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Cystic Neoplasms of the Liver: Biliary Cystadenoma and Cystadenocarcinoma

Kevin C Soares, MD¹, Dean J Arnaoutakis, MD¹, Ihab Kamel, MD, PhD², Robert Anders, MD, PhD³, Reid B Adams, MD, FACS⁴, Todd W Bauer, MD, FACS⁴, and Timothy M Pawlik, MD, MPH, PhD, FACS¹

¹ Department of Surgery, Division of Surgical Oncology, The Johns Hopkins University School of Medicine, Baltimore, MD

²Department of Radiology, The Johns Hopkins University School of Medicine, Baltimore, MD

³Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD

⁴Department of Surgery, Division of Surgical Oncology, University of Virginia Health System, Charlottesville, VA

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Introduction

Cystic diseases of the liver occur in about 5-10% of the population.(1) While simple cysts are most common, biliary cystic tumors (BCT), namely biliary cystadenoma (BCA) and cystadenocarcinoma (BCAC) can arise in a subset of patients. Hueter first reported BCA in 1887 and Keen reported the first BCA resection five years later.(2, 3) Since that time, there has been a relative paucity of data published on the surgical management of BCT. Due to the rarity of BCT, many clinicians may be unfamiliar with the diagnostic features, therapeutic management, and natural history of these liver neoplasms. We herein provide an evidence-based review of BCT with particular emphasis on early recognition and approach to management. A search of available electronic databases including MEDLINE/Pubmed using the terms “biliary cystadenoma”, “biliary cystadenocarcinoma”, and “non parasitic hepatic cysts” was conducted. Additionally, we searched the MeSH database under the heading “Liver Neoplasm” in combination with the above referenced terms and Boolean operator

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Correspondence address: Timothy M. Pawlik, MD, MPH, PhD Chief, Division of Surgical Oncology Professor of Surgery and Oncology John L. Cameron Professor of Alimentary Tract Surgery Department of Surgery, Blalock 688 600 N. Wolfe Street Baltimore, MD 21287 Phone: (410) 502-2387 Fax: (410) 502-2388 tpawlik1@jhmi.edu.

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AND or OR. Criteria for inclusion included English language articles using human subjects (Figure 1).

Incidence and Epidemiology

Biliary cystic tumors (BCT), such as biliary cystadenoma (BCA) and cystadenocarcinoma (BCAC), comprise less than 5% of all liver cysts.(4) While BCA occurs predominantly in females (90%), BCAC is more evenly distributed between men and women.(2, 5-10) The mean age at presentation of BCA is 45 years versus BCAC which typically presents a decade later.(7-11) While 10% of reported BCT originate in the extrahepatic biliary tree, the overwhelming majority arises from the intrahepatic biliary system.(12-15) BCT are typically slow growing lesions with a reported size that can range in diameter from 1.5 to 35 cm.(6, 10, 16, 17)

Based on the mesenchymal stroma and the epithelium resembling endodermal (primitive hepatobiliary) cells that can be seen in BCT, Wheeler and Edmondson hypothesized that BCA arise from ectopic rests of embryonic bile ducts.(18, 19) However, 50% of BCTs contain endocrine cells suggesting that they may originate from intrahepatic peribiliary glands.(10, 20) BCAC is thought to originate either *de novo* from formed biliary ducts induced by ischemia and carcinogens or from malignant transformation of a preexisting BCA.(18, 19, 21) The latter theory is supported by the multiple reports of benign epithelium within BCAC specimens.(8, 10, 18, 21, 22) For example, Devaney et al. (10) reported malignant transformation in 6 of the 18 BCAC in their series as well as cytological atypia/dysplasia in a number of BCA.

Presentation and Differential Diagnosis Considerations

The clinical presentation of BCT can vary significantly. Many patients with BCT will be asymptomatic; other patients with BCT can present with non-specific symptoms, most commonly abdominal pain and distention (55-90%).(3, 7, 11, 17, 18, 23) While laboratory values are normal in most patients, approximately 20% of patients present with elevated liver function tests such as an abnormal bilirubin level.(19, 24) Obstructive jaundice and cholangitis are rare and do not correlate with malignant disease and typically occur with extrahepatic BCT.(12, 25-30) Hemorrhage and cyst rupture are other recognized, yet very uncommon, presenting complications of these lesions.(31-33)

The differential diagnosis of patients with complex cystic lesions of the liver includes BCT, as well as hydatid cyst, post-traumatic cyst, liver abscess, polycystic disease, hemorrhagic cyst, embryonal sarcoma, primary or metastatic necrotic neoplasm, atypical simple cyst, and biliary intraductal papillary mucinous neoplasm (IPMN).(11, 24) Biliary IPMN is a recently recognized entity characterized by mucin production and prominent intraductal papillary proliferation.(34, 35) Biliary IPMN occurs equally in both genders with a mean age of 58 years.(34, 36) Some authors now advocate classifying BCT with biliary tree communication and no ovarian stroma as biliary IPMNs.(23, 35-37) In one study, Zen et al. (35) identified 9 cases of BCT noting 5 tumors with direct communication to the biliary tree. None of these 5 cases contained ovarian-like stroma and all had different clinicopathologic characteristics than BCT.(35) In a separate study, Nakagawa and colleagues (24) were able to

preoperatively differentiate BCA from biliary IPMN based on three main imaging characteristics. First, BCA typically have a smooth tumor wall with septa inside the tumor resulting in a “cysts-in-cyst” appearance. Second, papillary projections are typical in IPMN and less so in BCA. Finally, demonstration of cystic tumor and intrahepatic bile duct communication along with the presence of distal mucin is more characteristic of biliary IPMN.(24, 36, 38) Despite similar management principles as BCT, preoperative identification of cystic biliary IPMN can alert the surgeon to its typical superficial spreading tumor growth pattern.(34, 38)

Imaging

Cross-sectional imaging with either computed tomography (CT) or magnetic resonance imaging (MRI) can accurately define and characterize simple cystic lesions. In contrast, the accuracy of cross-sectional imaging to diagnose the different types of complex cystic lesions can be relatively low. Certain radiographic findings may be helpful when trying to differentiate BCT from other non-neoplastic pathologies. Specifically, ultrasound, CT and MRI combined with clinicopathological features can aid in preoperative differentiation and characterization of hepatic cystic tumors.

Sonographically, BCTs are anechoic with thickened irregular walls and internal septations (**Table 1**). (8, 16, 39) Septal thickening, papillary infolding, and mural nodules are characteristic of BCTs. (40, 41) BCAC is more likely to contain mural or septal nodules and papillary projections. (42-44) In the series by Seo et al. (45), the authors described their experience with 20 BCT and 19 resected simple cysts that mimicked BCT. BCAC was associated with intracystic debris, bile duct dilatation and mural nodules. (45) CT and ultrasound are complementary modalities in evaluating BCT. (46) Sonography is more sensitive at detecting septa in cystic lesions whereas CT more accurately demonstrates size and anatomic extent of these lesions. (33, 43) On CT, BCT lesions are isodense to water (less than 30 HU) with nodular areas enhancing with intravenous contrast. (8, 16, 30, 39, 47) Biliary duct dilatation, single cysts, and lesions in the left lobe of the liver can be predictive of BCT on CT. (48) In fact, multiple investigators have suggested that BCTs are more often located in the left hemi-liver and therefore BCT should be considered for suspicious cystic lesions in the left liver especially in the setting of an increase in alkaline phosphatase. (6, 7, 45, 48, 49) While there have been anecdotal reports on its potential usefulness in identifying malignancy with BCAC, no definitive conclusions can be made regarding the utility of PET-CT for BCTs. (8, 50)

MRI is another useful tool in evaluating BCT. BCT are typically multi-locular with irregular thick walls on MRI. (8, 51) A homogeneous low intensity T1 signal and high intensity T2 signal are characteristic (**Figure 2**). (39) MRI characterizes cyst fluid content by varying signal intensities on T1 weighted images depending on cyst fluid protein content. (52) Linear low signal intensity within high intensity cysts identifies septations on T2 weighted images. (16) MRI demonstrates the anatomic relationships within the liver and can aid surgical planning. (53) The addition of diffusion weighted MR to conventional MRI sequences aids in the qualitative and quantitative assessment of hepatic lesions with improved cyst characterization and detection of malignancy. (54) Further studies will be required to

establish the relative additional utility of diffusion weighted MR. MRCP can also be helpful in that it can demonstrate cyst communication with the biliary tree as well as identify internal septations.(52, 55) MRCP can better visualize the biliary tree proximal to an obstruction, unlike ERCP.(52) ERCP is uncommonly utilized for BCT, but in select circumstances may be helpful in obtaining tissue samples, identifying biliary tree communications, and extrahepatic BCTs.(17, 50)

On cross-sectional imaging BCT needs to be differentiated from other entities such as simple hepatic cysts, as well as infectious or hemorrhagic cysts. Cysts without internal septa or papillary projection are most likely simple hepatic cysts and can be managed conservatively.(56) Simple hepatic cysts have a better-defined tissue/fluid interface on imaging than BCT (**Figure 3**).(57) In addition, Choi and colleagues (58) identified the presence of a septum and septal thickening as significant predictors of BCA versus simple hepatic cysts in their series of 31 patients. Echinococcal cyst and liver abscesses are the two other cystic liver lesions that sometimes can be difficult to differentiate from BCTs. Echinococcal cysts present with debris or daughter cysts within the cysts.(59) Grisolia and colleagues (60) reliably differentiated non parasitic cysts from Echinococcal cysts without utilizing FNA by developing sonographic criteria in conjunction with routine serology. Their criteria included border irregularity, irregular shape, calcification, gender, ultrasound appearance at follow up and presence of septa (**Figure 4A**).(60) Liver abscesses typically have a septated or multilocular appearance along with irregular thicker wall, albeit thicker than that seen with BCT (**Figure 4B**).(43, 52, 59) The combination of imaging characteristics and serologic analysis along with culture of cyst fluid can aid in making an accurate diagnosis.(43, 61)

Differentiating hemorrhagic cysts from BCT can similarly be accomplished using multi-modality imaging. Ultrasound displays intracystic clots as irregular and nodular septal images. CT is less sensitive at detecting intracystic contents and generally demonstrates a homogeneous cyst even in the presence of blood within the cyst.(62) On MRI, high signal T1 and low intensity T2 weighted images from clot formation are also seen.(51) This characteristic discrepancy in US and CT along with the MRI findings suggest the diagnosis of hemorrhagic cyst.(62) Mesenchymal hamartoma and undifferentiated embryonal sarcoma have multiloculated cystic appearance but are generally seen in children and young adults without the characteristic female predominance of BCT.(52)

While cross-sectional imaging can more reliably differentiate BCTs from other non-BCT lesions, BCA and BCAC cannot be reliably differentiated with preoperative imaging. Both BCA and BCAC can appear as solitary, multilocular cystic lesions. Mural nodule, and irregular cyst wall thickness on CT may suggest a higher likelihood of malignancy, but these features are not pathognomonic for BCAC.(17, 23, 43, 52, 63) Wang and colleagues (9) proposed a novel scoring system using age, gender, duration of symptoms, and lesion location to differentiate BCA and BCAC. The authors validated this scoring system using two separate patient cohorts and demonstrated over a 90% sensitivity and specificity.(9) This scoring system, however, necessitates further validation before being adopted on a more widespread basis.

Image guided aspiration of suspected BCTs is sometimes undertaken. Aspiration of BCT often demonstrates bile tinged mucin and can allow differentiation from parasitic cysts, hematoma, or hemorrhagic cysts.(46) With adequate tissue sampling, cytology can reveal malignant glandular cells and mucin suggesting BCAC, although these cells are rarely identified.(33, 64, 65) The role of cyst fluid analysis with carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) has been studied. Pinto and Kaye (66) used intracystic CEA levels to differentiate BCT from benign (nonmucinous) cysts and abscesses with 100% sensitivity and 94% specificity. Other case reports demonstrated elevated serum and cystic fluid CA19-9 levels in patients with BCT.(8, 67-69) These findings, however, have not been replicated in other studies. The role of cyst fluid CEA, CA19-9, and serum tumor markers remains controversial.(45, 56, 58, 70) Although many providers may obtain a CA19-9, the sensitivity and specificity are not high enough to differentiate a BCA from a BCAC. Moreover, fine needle aspiration (FNA) of suspected BCAC has been associated with pleural and peritoneal dissemination.(7, 8, 56) Because of this risk, along with the low likelihood of identifying malignant cells, routine FNA and core needle biopsy of suspected BCT should generally be avoided.(23, 65, 66)

Pathological Characteristics

On gross pathology, BCT are generally solitary, multilocular cystic lesions with fluid contents;(10) multifocal BCT are rare.(21, 47, 71) Cyst walls (BCA or BCAC) can have dense fibrosis and even calcifications. BCA exhibit pure biliary immunophenotype with a single layer of cuboidal to columnar epithelium supported by fibrous connective tissue (**Figure 5**). (3, 19, 36, 72) Classically, BCA has been characterized by ovarian-type stroma that typically expresses estrogen and progesterone receptors (60-100%).(36) This finding may explain the high incidence among females, (10, 19, 36, 73, 74) as well as the reported finding that BCAs occurred more often in patients on hormonal therapy and can be known to increase in size during pregnancy.(19, 23, 74, 75) Wheeler and Edmondson (18) have defined BCA based on the presence of mesenchymal stroma.(76) This description of BCA is characterized by three distinct layers: (1) an epithelial layer of mucin producing cells; (2) a layer of undifferentiated mesenchymal cells under the epithelial lining and (3) a dense layer of collagenous connective tissue outside the stromal bands of cells.(18, 24). All 13 patients with ovarian-like stroma BCT reported in Wheeler and Edmondson's case series were female and had a mean age of 41.7 years.(18) A subsequent review of the literature identified an additional 27 cases of BCA with mesenchymal stroma. These patients were similarly all female and had a mean age of 44.1 years.(18) In contrast, patients with BCA lacking mesenchymal stroma, had a mean age at diagnosis of 53.4 years and were distributed equally between genders.(18) Defining BCA based solely on the presence of ovarian stroma may be insufficient since a number of reported BCTs lack this stromal component.(6, 18, 19)

In contrast to BCA, BCAC is identified by the presence of proliferating cytologically malignant epithelium.(10) Multilayered epithelium, frequent mitotic figures, loss of polarity and nuclear pleiomorphism are features that suggest a BCA has become a BCAC. The presence of mesenchymal (ovarian-like) stroma has important prognostic implications. Specifically, BCAC without mesenchymal stroma appears to progress to malignancy more

often, disseminate more rapidly, and is associated with a worse prognosis than BCAC without this distinctive component.(23, 56, 77) In one of the largest BCT series, Devaney and colleagues (10) noted a median survival of 3 years in patients with BCAC without mesenchymal stroma versus no deaths in 4-8 years of follow up in all cases of mesenchymal-associated BCAC. BCAC without ovarian stroma occurs in both men and women as opposed to the almost exclusive female incidence seen in BCAC with ovarian-type stroma.(77) BCA ovarian stroma may regress during malignant transformation.(10, 78)

Both BCA and BCAC epithelial cells are characterized by mucin production and immunoreactivities to cytokeratins (CAM5.2, AE1, AE3), CA19-9, epithelial membrane antigen, and CEA.(10, 36, 79) Immunohistochemical analysis has demonstrated CEA and CA19-9 in the epithelial component of BCT.(64, 69, 80) CEA is localized to the luminal surface of BCA epithelial cells whereas BCAC epithelium have CEA diffusely within the cytoplasm.(81) D'Errico and colleagues (82) noted markedly increased albumin messenger RNA in all 8 BCAC lesions they investigated while noting its absence in BCA and other benign biliary cysts.

Management

The risk of malignant transformation of BCA to BCAC can be as high as 20%.(25, 27, 37) Appropriate management is critical given the malignant potential and the propensity for the lesion to recur. Therefore, in general, attempts at percutaneous aspiration, ethanol injection, and unroofing are unnecessary and generally inappropriate.(6, 53, 65, 83) When aspiration is undertaken for a presumed simple cyst, rapid recurrence may denote misdiagnosed BCT.(65) In fact, fenestration, aspiration, sclerosis, internal drainage, marsupialization or partial resection with or without cavity ablation can result in recurrence rate as high as 80-90%.(19, 70, 84, 85) As such, formal surgical resection with negative margins is recommended.(6-8) Appropriate surgical therapies may include liver resection or enucleation depending on the individual patient, anatomic position of the cyst, and surgeon experience.(6, 8, 70) While peripheral lesions or those BCTs relegated to one side of the liver should be treated with formal resection, centrally located lesions that involve central vascular or biliary structures may require enucleation. Extrahepatic BCTs will require complete resection in conjunction with resection of the bile duct followed by biliary diversion.(12, 86) A few case reports of laparoscopic BCT management have been published and reveal acceptable morbidity with recurrence rates similar to open series.(70, 87, 88) In the largest BCT laparoscopic resection series, Koffron et al. (70) resected 22 BCT laparoscopically, performing lobectomy (n=1), segmentectomy (n=8), marsupialization with remnant cyst fulguration (n=10), enucleation (n=2) and subtotal resection (n=1). With a mean follow up of 16 months, they reported 1 recurrence (5%) in a patient who had undergone marsupialization while noting less morbidity in the laparoscopic cohort compared to their open cohort of 12 patients (**Table 2**). (70) Whether the operative approach is open or laparoscopic, the surgeon should strive for complete extirpation of the BCT. Leaving residual BCA based on intra-operative frozen section analysis that shows no evidence of overt malignancy (e.g. BCAC) should generally be avoided. Intra-operative frozen section analysis is often insensitive most likely due to small focus of neoplastic cells that may be missed by partial sampling.(6, 8, 49, 53, 74)

In addition to surgical resection, a few single case reports of orthotopic liver transplantation (OLT) for BCT management have been reported.(3, 7, 85) For example, Romagnoli and associates (85) reported a successful outcome after performing OLT in a symptomatic BCT deemed unresectable. Given BCAC's indolent course, the use of liver transplantation should be utilized only in rare circumstances when formal resection is not possible and only after multi-disciplinary review by an experienced team.(7, 85)

Outcomes and Prognosis

Due to the rarity of these lesions, relatively little is known regarding the prognosis of BCTs. Based on the few small series that have been published, recurrence rates for BCAs seem to be extremely low after appropriate surgical management (5-10%).(6, 50) Most often BCAC recurs locally in the liver, perhaps due to initial inadequate local management.(7) Recurrent extrahepatic disease is relatively uncommon, but does occur in a subset of patients (20%).(7) However, at least one series reported that even some patients with metastatic disease, depending on the subtype, may live beyond 10 years.(6) Regarding overall survival, surgical resection of BCTs is associated with an improved prognosis compared with other malignant liver tumors such as hepatocellular carcinoma and cholangiocarcinoma (57% vs. 40% vs. 22% 5-year survival, respectively).(7, 8, 10, 69, 83) In fact, overall survival for patients with benign BCA in one large series was greater than 90% with 18 years of follow up.(18) Among patients with BCAC, the prognosis is worse than BCA but still better than other primary malignancies of the liver. Several series have reported that complete surgical resection of BCAC can result in 5-year survival of 65% to 70%.(6, 7, 10, 36, 50) In contrast, at least one series noted that partial excision of BCAC had a significantly worse 5-year survival of only 36%.(7)

Prognostic factors associated with survival following resection of BCAC include tumor subtype, as well as the type of stroma found in the tumor. Nakajima and colleagues (80) classified BCAC into two subtypes: invasive and non-invasive based on the carcinoma extension into the liver. The authors reported a significant difference in survival. Specifically, there were no recurrences or deaths noted among patients with non-invasive BCAC compared with a median survival of only 7 months among those patients who had the invasive subtype.(80) In a separate study, Devaney et al. (10) reported that patients with a BCAC characterized by ovarian-like stroma on pathology had a significantly better long-term prognosis compared with patients who had a BCAC whose tumors lacked ovarian-like mesenchymal stroma. Vogt and colleagues (6) similarly noted a worse prognosis among men with BCAC, probably due to the higher likelihood of BCAC without mesenchymal stroma in males.

Very few reports exist regarding the role of chemotherapy and radiation for BCAC. Anecdotal case studies have reported salvage or adjuvant chemotherapy, radiation, or transcatheter arterial chemoembolization.(8) Lauffer et al. (7), in their meta-analysis of 112 invasive BCAC cases, reported a 33% 5-year survival for patients with unresectable BCAC who were treated with definitive chemotherapy and radiation. Due to the lack of data, no evidence-based recommendations can be made the role chemotherapy and radiation therapy

in BCAC. However, given the excellent long-term outcomes following surgery alone for BCAC, there is probably no role for adjuvant therapy.

Conclusion

Improving imaging modalities and increased abdominal imaging has led to higher detection rates of cystic lesions of the liver. BCT incidence correlates significantly with sex and age and should be the primary diagnostic consideration in a middle-aged woman with a well-encapsulated, multi-locular cystic liver mass. Diagnostic modalities, such as ultrasound, CT, MRI, and ERCP yield important information regarding the nature of the cyst, but cannot reliably distinguish BCA from BCAC. As such, suspected BCTs should be extirpated surgically with complete removal of the lesion when feasible. Following excision of BCA long-term outcomes are good, however patients with BCAC have a worse long-term prognosis. Due to the rarity of this disease, future multi-institutional studies will be needed to better understand the management, biology, and prognosis of patients with BCTs.

Abbreviations

BCT	Biliary cystic tumors
CT	Computed tomography
MRI	Magnetic resonance imaging
BCA	Biliary cystadenoma
BCAC	Biliary cystadenocarcinoma
IPMN	Intraductal papillary mucinous neoplasm
CEA	Carcinoembryonic antigen
CA 19-9	Carbohydrate antigen 19-9
FNA	Fine needle aspiration

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Figure 1.

A PRISMA diagram defining the method of inclusion and exclusion for studies utilized in the review.

Figure 2. Biliary cystadenoma in a 53 year old female. (A) T2 and (B) post-contrast T1 weighted images in the axial plane reveal a 3.5 cm multiseptated mass in the left lobe of the liver, with associated ductal dilatation in the left lobe. Left lobectomy revealed biliary cystadenoma.

Figure 3. Incidental simple cyst in a 60 year old female. (A) Axial and (B) coronal CT images obtained in the portal venous phase show a large 7 cm well-defined simple cyst, with no internal septations or enhancing mural nodules. (C) Coronal T2 weighted MR image shows a well-defined hyperintense lesion compatible with simple cyst.

Figure 4.

(A) Echinococcal cyst in a 43 year old female. CT of the liver in the portal venous phase shows a heterogenous cyst with rim calcification as well as lamellated serpiginous internal enhancement. These findings are consistent with Echinococcal cyst. Serology was also positive. (B) Bacterial abscess in a 44 year old male with fever and transaminitis. CT of the liver in the portal venous phase shows a multiseptated cystic mass in the right lobe of the liver, with adjacent edema.

Figure 5.

Simple hepatic cyst (A) with flat epithelium supported by a thin layer of fibrous stroma overlying hepatic parenchyma (*). Biliary cystadenoma (40X magnification, H&E stain) (B) with simple columnar epithelium lining. Ovarian stroma highlighted by a progesterone immunohistochemical stain (C) and mucin production (red, arrow head) as shown by a mucin histochemical stain (D). Biliary cystadenocarcinoma (E) with architectural and extensive cytologic atypia.

Table 1**Radiologic Characteristics**

Biliary cystic tumors	Hepatic simple cysts	Echinococcal cysts
Multiloculated cyst	Anechoic	Daughter cyst within main cyst
Internal septation	Smooth borders	Intracystic debris
Enhancing cyst wall	No perceptible wall	Low signal intensity rim on T2-weighted MRI
Calcifications	No septations	
Papillary wall nodules	No enhancement on CT with IV contrast	
Thickened irregular wall	Water attenuation on CT	
Enhancement on CT with IV contrast		
Water attenuation on CT		

Table 2

Biliary Cystic Tumor Case Series

First author, year	Patients	Operative procedure	Outcomes
Martel, 2012 (49)	n=13 (12 Ff) BCA (n=11), BCAC (n=2) Mean age 51 y	Liver resection (3) Enucleation (6) Unroofing (4)	No mortality Median follow up 23.1 mo No BCA or BCAC recurrences
Pillai, 2012 (23)	n=13 (BCA, 11 F) Mean age 46 y	Hepatectomy (5) Segmentectomy (5) Enucleation (3)	No mortality Median follow-up 22 mo No recurrence
Ratti, 2012 (61)	n=12 (BCA, 12 F) Mean age 45 y	Hepatectomy (12)	No mortality Morbidity 16.7% Median follow-up 16 mo No recurrence
Sang, 2011 (8)	n=33 BCA (n=19, 17 F), Mean age 44.2 y BCAC (n=14, 5 F), Mean age 57.0 y	Enucleation 3 (BCA 3) Fenestration 2 (BCA 1) (BCAC 1) Segmentectomy 6 (BCA 5) (BCAC 1) Sectionectomy 7 (BCA 5) (BCAC 2) Hemihepatectomy 7 (BCA 5) (BCAC 4) Trilobectomy 1 (BCAC 1)	BCA 1 patient death 8 mo postoperatively, secondary to metastatic disease after BCA resection Median follow-up 2.5 mo No recurrence in fenestration patient, 14.4 mo of follow-up BCAC Median follow-up 5.5 mo 2 mortalities secondary to metastatic disease
Erdogan, 2010 (37)	n=15 (13 F) BCA (n=12) BCAC (n=3)	Hepatectomy (6) Enucleation (9)	No mortality Morbidity 13% No follow up recorded
Teoh, 2006 (65)	n=20 (BCA, 16 F) Mean age 58 y	Hepatectomy (10) Enucleation (10)	Mortality rate not reported Mean follow-up 5.5 y 1 lost to follow-up No recurrences after resection
Daniels, 2006 (74)	n=12	Hepatectomy (2)	25% morbidity rate

First author, year	Patients	Operative procedure	Outcomes
Thomas, 2005 (50)	BCA, 12 F, Mean age 50.5 y	Enucleation (4)	Wound infection (1)
		Combination hepatectomy enucleation (7)	Pulmonary embolus (1)
			Bile fistula (1)
			No mortality
Vogt, 2005 (6)	n=19 (18 F)	Hepatectomy (12)	No mortality
	BCA (n=18)	Enucleation (6)	Mean follow-up 4 y
	BCAC (n=1)	Fenestration (1)	No recurrences
	Mean age 48 y		
Vogt, 2005 (6)	n=22	Hepatectomy (14)	2 deaths at 6 and 12 mo in secondary to metastatic BCAC
	BCA (n=18, 18 F) Mean age 48 y	Enucleation (8)	
	BCAC (n=4, 3 F) Mean age 60 y		
Kofron 2004 (70)	n=34	Open resection (11)	No mortality
	BCA (n=33)	Open enucleation (1)	1 recurrence after BCA laparoscopic marsupialization
	BCAC (n=1)	Laparoscopic resection (10)	
		1 subtotal resection	
		Laparoscopic enucleation (2)	
Laparoscopic marsupialization (10)			

BCA, biliary cystadenoma; BCAC, biliary cystadenocarcinoma; F, female.