Imaging and staging of biliopancreatic malignancy: Role of ultrasound

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Summary

Most patients with a pancreatic head carcinoma, periampullary carcinoma or a cholangiocarcinoma of the liver hilum (Klatskin tumor) present with obstructive jaundice and therefore ultrasound often is the first imaging modality. Visualization is sufficient in more than 90% of cases for adequate diagnosis and staging. Even most small papillary tumors can be diagnosed with conventional abdominal ultrasound. In pancreatic head and periampullary carcinoma vascular involvement is the most important determinant for local irresectability and can often be assessed by color Doppler US. An abnormal pulsed Doppler signal obtained from the portal venous system due to severe narrowing or occlusion is highly suspicious for major involvement and irresectability of the tumor. However, a normal pulsed Doppler signal does not exclude involvement, if the tumor has continuity with the vessel with interruption of the hyperechoic tumor vessel interface. Enlarged lymph nodes are not a major diagnostic parameter, because a reliable differentiation between reactive and malignant lymph nodes is generally not possible. Very tiny liver and peritoneal metastases are missed by abdominal US and only detectable by laparoscopy and/or laparoscopic US. In cholangiocarcinoma of the liver hilum extensive biliary and vascular involvement are considered the most important factors for determining irresectability. Portal venous involvement can be assessed by color Doppler US with a high accuracy (91%). Although cholangiography (ERCP and PTC) is considered the best imaging modality in detecting proximal extension of the tumor into the biliary system US can provide useful additional information. If dilated ducts are seen without clear communication among each other within a liver lobe, extension of the tumor into the segmental bile ducts can be concluded.

We consider color Doppler US, a valuable tool for preoperative imaging and staging of biliopancreatic malignancy.

Key words: Bile ducts, neoplasms; Bile ducts, US; Neoplasms, diagnosis; Neoplasms, staging; Pancreas, neoplasms; Pancreas, US; Portal vein; Ultrasound (US); Doppler studies.

Introduction

The majority of patients with pancreatic or bile duct malignancies present with obstructive jaundice ultrasonography is often the first imaging modality because it is very accurate in defining dilatation of bile ducts, level and cause of obstruction [1,2]. Currently dynamic incremental computed tomography (CT) and, more recently, (twin) helical CT are the gold standards for diagnosis and staging of patient suspected of having pancreatic carcinoma [3,4]. In the last decade Magnetic Resonance Imaging (MRI) is playing an increasing role. Unfortunately, at the time of presentation and diagnosis most biliopancreatic malignancies are already irresectable, which can be assessed by color Doppler ultrasonography as first imaging modality. We will discuss the literature and our own experiences with respect to color Doppler imaging in diagnosis and staging of biliopancreatic malignancies.

Pancreatic Carcinoma

General Characteristics

A total of 60-80% of pancreatic tumors originate in the head of the pancreas, and surgical options for curative resection (pancreaticoduodenal resection and subtotal pancreatectomy) are mostly done for tumors in this location [5]. Tumors in the body or tail usually present in an even more advanced stage and therefore are rarely resectable. Most patients with pancreatic head carcinoma present with symptoms indicating tumor extension beyond the boundaries of the gland (local infiltration), which for most surgeons indicates irresectability. In most instances, conventional abdominal ultrasound is the first imaging technique [6]. US is a noninvasive technique and does not present any of the risks inherent to contrast studies. Although the cost of US with color flow Doppler is less than that of CT scan, the real cost savings will come from early and efficient identification of patients, in whom surgery should be avoided and less costly palliative therapy can be done [7]. In the past, 20-25% of pancreatic sonographic examinations were technically inadequate, because of the deep location of the tumor and gastrointestinal superimposed bowel gas obscuring the pancreas or both; however with improved techniques and the operator's increasing skill, the limitations of sonographic assessment of the pancreas have been reduced. With real-time sonography, tumor involvement of the portal venous system can be assessed [8] The addition of pulsed Doppler sonography (PDS) and color Doppler has contributed much to assessing tumor involvement of the portal venous system, a main determinant of irresectability. The duplex Doppler imaging techniques in the study of vascular involvement by pancreatic neoplasm has, so far, been described by only a few authors [6]. Recently the additional application of color Doppler imaging to such patients has been described [7]. Duplex Doppler Imaging combines real-time and PDS. Narrowing of the portal venous system, caused by compression or tumor ingrowth, results in changes in blood flow velocities, which can be detected by PDS [6]. Apart from vascular involvement, other criteria for irresectability...
are local infiltration of the tumor, regional lymph node metastases, liver metastases, and peritoneal metastases.

**Pancreatic head carcinoma**

**Diagnosis, tumor detection**

A pancreatic head carcinoma usually presents as a lesion which is hypoechoic relative to adjacent normal pancreatic tissue. In our patient material, both the pancreatic duct (PD) and the common bile duct (CBD) were dilated in 87% of patients. The PD was dilated in 91%, and the CBD in 93% of patients. The sensitivity of sonographic tumor detection ranges from 72% to 98% [9-12]. This may in part reflect patient selection and the investigator's experience. The specificity exceeds 90% [12]. Sonographic measurement of tumor size is accurate because it correlates well with the findings of the pathologic specimen [13].

A variety of other disease processes, may sonographically mimic pancreatic head carcinoma, including chronic pancreatitis, focal pancreatitis, often malignancies such as lymphoma and metastasis and occasionally rare inflammatory processes as retroperitoneal fibrosis or cat scratch disease [14]. The diagnosis of pancreatic cancer coexisting with pancreatitis is especially difficult both on cross-sectional imaging and on the basis of ERCP [15]. Any hypoechoic lesion in the head of the pancreas causing a dilatation of both the CBD and the PD suggests carcinoma. A large pancreatic head (4-5 cm diameter) carcinoma is hardly ever encountered without the "double duct" sign. If the lesion is located in the uncinate process, one or both ducts may have a normal diameter. Patients with pancreatitis of the head of the pancreas may often present with only dilatation of the PD or the CBD. Abrupt termination instead of gradual tapering of the CBD or the PD suggests pancreatic carcinoma. In pancreatic head carcinoma, the hypoechoic lesion is occasionally surrounded by a rim of normal, more hyperechoic pancreatic tissue between the tumor and duodenum. Reactive pancreatitis occurring proximal to the tumor mass may hinder differentiation between the tumor and the pancreatic body or tail. Calcifications and pseudocysts suggest chronic pancreatitis. In chronic pancreatitis, a discrepancy can be expected between the size of the mass and the involvement of the portal venous system. If a large hypoechoic mass is seen in the head of the pancreas and PDS yields normal blood flow velocities, pancreatic cancer is unlikely. Enlarged lymph nodes are not helpful in the differentiation between carcinoma and pancreatitis. Irregular dilatation of the PD suggests pancreatitis. Of those patients, who underwent resective surgery under the presumptive diagnosis of pancreatic head carcinoma in our Institution in the period from 1983 to 1993, 6% proved to have benign chronic pancreatitis [16].

**Staging**

**Vascular involvement: portal venous system; major peripancreatic arteries**

Loss of the hyperechoic interface between the tumor and the vessel is an indication of infiltration. However, in color Doppler imaging of pancreatic carcinoma the resolution of ultrasound is not always enough to confirm this. Angeli et al. considered absence of contact or a short contiguity (< 2 cm) between tumor and vessel as a sign of absence of vascular ingrowth; a long contiguity (> 2 cm), compression, encasement (more that 50% of the vascular circumference surrounded by tumor) or thrombosis were considered to be signs of vascular ingrowth (Figure 1). For diagnosis of vascular involvement the sensitivity, specificity, accuracy, positive and negative predictive values were 79%, 89%, 84%, 89% and 79%, respectively [17]. No false-positive diagnoses occurred when vascular encasement was revealed by color Doppler imaging. This was confirmed by Wren et al in comparison with operative findings and histologic resection margins [7].

![Figure 1. Pancreatic head carcinoma. US sign of vascular ingrowth. US transverse view: hypoechoic mass (T) in the pancreatic head surrounds the superior mesenteric vein (SMV) more than 50% of the circumference (arrows). SMA= superior mesenteric artery](image)

When tracing the portal venous system in duplex Doppler sonography -a combination of real-time imaging and pulsed Doppler- an abrupt increase in Doppler shift is considered indicative of narrowing caused by compression or tumor ingrowth. A stenosis of more than 50-70% creates an obvious increased Doppler shift with corresponding blood flow velocities of more than 1 m/sec which is considered to be abnormal. Beyond such a significant stenosis, blood turbulence creates spectral broadening, which is the reflection of the presence of a large and increased range of blood flow velocities at a given point in the pulse cycle [6,18]. Where there is complete occlusion, no Doppler signal can be detected. Where there is severe stenosis or occlusion anywhere in the portal venous system, collaterals can be shown with color Doppler sonography. Color Doppler sonography allows the fastest and most accurate sampling of the portal venous system.

In our series of patients with pancreatic head carcinoma (n=191) no patient with an abnormal PDS who underwent laparotomy (n=15) had a tumor with a chance for curative resection. In patients with an abnormal pulsed Doppler study who did not undergo laparotomy and in whom angiography was performed (n=21), angiography was positive in 95% of cases. Therefore an abnormal pulsed Doppler study is highly suspicious of major involvement of the portal venous system.
and indicates irresectability of the tumor. A normal pulsed Doppler signal does not exclude infiltration of the portal venous system. Loss of the hyperechoic interface between the tumor and the vessel is an indication of infiltration. A high Doppler shift due to narrowing of the portal venous system can be masqueraded by chronic pancreatitis, lymphoma, and metastases [18]. Tumor involvement of the superior mesenteric artery or the celiac trunk indicates irresectability. However, pulsed Doppler examination of these vessels is of limited importance because narrowing of the lumen, resulting in an abnormal Doppler signal, will only occur in advanced disease. Arterial encasement is reflected in the loss of the hyperechoic interface between tumor and vessel. In pancreatic head carcinoma involvement of the portal venous system will almost always precede encasement of the major peripancreatic arteries. Kosuge et al. described thickening of the area around the superior mesenteric artery, with or without decreased echogenicity ("cuff sign"), as a reliable sign of tumor infiltration in patients with pancreatic carcinoma. These authors found a sensitivity, specificity, and accuracy of 91%, 100% and 96%, respectively [19].

Regional lymph node metastases

Because survival correlates with nodal status, the identification of lymph node metastases is important [20]. Lymph nodes that are adjacent to the tumor mass cannot be detected by US. Campbell and Wilson reported lymphadenopathy in 16 of 50 patients (32%) with pancreatic neoplasms (adenocarcinoma, n=30; other malignant tumors, n=10; unknown, n=10) [21]. A typically benign lymph node is long with a small short axis and a hyperechoic center. Such a lymph node can often be seen in the region of the hepatic artery and posterior to the pancreatic head (portal-caval node). Large oval-shaped hypoechoic lymph nodes can indicate both inflammation and malignancy. However, reliable differentiation between reactive lymph nodes and lymph node metastases is generally not possible. This is even difficult with endosonography [22]. Therefore lymph node enlargement alone may not indicate irresectability. Small lymph nodes that are not even identified by sonography may contain tumor.

Liver and peritoneal metastases

At presentation, most liver metastases measure 1-3 mm in diameter. At laparoscopy Warshaw et al. found liver metastases in 13 of 55 patients (24%) with a carcinoma of the pancreatic head [5]. However, a previous contrast-enhanced CT scan of the liver in these patients was negative for metastases. Because of their size (1-3 mm), the lesions were below the detection level of preoperative imaging techniques, including US. Laparoscopy or laparoscopic sonography with biopsy are more sensitive diagnostic techniques. Metastatic liver lesions larger than approximately 1 cm can be detected by sonography, depending on location and echogenicity relative to the adjacent liver parenchyma. Liver metastases are usually hypoechochogenic. There is an important role for the near-field scanning technique because most liver metastases are superficial. For this purpose additional scanning with a 7.5-MHz linear or curved array probe is recommended. Peritoneal metastases are also usually tiny and only detectable by laparoscopy.

Ampullary carcinoma

Ampullary tumor, usually a polypoid adenocarcinoma protruding from the papilla, is less common than pancreatic carcinoma and can usually best be identified during endoscopy. The tumors are usually small (50% measuring < 3 cm) when discovered, since the lumen of the CBD does not permit much encroachment before it becomes obstructed [23,24]. Early detection may allow curative resection [25]. An impacted stone with secondary edema may mimic a friable ampullary mass. US may demonstrate both a dilated CBD and a dilated PD, and occasionally a mass lesion. The actual tumor may be small, but the dilated CBD may prolapse into the duodenum, thus mimicking a larger mass. The differential diagnosis between benign ampullary stenosis and small tumor is hindered by the fact that inflammatory stenosis, especially after endoscopic sphincterotomy, can also lead to an hypoechoic lesion mimicking a true neoplasm [26]. Duplex Doppler US, endo-ultrasonography, CT and MRI and in some selected cases angiography may be helpful in further evaluating resectability preoperatively.

Primary Cholangiocarcinoma

General Characteristics

In cholangiocarcinoma, three morphological types need to be considered: focal stenotic carcinoma (pathologically high-grade tapered lesions, 1-3 cm long with secondary narrowing or obstruction of a bile duct segment), polypoid carcinoma, (pathologically low-grade papillary lesions protruding into the lumen of the bile duct), and high-grade diffuse sclerosing carcinoma (lesions obstructing multiple intrahepatic bile duct segments) [27]. Patients with an extrahepatic low-grade (polypoid) carcinoma have the best prognosis. In differentiating obstructive from nonobstructive jaundice, US has an accuracy of over 90% for common bile duct dilatation and is the screening procedure of choice [1]. In one report, information about the level of obstruction was obtained with US and CT in 100% of cases [28].

Hilar Cholangiocarcinoma (Klatskin Tumor)

The most common type of hilar cholangiocarcinoma is a sclerosing mass extending along the bile ducts. This infiltrating type of neoplasm, which invades adjacent liver tissue, is pathologically a sclerotic lesion with abundant fibrous tissue and exhibits as a desmoplasic and inflammatory stroma response and perineural growth [29]. Although the surgical results are poor, with a median survival rate of 6-22 months, complete excision is still considered to be the treatment of choice for this tumor [30,31]. For determining resectability, extensive biliary and
vascular involvement are considered the most important factors. The aim of radiological investigation is early detection and accurate preoperative assessment of resectability of these tumors in terms of curative or a palliative surgery [28].

**Diagnosis, tumor detection**

Usually, a Klatskin tumor presents as a small solid mass at the bifurcation, causing dilatation of the intrahepatic bile ducts with non-union of the right and left hepatic ducts. Most tumors are more or less isoechoic to the adjacent liver parenchyma (45-56%) and therefore difficult to delineate [28,18]. The sonographic character of these tumors can be hyperechoic (16-42%), hypoechoic (16-27%) or mixed (1%) [28,18]. US can correctly visualize the tumor in 83-89% of patients [28,18]. The CBD has a normal calibre. If the tumor distally terminates above the orifice of the cystic duct, the gallbladder collapses. A large gallbladder can indicate that the tumor infiltrates the cystic duct.

Hilar cholangiocarcinoma needs to be discriminated from various other benign and malignant lesions affecting the hilar or subhilar region such as gallbladder carcinoma, primary sclerosing cholangitis, with or without cholangiocarcinoma, benign fibrosis, biliary stones, metastasis and lymphoma.

Benign fibrosing or localized sclerosing tumors at the hepatic confluence, although notorious for mimicking proximal bile duct cancer, have rarely been described in the literature [32,33]. Of the 82 patients who underwent resective surgery under the presumptive diagnosis of hilar cholangiocarcinoma (Klatskin tumor) in our Institute in the period from 1984 to 1990, 11 (13.4%) proved to have benign fibrosing or localized sclerosing lesions [32]. However, differentiation using duplex Doppler imaging is also not possible.

Percutaneous intraluminal US of the bile ducts and percutaneous cholangioscopy can discriminate reliably between benign and malignant hilar lesions [34,35]. These are invasive techniques with a risk of tumor spill.

**Staging**

**Proximal extension into the biliary system**

If dilated ducts are seen within a liver lobe without clear communication among each other, extension of the tumor into the segmental bile ducts can be concluded. US has the advantage over cholangiography that all dilated bile ducts can be visualized. Proximal intraluminal tumor extension can correctly be established sonographically in 80% [28].

**Tumor infiltration into the liver**

Loss of the hypoechoic interface between bile ducts and liver may indicate invasion into the liver [36] and can be identified in 55% [28]. However, because most tumors are isoechoic, the extent of infiltration is often difficult to define.

**Vascular involvement**

Duplex US can correctly diagnose vascular infiltration in 85-91% of the cases; angiography does the same in 82-86% [18,28]. This has made angiography in most cases an obsolete procedure with no additional information. Duplex Doppler US may assist in the selection of patients for attempted resection and, more importantly, noninvasively identify patients whose tumors are clearly irresectable but who might be considered as candidates for nonoperative palliation [28,36] (Figure 2). Doppler US can give false-negative results, firstly for technical reasons, e.g. if the portal vein (especially the left one) courses deeply or the Doppler angle is not shallow enough, and secondly if tumor infiltration of the vessel wall does not result in narrowing of the vessel. Doppler US can give a false-positive result if narrowing of the portal vein is caused by compression without tumor infiltration. Lobar atrophy, due to longstanding severe biliary obstruction and/or severe portal venous stenosis or occlusion, is an important predictive factor arguing for irresectability but does not affect the overall patient prognosis disproportionately [37,38].

The presence of an atrophy/hypertrophy complex (AHC), which may indicate marked progression of local tumor growth, determines the type of liver resection to be carried out (hemihepatectomy, extended hemihepatectomy) and can be appropriately documented with CT or with (color) Doppler US if CT is indeterminate [39,1,28,36,40]. No liver resection should be performed that leaves an atrophic remnant! In the presence of lobar atrophy, axial rotation or compression by the contralateral hypertrophic liver lobe can result in stenosis of the portal vein without tumorous infiltration [28,36]. On Doppler US, the portal vein may be gracile without involvement and may show a low-velocity hepatopetal blood flow or even a hepatofugal blood flow. Tumor infiltration into the hepatoduodenal ligament is inadequately shown by US and/or CT. Intraportal US may provide more valuable information on changes of the portal venous wall than duplex Doppler, arterial portography and/or direct portography [41].

The accuracy of nonresectability in a Klatskin tumor is higher, when different methods (US, CT, endoscopic retrograde cholangiography (ERC), angiography) are combined (70-90%) than with any single modality (42-71%) [1,37].
Regional lymph node metastases; liver metastases

In hilar cholangiocarcinoma, regional lymph node metastases are reported in approximately 30% of cases. The nodes most commonly involved are the nodes of the foramen of Winslow, the superior pancreaticoduodenal nodes, the posterior pancreaticoduodenal chain, and the nodes on the coeliac trunk. However, US and CT are not reliable in predicting lymph node metastases, since lymph nodes that are metastatically invaded but not enlarged cannot be detected with these methods. At our institute we investigate regional lymph node status preoperatively using laparoscopy combined with laparoscopic US. In hilar cholangiocarcinoma metastases to the liver are rare. Therefore metastases should be distinguished from benign lesions.

Conclusion

A majority of patients with biliopancreatic malignancy present in an advanced stage of disease. Color Doppler US, as first imaging modality in obstructive jaundice can often assess local irresectability due to vascular involvement in pancreatic malignancy and vascular or extensive biliary involvement in hilar cholangiocarcinoma, obviating other imaging modalities.

Acknowledgements

This article is adapted from original version: Chapter 14, Ultrasonography, Duplex Color Doppler Imaging and Laparoscopic Sonography in Patients with Pancreatic Head and Bile Duct Malignancies. Jacques WJAJ Reeder, Nico J Smits in: Hepatobiliary and Pancreatic Imaging (DJ van Leeuwen, JWAJ Reeders, J Ariyama Eds), WB Saunders, London, 1999

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