RAPID COMMUNICATION



Differentiation of malignant and benign proximal bile duct strictures: The diagnostic dilemma

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Abstract

AIM: To identify the criteria for the differentiation of hilar cholangiocarcinoma (HCCA) from benign strictures.

METHODS: A total of 68 patients underwent resection of lesions suspicious for HCCA between 1998 and 2006. The results of laboratory investigations, imaging studies and brush cytology were collected. These findings were analyzed to obtain the final diagnosis.

RESULTS: Histological examination of the resected specimens confirmed HCCA in 58 patients (85%, group I) whereas 10 patients (15%, group II) were diagnosed to have benign strictures. The most common presenting symptom was obstructive jaundice in 77% patients (79% group I *vs* 60% group II, *P* = 0.23). Laboratory findings showed greater elevation of transaminase levels in group I compared to group II. The various imaging modalities showed vascular involvement exclusively in the malignant group (36%,

P < 0.05). Brush cytology was positive for malignant cells in only 50% patients in group I whereas none in group II showed malignant cells.

CONCLUSION: Despite improvements in imaging techniques, 10 patients (15%) with a presumptive diagnosis of HCCA were ultimately found to have benign strictures. Except for vascular involvement which was associated significantly with malignancy, there were no conclusive features of malignancy on regular imaging modalities. This uncertainty should be taken into account when patients with a suspicious lesion at the liver hilum are considered for resection.

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Key words: Biliary stricture; Hilar cholangiocarcinoma; Benign; Radiological; Vascular involvement

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INTRODUCTION

Hilar resection en bloc with liver resection is the only curative treatment option for patients with carcinoma at the hepatic duct confluence. Although mortality rates associated with partial hepatectomy have decreased markedly in the past decades, postoperative morbidity is considerable and can exceed 50 percent^[1-4]. Undertaking partial hepatectomy for hilar cholangiocarcinoma (HCCA) becomes even more a subject of discussion when histopathology of the resected specimen shows benign disease. A variety of benign lesions at the liver hilum can mimic malignancy. In particular, inflammatory lesions may present with the same clinical and radiological features as a malignant tumor.

In the past decade, imaging techniques have improved and the diagnostic work-up of patients suspected of HCCA usually comprised of ultra-sonography (US), contrast enhanced multi-slice computed tomography (CT) and magnetic resonance cholangiography (MRC). In experienced hands, colour Doppler US is very useful in assessing proximal biliary extension of the tumor and vascular invasion, but has limited value in distinguishing HCCA from inflammatory lesions^[5]. Contrast enhanced CT and MR imaging (MRI) provide important information regarding resectability and vascular involvement^[6-8]. Furthermore, these cross-sectional imaging modalities are accurate in detecting a tumor mass and signs of lymphadenopathy, although both features may also be present in benign diseases. Cholangiography in combination with brush cytology has a low sensitivity, and although the specificity is higher, it is not 100% since longstanding stenting of the biliary duct may give rise to false positive cytology results^[9]. Overall, an extensive work-up with multiple imaging techniques may improve the differentiation between malignant and benign proximal bile duct strictures.

Several studies have noted that approximately 14% to 25% of patients resected for presumed HCCA prove to have a benign lesion at histopathology^[10-14]. A recent study attempted to identify potential criteria for distinguishing patients with HCCA from those with an alternative diagnosis^[15]. However, the non-HCCA patients in this series comprised of benign and malignant diseases (for instance gallbladder cancer), which makes any conclusions difficult to interpret. In a previous series of 132 patients who had undergone surgical treatment for suspicious HCCA at our center from 1983 to 1998, 15% (20/132) of the patients had benign lesions^[16]. In the present study, which covers a more recent period during which improved imaging techniques were used, the rate of mis-diagnosed benign lesions was reexamined and the diagnostic features of benign and malignant lesions was compared. The aim of the study was to identify criteria that can differentiate HCCA from benign proximal bile duct strictures.

MATERIALS AND METHODS

Between January 1998 and December 2006, a total of 143 patients underwent a diagnostic laparoscopy for staging of HCCA, and 13 patients underwent laparotomy without diagnostic laparoscopy. Unresectable disease was found in 36 patients undergoing laparoscopy, and in the majority of these cases the diagnosis was confirmed by histology (Figure 1). Another 52 patients were found to have unresectable disease during subsequent laparotomy which was confirmed by histology. Finally, 68 consecutive patients underwent resection and are the subject of the present study (Figure 1). These patients had hilar resection with complete lymphadenectomy of the hepato-duodenal ligament usually en bloc with (extended) hemi-hepatectomy including resection of the caudate lobe and left or right portal vein^[17]. Although in the majority of the patients included in the study,

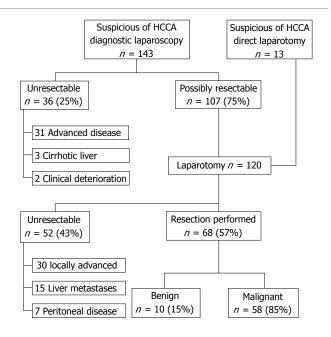


Figure 1 Flow chart of patients eligible for resection of hilaire cholangiocarcinoma (HCCA) with final histopathological outcome in the period from January 1998 to December 2006.

the initial diagnostic evaluation was performed at the referring hospital, imaging studies such as US, CT and MRC were usually repeated in our center. The medical data of patients obtained from these hospitals and from our center included demographic features, relevant medical history, presenting symptoms, laboratory investigations, results of imaging studies (including cholangiography, CT, MRC, duplex US), radiological and endoscopic interventions including placement of a stent, brush cytology and intra-operative findings.

The results of biliary brush cytology obtained during antegrade percutaneous transhepatic cholangiography (PTC) or endoscopic retrograde cholangiopancre aticography (ERCP) were categorized as follows: highly suspicious for adenocarcinoma, atypical cells/ inconclusive, and no malignant cells. Data from imaging studies were collected for staging purposes. The data recorded from these studies included: the presence of a mass lesion, proximal extent of the tumor within the biliary tree according to the Bismuth-Corlette classification system, vascular involvement (hepatic artery, portal vein), liver lobe atrophy, and lymphadenopathy. Ultrasonography, CT and MRI were used to detect a mass lesion, to determine the size of the lesion and the level of the biliary obstruction. Findings on PTC and/or ERCP showing an irregular and eccentric stenosis and/or a blunt end rather than a smooth tapering narrowing of the duct were considered more suggestive of a malignant lesion. Vascular invasion on colour Doppler US was defined as an increase in flow compatible with stenosis or absence of flow compatible with occlusion. Furthermore, on contrast enhanced CT, presence of vascular stenosis or occlusion of the portal vein and encasement of the artery were indicative of vascular involvement.

The final histological diagnosis was correlated with

the preoperative clinical and laboratory findings as well as with the radiological data in an effort to identify criteria which may be useful for the differentiation of HCCA (group I, 58 patients) from benign proximal bile duct stricture (group II, 10 patients). The resected specimens of the benign lesions were re-assessed by a single pathologist, specialized in hepatobiliary pathology (FJ. tK.). The results obtained are expressed as the mean (SEM). The differences between categorical variables were evaluated by chi-square analysis, while Student's t test was used for all comparisons among continuous variables. A two-tailed P value less than 0.05 was considered to indicate significant differences. All statistics were carried out using the SPSS Base 12.0 for Windows Statistical Package for Social Sciences (SPSS®, Chicago, IL).

RESULTS

The demographic features, presenting symptoms, and preoperative laboratory findings are shown in Table 1. The mean age and male-female gender ratio were equal in the two study groups. Although 9 patients (groups combined) had a prior cholecystectomy, none of the patients had a complicated procedure with bile duct stricture. In the group with benign lesions, one patient had history of alcohol abuse and related chronic pancreatitis, and another patient had history of inflammatory bowel disease (ulcerative colitis). In the malignant group, one patient had history of alcohol abuse and one patient had Crohn's colitis with primary sclerosing cholangitis (PSC).

There were no statistically significant differences between the two groups with respect to the clinical presentation. Jaundice was present in 79% of the patients in group I and 60% of group II. Abdominal pain, usually located in the right upper abdomen or in the epigastric region was mostly vague and nonpersistent. Weight loss was observed in both groups with a median loss of 6.4 kg in group I (range 2-16) and 7.3 kg (range 2-10) in group II. No differences were observed in the results of the laboratory tests, except for serum transaminase levels which showed higher levels in group I compared to group II (P <0.05, Table 1). Assessment of tumor markers, including carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) was not performed routinely.

The majority of patients underwent imaging studies, and interventions such as ERCP, PTC and diagnostic laparoscopy (Table 2). The mean number of imaging procedures was 3.3 per patient in both groups. CT scan was performed most frequently, with an overall rate of 96%. Sixty patients (88%) underwent colour Doppler US, while MRI was performed in 21 patients (31%). Cholangiography (either ERCP or PTC) was performed in 63 patients (93%). Forty-seven patients underwent ERCP and 15 patients underwent PTC with at least one bile duct stent or drainage tube inserted. Five patients underwent both ERCP and PTC to achieve biliary decompression. Examination of brush cytology, shown

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Table 1 Demographic features, presenting symptoms and laboratory findings in patients resected for presumed HCCA

	$\begin{array}{l} \text{Malignant} \\ (n = 58) \end{array}$	Benign $(n = 10)$	Р
Demographics			
Gender male/female	35/23	3/7	0.09
Mean age (range)	62 (30-80)	61 (40-71)	0.62
Prior history of cholecystectomy	6 (10%)	3 (30%)	0.12
Presenting symptoms			
Jaundice	46 (79%)	6 (60%)	0.23
Abdominal pain	27 (47%)	6 (60%)	0.51
Weight loss	34 (59%)	4 (40%)	0.32
Fever	2 (3%)	2 (20%)	0.10
Preoperative laboratory findings			
Bilirubin (μmol/L)	144 (± 15)	107 (± 35)	0.36
AP (U/L)	430 (± 61)	371 (± 64)	0.73
AST (U/L)	119 (± 12)	58 (± 15)	0.02
ALT (U/L)	190 (± 21)	88 (± 22)	0.03
GGT (U/L)	675 (± 89)	405 (± 114)	0.32
LDH (U/L)	313 (± 20)	277 (± 30)	0.42
PT (Prolonged-Normal)	3-33 (8%)	1-6 (14%)	0.62

HCCA: Hilar cholangiocarcinoma; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma glutamyl transpeptidase; LDH: Lactate dehydrogenase; PT: Prothrombin time; AP: Alkaline phosphatase.

Table 2	Imaging	studies	and	interventions	in	patients
resected f	for presum	ed HCC/	4			

	$\begin{array}{l} \text{Malignant} \\ (n = 58) \end{array}$	Benign $(n = 10)$	P
No. of imaging studies			
ERCP	51 (88%)	9 (90%)	
PTC	13 (22%)	3 (30%)	
US + colour Doppler	52 (90%)	8 (80%)	
CT	56 (97%)	9 (90%)	
MRC	17 (29%)	4 (40%)	
Mean No. of procedures per patient	3.3	3.3	
Stent placement procedure			
ERCP	40	7	
PTC	12	3	
ERCP and PTC	4	1	
Biliary brushing			
No. of brushings performed	30/58 (52%)	6/10 (60%)	0.74
Highly suspicious	15/30 (50%)	0/6 (0%)	0.03
No malignant cells	9/30 (30%)	4/6 (67%)	0.16
Atypical cells, inconclusive	6/30 (20%)	2/6 (33%)	0.60
Diagnostic laparoscopy			
No. of laparoscopies performed	53 (91%)	8 (80%)	
Intra-operative US performed	15	1	

in Table 2, showed malignant cells in 50% of patients in group I, whereas none in group II showed malignant cells (P < 0.05). Furthermore, brush cytology in 9 patients in the malignant group proved false negative. Atypical cells were found in 6 and 2 patients in group I and II, respectively.

The findings obtained with the imaging studies are shown in Table 3. A mass lesion at the hepatic duct confluence was seen in 56 patients (97%) in group I and 8 patients (80%) in group II. The presence and size of a mass could not distinguish between benign or malignant disease. The extent of bile duct involvement classified according to the Bismuth-Corlette system was similar in the two groups. Vascular involvement was

findings in patients resected for presumed HCCA						
	$\begin{array}{l} \text{Malignant} \\ (n = 58) \end{array}$	Benign $(n = 10)$	P			
Findings on preoperative imaging						
Presence of mass	56 (97%)	8 (80%)	0.10			
Mean size (range, cm)	2.5 (0.7-7.0)	2.6 (1.0-3.7)	0.62			
Bismuth classification						
Туре І, П	14	3	0.70			
Type Ⅲa/b, IV	39	6				
Intrahepatic	5	1				
Vascular involvement ¹	21 (36%)	0 (0%)	0.03			
Portal vein	19	0				
Hepatic artery	6	0				
Lobar atrophy	10 (17%)	1 (10%)	1.00			
Lymph nodes (> 1 cm)	12 (21%)	1 (10%)	0.67			
Intra-operative findings						
FS performed ²	57/58 (99%)	10/10 (100%)				
FS positive for malignancy	20/57 (35%)	0/10 (0%)	0.03			
Suspicious ³ -Not suspicious	51-7	5-5				
Type of resection						
Local bile duct resection	17 (29%)	3 (30%)				
Concomitant partial hepatectomy	41 (71%)	7 (70%)				

Table 3 Results of imaging studies and intra-operativefindings in patients resected for presumed HCCA

FS: Frozen section. ¹Non cumulative, patients with simultaneously portal v. and hepatic a. involvement; ²FS from suspicious lesions, lymph nodes and/or resection margins; ³A positive FS and/or palpable mass.

observed only in patients with malignant disease (P < 0.05), although lobar atrophy was not more frequent in the malignant group. Lobar atrophy was present in one patient in the benign group, probably caused by segmental biliary obstruction. Moreover, the presence of enlarged lymph nodes (> 1 cm, short axis diameter) could not differentiate the two groups. After taking into consideration the clinical presentation, laboratory findings, imaging studies, prior interventions and brush cytology, all 68 patients were diagnosed to have a lesion suspicious of HCCA.

During surgical exploration, frozen sections were obtained of suspicious lymph nodes, tissue suspicious of tumor infiltrating the vessel walls, and the resection margins to ensure radical resection in all patients except one (Table 3). The frozen section examination confirmed malignancy in 35% of the patients in group I, and no false positive results were obtained in group II (P < 0.05). A palpable, suspicious hilar tumor was found in 5 patients (50%) in the benign group and in 51 patients (88%) in the malignant group. Eventually, 70% of all patients underwent hilar resection, in combination with partial liver resection; the prevalence of local bile duct excision was equally divided between the two groups. Histological analysis of the resected specimens showed a benign bile duct stricture in 10 patients, diagnosed as chronic fibrosing lesion, erosive inflammation, sclerosing cholangitis or autoimmune cholangitis (IgG4-related) (Table 4). In the remaining 58 resection specimens, histology confirmed HCCA.

DISCUSSION

Cholangiocarcinoma and benign, inflammatory lesions of

the biliary tract may have a similar clinical presentation. Differentiating the two conditions is complex because on the one hand, HCCA is frequently associated with secondary inflammatory changes, and on the other hand, conditions such as PSC predispose to malignancy of the bile ducts (with a reported prevalence of 30%)^[18]. A combination of different imaging modalities is usually employed in the diagnosis of hilar bile duct lesions^[8]. However, to date, no single investigation has been found to reliably differentiate HCCA from benign proximal bile duct strictures.

In the present study, the rate of patients (15%) with benign lesions misdiagnosed as malignancy was similar to the rate (15%) observed in a previous study performed at our center a decade earlier (1983-1997)^[16]. Despite considerable improvements in imaging techniques (contrast enhanced multi-slice CT and MRC), and an increase in the number of imaging procedures (a mean of 3 modalities in comparison to 2 in the previous study), patients still required unnecessary extensive resections, for achieving adequate biliary drainage. Case series from other groups worldwide, have noted comparable rates of benign lesions in resections performed for presumed HCCA (Table 5). Our observations confirm the findings of these studies and emphasize the difficulty in differentiating benign from malignant lesions at the liver hilum, despite use of stateof-the-art imaging modalities.

Clinical features alone cannot differentiate HCCA from benign proximal bile duct strictures. With regard to laboratory tests, plasma transaminase values were significantly elevated in the malignant group compared to patients with benign hilar lesions. Although raised transaminase values may occur in patients with benign proximal bile duct strictures (usually in conjunction with cholangitis), our results show that this is an uncommon finding. Other laboratory tests failed to identify patients with a malignancy. The diagnostic value of tumor markers such as CA 19-9 and CEA in biliary cancer has been extensively studied. One study showed 100% sensitivity using a combination of CA 19-9 and CEA^[19], but these results could not be confirmed by other workers^[9,10]. Another, potentially useful test is serum IgG4. Recently, IgG4-related lymphoplasmacytic sclerosing disease was observed in patients with strictures of the pancreatic duct mimicking carcinoma^[20]. In a study from our center, it was shown that IgG4-related sclerosing disease also occurs in patients with benign proximal bile duct strictures^[21]. In the present series, two of the ten patients with benign proximal bile duct strictures showed infiltration by IgG4-plasma cells with histological features suggestive of an autoimmune disorder. Serum levels of IgG4 have potential to differentiate benign disease from HCCA, although the diagnostic value of this marker and the role of immunomodulatory drugs requires further investigation^[22].

The findings obtained with the different imaging studies revealed that only one feature, i.e. vascular involvement, was significantly different between the Table 4 Patients with benign proximal bile duct strictures: Preoperative, intra-operative and histological findings

Number of patient	Age/Gender	Medical history	Bismuth classification	Brush cytology	Intra-operative findings	Treatment	Final histological diagnosis
1	40/F	LC	Intrahepatic	Atypical cells	Suspicious	Hemihepatectomy le	Fibrosing cholangitis
2	54/F	-	Туре Ша	No malignancy	Suspicious	Hemihepatectomy ri ¹	Sclerosing cholangitis
3	56/M	IBD	Type Ⅲb	-	Not suspicious	Hemihepatectomy le ^{1,2}	Sclerosing cholangitis
4	60/F	-	Туре II	No malignancy	Not suspicious	Local resection	Fibrosing cholangitis
5	63/F	LC	Туре II	Atypical cells	Suspicious	Local resection	Erosive inflammation
6	65/F	-	Туре Ша	-	Not suspicious	Hemihepatectomy ri	Autoimmune-like cholangitis
7	68/F	LC	Туре Ша	-	Suspicious	Hemihepatectomy ri	Fibrosing cholangitis
8	69/F	-	Type Ⅲb	-	Not suspicious	Hemihepatectomy le	Sclerosing cholangitis
9	70/M	-	Туре II	No malignancy	Not suspicious	Local resection	Erosive inflammation
10	71/M	CP	Туре Ша	No malignancy	Suspicious	Hemihepatectomy ri ¹	Autoimmune-like cholangitis

CP: Chronic pancreatitis; LC: Laparoscopic cholecystectomy; IBD: Inflammatory bowel disease. ¹Partial liver resection + local resection; ²Partial liver resection was performed because of atrophic liver lobes.

Table 5Incidence of benign lesions in patients resected forpresumed HCCA:Review of literature

Source, yr ¹	Period of inclusion	Number of patients ²	Number of benign lesions (%)
Hadjis et al 1985 ^[34]	1979-1983	104^{3}	8 (8)
Wetter et al 1991 ^[35]	1985-1990	59^{4}	8 (14)
Verbeek et al 1992 ^[36]	1984-1990	82	11 (13)
Nakayama et al 1999 ^[10]	1990-1997	99	14 (15)
Gerhards et al 2001 ^[16]	1983-1997	132	20 (15)
Knoefel et al 2003 ^[12]	1996-1999	33	6 (18)
Khalili et al 2003 ^[13]	2000-2001	20	4 (20)
Koea et al 2004 ^[37]	1998-2002	49	12 (24)
Corvera et al 2005 ^[38]	1992-2003	275 ³	22 (8)
Are et al 2006 ^[15]	1997-2001	59	9 (15)
Uhlmann et al 2006 ^[39]	1998-2004	49	7 (14)
Present study	1998-2006	68	10 (15)

¹Listed chronologically; ²Indicates only patients undergoing resection; ³Patients evaluated of suspected hilar cholangiocarcinoma (not all resected); ⁴Patients resected for papillary tumours were excluded (n = 5).

benign and malignant groups. Even a mass lesion was not able to differentiate between the two groups. Furthermore, in contrast to the report by Are and coworkers^[15], we did not find any difference between the benign and malignant groups with respect to either the level of obstruction or the extent of lesion. Moreover, there was no difference in rate of liver lobe atrophy. Portal vein occlusion of one side of the liver typically gives rise to ipsilateral lobar atrophy and compensatory hypertrophy of the contralateral lobe. However, it is possible to develop lobar atrophy without portal vein occlusion. In benign disease, lobar atrophy can develop secondary to longstanding cholestasis. In a series of 162 patients with intrahepatic cholelithiasis, lobe atrophy was observed in 7% of the patients^[23]. Overall, the finding of lobar atrophy is uncommon with benign disease and should be considered as a manifestation of vascular involvement and therefore of malignancy. Occlusion of the portal vein obviously suggests malignancy, however two cases have been reported of a benign inflammatory pseudotumor mimicking HCCA with vascular involvement^[24,25]. Therefore, although uncommon, even vascular involvement may be seen in benign lesions at the liver hilum.

Brush cytology of a biliary stricture is often undertaken during ERCP or PTC. Unfortunately, the diagnostic yield is poor with sensitivity rates around 50%^[9,26]. Moreover, the specificity is not 100% since longstanding stenting of the biliary duct induces chronic inflammation, which makes it difficult to differentiate benign from malignant cells, resulting in false positive results^[9]. The present study showed similar rates which is consistent with previous studies. Fluorescence in situ hybridization (FISH) has been increasingly used to facilitate the identification of neoplastic cells in cytologic specimens^[27]. In one study, 20% of patients with cholangiocarcinoma missed by conventional cytology were identified by FISH without affecting the specificity^[28]. Several studies have evaluated the diagnostic yield of endoscopic US fine needle aspiration in patients with biliary strictures^[29-32]. In one of the studies, the sensitivity and specificity of biopsy were 89% and 100%, respectively^[30]. Moreover, the planned surgical approach was changed in 27 of 44 patients. Therefore, biopsy from either the mass or the surrounding malignant-appearing lymph nodes appears to have a higher sensitivity than ERCP or PTC with brush cytology. More recently, techniques such as intraductal ultrasound (IDUS) and cholangioscopy have been used to obtain direct biopsy specimens. IDUS with biopsy increased the accuracy of ERCP from 58%-60% to 83%-90% in distinguishing benign and malignant strictures^[33]. These diagnostic modalities appear very promising in differentiating benign and malignant biliary lesions, although they are highly expert-dependent and are still not widely available.

In one-half of the patients diagnosed to have a benign lesion at the liver hilum, the intra-operative findings were consistent with a malignant tumor (i.e. positive frozen section diagnosis and/or evident palpable mass). Furthermore, 7 patients in the malignant group were not found to have a suspicious lesion during laparotomy. Thus, even at surgery it is difficult to determine the nature of a hilar lesion, and resection is the only way to rule out malignancy.

In conclusion, despite improvements in the quality and increase in the number of imaging studies, 10 out of 68 (15%) patients with presumed HCCA, were misdiagnosed. Vascular involvement showed a significant association with malignant lesions. However, there was no feature on imaging studies or laboratory tests that reliably distinguished HCCA from benign proximal bile duct lesions. Therefore, differentiation of benign from malignant lesions at the liver hilum remains difficult and this should be taken into account when considering resection in patients with suspicious hilar lesions.

COMMENTS

Background

The main etiology of proximal bile duct stricture is hilar cholangiocarcinoma (HCCA). However, the differentiation of benign and malignant strictures is difficult which has obvious important consequences for management. Extensive work-up including multi-slice computed tomography and magnetic resonance cholangiography may help improve the diagnostic dilemma.

Research frontiers

The differentiation of benign and malignant lesions at the liver hilum remains a diagnostic dilemma despite improvements in the quality and increase in the number of imaging techniques. Novel diagnostic and imaging techniques are discussed, although none have shown a high rate of accuracy. The most promising diagnostic modality appears to be intraductal ultrasound in combination with cholangioscopic biopsy.

Innovations and breakthroughs

The authors observed that vascular involvement had a significant association with malignant lesions. No other feature on imaging studies or laboratory tests was able to reliably distinguish HCCA from benign proximal bile duct lesions.

Applications

Vascular involvement emerged as the most important diagnostic feature.

Terminology

Vascular invasion on colour Doppler ultrasonography was defined as an increase in the portal and/or hepatic arterial flow compatible with stenosis, or absence of flow compatible with occlusion. Furthermore, on contrast enhanced computed tomography a vascular stenosis or occlusion was considered as vascular involvement.

Peer review

This is a retrospective study of 68 patients with suspicion of cholangiocarcinoma. Fifteen percent of patients were found to have benign strictures after resection. The authors concluded that despite the use of sophisticated diagnostic tests and imaging studies, differentiation of malignant from benign hilar lesions remains a dilemma.

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