

PORCELAIN GALLBLADDER AND GALLBLADDER CANCER

PORCELAIN GALLBLADDER

- Porcelain gallbladder is an uncommon manifestation of chronic cholecystitis characterized by intramural calcification of the gallbladder wall.
- Patients with a porcelain gallbladder are often asymptomatic but are at increased risk for the development of gallbladder carcinoma, which has a poor prognosis.
- Epidemiology — The incidence of a calcified gallbladder at autopsy ranges from 0.06 to 0.08%.
 - It is more common in females than in males with a ratio of 5:1.
 - The mean age at presentation varies from 38 to 70 years.
 - The incidence of gallbladder carcinoma in patients with a calcified gallbladder ranges from 7 to 33%[1].
- Pathogenesis And Histopathology — Porcelain gallbladder is associated with cholelithiasis in more than 95 percent of patients.
 - The most common type of malignancy associated with porcelain gallbladder is adenocarcinoma.
- Diagnosis — The lesion is usually discovered incidentally on a plain abdominal roentgenogram.
 - A computerized tomogram or ultrasound should then be performed to confirm the diagnosis.
- Treatment — Because of the risk of gallbladder cancer, porcelain gallbladder is an indication for cholecystectomy even in asymptomatic patients.
 - Open rather than laparoscopic cholecystectomy is usually recommended, however, laparoscopic cholecystectomy may be possible.

GALLBLADDER CANCER

- Epidemiology And Risk Factors
 - In the United States, GB cancer is the fifth most common GI cancer, and the most common involving the biliary tract.
 - High rates of GB cancer are seen in South American countries.
 - These populations all share a high prevalence of gallstones and/or salmonella infection, both recognized risk factors for GB cancer.
 - Gallstones are present in 70 to 90 percent of patients with GB cancer.
 - The overall incidence of GB cancer in patients with cholelithiasis is 0.5 to 3%.
 - Incidence steadily increases with age
 - women are affected two to six times more often than men.
 - Other risk factors include adenomatous polyps, choledochal cysts and anomalous pancreatobiliary duct junction.
- Diagnostic Evaluation
 - Ultrasound — The overall accuracy of US for staging the local and distant extent of a suspected GBC is limited.
 - Endoscopic ultrasound — (EUS) is more accurate for imaging the gallbladder. EUS is a useful modality to assess the depth of tumor invasion into the wall of the gallbladder and for defining lymph node involvement.
 - CT and MRI — Liver invasion, suspected nodal involvement, or distant metastases may be shown. MRCP can help to differentiate benign from malignant gallbladder lesions and provide information as to disease extent.

MRI is particularly useful for visualizing invasion into the hepatoduodenal ligament, portal vein encasement, and lymph node involvement.

- Staging
 - The AJCC staging system was revised to recognize that locally advanced tumors are potentially resectable for cure.
 - Lymph node metastases are now classified as stage IIB rather than stage III
 - stage III indicates locally unresectable disease
 - stage IV indicates distant metastatic disease
 - peripancreatic lymph nodes are now considered to represent metastatic (M1) disease.

TNM Staging Gallbladder Cancer*

Definition of TNM

Primary tumor (T)

TX Primary tumor cannot be assessed
 T0 No evidence of primary tumor
 Tis Carcinoma in situ
 T1 Tumor invades lamina propria or muscle layer
 T1a Tumor invades lamina propria
 T1b Tumor invades muscle layer
 T2 Tumor invades perimuscular connective tissue; no extension beyond serosa or into liver
 T3 Tumor perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure, such as the stomach, duodenum, colon, or pancreas, omentum or extrahepatic bile ducts.
 T4 Tumor invades main portal vein or hepatic artery, or invades multiple extrahepatic organs or structures.

Regional lymph nodes (N)

NX Regional lymph nodes cannot be assessed
 N0 No regional lymph node metastasis
 N1 Regional lymph node metastasis

Distant metastasis (M)

MX Distant metastasis cannot be assessed
 M0 No distant metastasis
 M1 Distant metastasis

Stage grouping

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage III	T4	Any N	M0
Stage IV	Any T	Any N	M1

* Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Sixth Edition (2002) published by Springer-Verlag New York, Inc.

- Surgical Treatment —
 - Surgery is the only potentially curative therapy, but only 10 to 30 percent of patients are eligible for resection at presentation.
 - Among the absolute contraindications to surgery are:
 - liver or peritoneal metastases
 - ascites
 - encasement or occlusion of major vessels.
 - Direct involvement of colon, duodenum, or liver is not an absolute contraindication.

- Outcome —
 - Improved outcomes have been noted in the last decade, and attributed to more aggressive surgery, and the use of postoperative adjuvant therapy [2,3].
 - T1 disease- 85 to 100 percent.
 - T2 disease- 30 to 40 percent; possibly as high as 80 to 90 percent with more radical resection [4].
- Incidental GB cancer at cholecystectomy — Frozen section can reliably indicate whether a lesion is benign or malignant but it cannot reliably predict the depth of tumor invasion [5].
- Laparoscopic cholecystectomy
 - If GB cancer is strongly suspected, an open rather than laparoscopic procedure should be performed.
 - Although available data suggests that a laparoscopic approach does not diminish the survival of patients with incidentally found GB cancer, port site recurrences have been described [6].
 - Because of this, laparoscopic port sites should be removed at the time of reexploration.

Optimal surgical approach — Surgical options include:

- Simple cholecystectomy.
- Radical cholecystectomy, which includes removal of the gallbladder plus at least 2 cm of the gallbladder bed, and dissection of the regional lymph nodes from the hepatoduodenal ligament behind the second portion of the duodenum, head of the pancreas and the celiac axis.
- Radical cholecystectomy with resection of liver (generally segments IVb and V).

Morbidity and mortality — Morbidity and mortality rates from resection for GB cancer vary widely, with major morbidity rates ranging from 5 to 54 percent, and perioperative mortality rates from 0 to 21%.

Management of T1 lesions —

- Simple cholecystectomy may be sufficient for many patients with T1 lesions.
- Cure rates following simple cholecystectomy range from 73 to 100% [4,7], even among those diagnosed following laparoscopic cholecystectomy [8].
- T1b tumors are associated with a higher incidence of lymph node metastases than are T1a tumors (15 versus 2.5%).
- Thus, most surgeons favor simple cholecystectomy for patients with T1a cancers, while more radical resection should be considered for patients with T1b tumors.

Management of T2 lesions —

- Reexploration with radical resection should be strongly considered and will reveal residual tumor in 40 to 76% of cases.
- Five-year survival rates can be expected to increase from between 24 and 40%, to between 80 and 100% with radical surgery.
- Even patients with involved cystic and portal and lymph nodes may be curable by extended lymphadenectomy [4].
- In contrast, few if any patients with peripancreatic, celiac, and/or superior mesenteric nodal involvement are long-term survivors, and resection cannot be recommended.

Locally advanced (T3/4) —

- Radical surgery should not be performed for the purpose of debulking.

Summary and recommendation —

- Surgery is the only potentially curative treatment for GB cancer.
- In general, surgical approach to potentially resectable GB cancer consists of total removal of the gallbladder, a portion of the underlying liver (generally segments IVb and V), and dissection of the regional lymph nodes.
- For patients who are diagnosed incidentally at the time of cholecystectomy, reexploration and radical resection is warranted if disease extent is T2.
- The benefit of reexploration for patients with incidentally diagnosed T1 disease is more controversial, but it should be considered for healthy patients with T1b disease.
- Patients with locally advanced unresectable disease are candidates for chemoradiotherapy.

Adjuvant Therapy

Radiation and chemoradiotherapy —

- Although several retrospective series report encouraging results with RT, with or without chemotherapy (generally, 5-FU), it is difficult to conclude from these small series that adjuvant therapy provides clear survival benefit.
- Nevertheless, the use of adjuvant chemoradiotherapy is common in the United States.

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