negative resection with preoperative diagnostic technique.

House [5] tried to understand if MDCT is able to predict a margin negative (R0) or margin positive (R1) surgical resection. A margin-negative resection can be predicted based on the presence of a clear tissue plane between the neoplasm and the SMA, and noncircumferential involvement of the SMV-PV confluence. The overall accuracy in predicting margin-positive (R1) resection was 83%.

Comparing MDCT and EUS, Bao [30] tried to retrospectively define the potential of these two diagnostic techniques in predicting a margin-negative (R0) resection on 46 patients affected by pancreatic cancer.

EUS vessel "abutment" was defined as a loss of the hyperechoic interface between the tumor and vessel, whereas vessel "invasion" was defined as visualization of tumor within the lumen, vessel encasement, or vessel occlusion. In this study, EUS accuracy is highly affected by the presence of biliary stents.

Venous involvement $>180°$ and arterial involvement $>90°$ by CT were considered predictive signs of margin positive (R1) resection.

Bao assessed that venous involvement $>180°$ and arterial involvement $>90°$ by CT had 100% positive predictive value for failure to achieve R0. Excluding patients with preoperative biliary stents, EUS venous abutment or invasion also predicted R0 failure.

Conclusion

In this review article it has been demonstrated that MDCT, EUS, and color Doppler imaging are diagnostic techniques with high accuracy in the evaluation of vascular involvement.No studies have been reported comparing studies with these three different imaging modalities. As correctly said by DeWitt [48], prospective studies with state-of-the-art imaging are needed to further define the role of each test. In particular, in our opinion, prospective, single or multicenter study is needed to compare EUS, MDCT, and color Doppler imaging in periampullary tumors. Moreover, this study may be performed in a high volume hospital, where a periampullary cancer unit is operative, with radiologists and gastroenterologists particularly skilled in periampullary tumors and where a clear cooperation can be found.

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