



**ORIGINAL RESEARCH PAPER**

**Surgery**

**ANTICIPATORY EXTENDED  
CHOLECYSTECTOMY FOR SUSPICIOUS  
GALLBLADDER CARCINOMA**

**KEY WORDS:**

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**INTRODUCTION:**

Gallbladder carcinoma represents the most frequently encountered malignant tumor originating from the biliary tract, with a low rate of diagnostic, a low rate of surgical treatment, and an extremely poor long-term prognostic (overall 5 year survival rate is 5% and median survivals of <6%). In advanced and untreated cases, the median survival is usually 2 to 5 months.

It has been demonstrated that women are more commonly affected by this malignancy; in regard to the patients' age, it seems that the incidence of gallbladder cancer significantly increases after the age of 40. In terms of race, it seems that the highest risk for gallbladder carcinoma has been reported among people from Chile, Poland, India, Japan, and Israel.

Frozen section diagnosis is effective for determining the presence of cancer and its depth. In order to find gallbladder cancer during surgery, it is recommended that resected gallbladder specimens should be opened in the operating room and the mucosa of the gallbladder should be carefully examined. In cases in which there is a suspicion of malignancy, frozen section diagnosis should be obtained. The results were compared with those of pathological diagnosis of postoperative entire cross sections to determine whether invasion.

Ultrasonography (US) is often the default initial investigation for gallbladder pathology, concerning features include: gallbladder-replacing or invasive mass, irregular wall thickening and intraluminal polypoid lesions. However, for full assessment of suspected gallbladder cancers, a combination of thoracic, abdominal, and pelvic computed tomography (CT), liver magnetic resonance imaging (MRI), and endoscopic ultrasound (EUS) can be performed. While preoperative imaging is helpful, often there is only a suspicion of gallbladder cancer with the absence of tissue confirmation before surgery. Small studies utilizing endoscopic techniques: ultrasound-guided fine needle aspiration (EUS-FNA), have had varied success in differentiating malignant disease from benign disease.

**OBJECTIVE:**

Whenever gallbladder cancer is suspected, the therapeutic desiderate consists of complete tumor resection with negative resection margins. In early stages of the disease, this desiderate is achieved if cholecystectomy en bloc with the surrounding liver bed and the regional lymph nodes are excised. In cases in which surgery is planned for a presumed benign disease and at the time of exploration the suspicion of malignancy is raised, hepatic resection should be associated.

**Risk Factors:**

**1. Acute Cholecystitis:**

It is the fourth most common cause of hospital admissions for patients presenting with acute abdomen, and it of concern

when a thick walled gallbladder is found at imaging. The most important risk factor for the development of gallbladder cancer is gallstones, with an 8.3x higher risk than the general population.

Among patients with gallbladder cancer, 70–90% has a history of cholelithiasis. Larger stones portend a greater risk, with stones >3 cm being 9.2–10.1 times greater than stones <1 cm. This increased risk is most likely,

- Attributable to greater local epithelial irritation.
- Acute calculus cholecystitis imaging studies:
- Obstructing gallstone
- Hydropical dilatation of gallbladder
- Positive sonographic murphy's sign
- Pericholecystic inflammation or fluid

**2. Chronic Inflammation:**

Chronic inflammation is considered a major factor in carcinogenesis, causing DNA damage, tissue proliferation, and cytokine and growth factor release. Another result of chronic inflammation is deposition of calcium within the gallbladder wall, causing the gallbladder to develop a bluish hue and become fragile—the “porcelain gallbladder.” While less than 1% of gallbladder specimens demonstrate this change, it is frequently (~25%) associated with gallbladder cancer.

**3. pancreaticobiliary Maljunction Anomalies:**

Pancreaticobiliary maljunction is an abnormal union of the biliary and pancreatic ducts located outside the duodenal wall in which a sphincter is not present. This congenital anatomic anomaly allows pancreatic fluids to reflux into the biliary system, causing chronic inflammation and genetic alterations, leading to increased cellular proliferation resulting in hyperplasia/dysplasia/carcinoma. This anomaly may be detected by cholangiography either with endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance cholangiopancreatography (MRCP) or through endoscopic ultrasound (EUS) imaging. EUS shows two thickened layers with epithelial hyperplasia and subserosal fibrosis, with or without a third layer containing a hypoechoic hypertrophic muscular layer.

**4. Infection:**

An association between Helicobacter infection of the bile and gallbladder carcinogenesis may be related to bacterial-induced degradation of bile acid; however, precise mechanisms remain poorly understood. Liver flukes, particularly Clonorchis sinensis and Opisthorchis viverrini, have been implicated in cancer of the gallbladder.

**Pathogenesis:**

Gallbladder cancer may arise in the gallbladder's fundus (60%), body (30%), or neck (10%) . The development of gallbladder cancer is proposed to occur over a span of 5–15 years, with tissue alterations including metaplasia, dysplasia, carcinoma in situ, and invasive cancer.

The anatomy of the gallbladder is unique and predisposes the cancer to direct invasion as histologically the gallbladder wall is composed of a mucosa, lamina propria, smooth muscle layer, perimuscular connective tissue, and serosa: note the lack of submucosa in the gallbladder. Additionally, no serosa is present where the gallbladder attaches to the liver and, as such, direct infiltration of gallbladder cancer to the liver is the most common form of direct local spread.

**Patterns of Spread:**

**Spread of gallbladder cancer occurs via four routes:**

- (a) Local invasion of the liver or other nearby structures,
- (b) Lymphatic dissemination,
- (c) Peritoneal spread, and
- (d) Hematogenous spread.

Direct extension of gallbladder cancer typically involves the liver (segments IV and V), bile duct, duodenum, colon, parietal wall, and/or abdominal viscera. Hepatic metastasis is most often the result of direct liver and portal tract invasion. Portal tract invasion can also be the result of lymphatic spread.

**Methodology:**

A retrospective study was conducted in Department of General Surgery of Meenakshi Medical College, Kanchipuram India Between May 2020 to July 2021. It included 30 patients and all of them were symptomatic for gall stone disease.

An initial critical diagnostic observation regarding gallbladder wall thickening (>3mm), single (>1 cm)/ sessile polyp, pericholecystic stranding, GBC, XGC, is important for diagnosis and appropriate management.

Patient's demographic data and clinical symptoms and signs were recorded and laboratory investigations, preoperative ultrasonography of abdomen, CT of abdomen in all patients suspicious for the above mentioned features, AEC were performed as a protocol.

**RESULTS:**

Of the 30 patients who were included in the study 17(56.7%) were females and 13(43.3%) were males [fig 1]. 30 patients were symptomatic for gallstones and thick walled gallbladder. An ultrasound revealed gallstones and thick-walled gallbladder in 30 patients. USG raised suspicion of carcinoma in 9(30%), gallbladder polyp in 2(6.7%), chronic cholecystitis in 19(63.3%) patients respectively in the given study group [fig 2]. Gallbladder wall thickening was noted in 30 patients on ultrasound. These cases were subjected to CT scan further. CT raised suspicion of GBC in 9(30%), GB polyp in 2(6.7%), chronic cholecystitis in 11(36.7), acute calculus cholecystitis in 8(26.7%) patients in the given study group [fig 3].

After pre anesthetic evaluation and stabilizing all the patients, Anticipatory extended cholecystectomy was done for all the patients as triage and specimen was sent for frozen section histopathological examination, if negative for malignancy specimen is sent for routine histopathological evaluation, if frozen section is positive for malignancy AEC is converted to EC (extended cholecystectomy) for performing lymphadenectomy. Frozen section biopsy was done on 24 (80%) cases which showed GBC in 1(3.3%), GB polyp in 2(6.7%), chronic cholecystitis in 11(36.7%), acute calculus cholecystitis in 2(6.7%), intracholecystic papillary tubular neoplasm in 1(3.3%), GB perforation in 1(3.3%), XGC in 6(20%) of the patients in the given study group. All the specimens obtained during surgery were subjected to routine histopathological examination. This revealed GBC in 1(3.3%), GB polyp in 2(6.7%), chronic cholecystitis in 11(36.7%), acute calculus cholecystitis in 8(26.7%),

intracholecystic papillary tubular neoplasm in 1(3.3%), GB perforation in 1(3.3%), XGC in 6(20%) patients in the given study group [fig 4] According to this report 1(4.2%) patient with GBC underwent EC, 1(4.2%) patient with intracholecystic papillary tubular neoplasm underwent AEC, 1(4.2%) patient with GB perforation underwent AEC, 6(25.0%) with XGC underwent AEC, 2(8.3%) with GB polyp underwent AEC, 11(36.7%) patients with chronic cholecystitis underwent Laparoscopic cholecystectomy, 8(26.7%) patients with acute calculus cholecystitis underwent laparoscopic cholecystectomy in the given study [fig 5]. 10(33.3%) patients with suspicious carcinoma which proved to be benign on histopathological examination underwent AEC, 1(3.3%) had malignant etiology on histopathological and frozen section examination underwent EC, 19(63.3%) patients with benign etiology on histopathological evidence underwent laparoscopic cholecystectomy [Fig 6].

**Figure 1 :**

	FREQUENCY	PERCENT
<b>MALE</b>	<b>13</b>	<b>43.3</b>
<b>FEMALE</b>	<b>17</b>	<b>56.7</b>
<b>TOTAL</b>	<b>30</b>	<b>100.0</b>

In this figure, 13(43.3%) were males and 17(56.7%) were females with a p value of which is significant. Hence, Gall stone pathology is more frequently encountered in women especially GBC which is more common in woman population.

**Figure 2:**

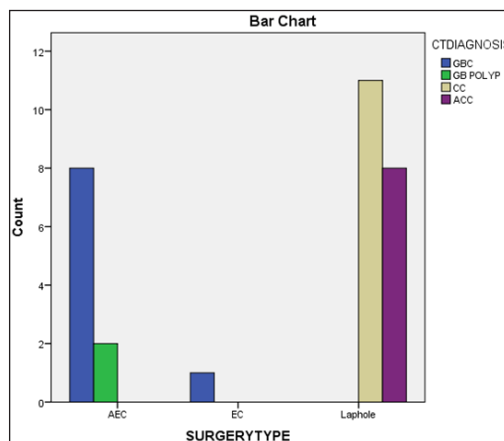
	FREQUENCY	PERCENT
<b>GBC</b>	<b>9</b>	<b>30</b>
<b>GB POLYP</b>	<b>2</b>	<b>6.7</b>
<b>CHRONIC CHOLECYSTITIS</b>	<b>19</b>	<b>63.3</b>

In this figure, different diagnoses were confirmed on ultrasound, which revealed GBC in 9(30%) cases, GB polyp in 2(6.7%) and chronic cholecystitis in 19(63.3%) in the given study group.

**Figure 3:**

	FREQUENCY	PERCENT
<b>GBC</b>	<b>9</b>	<b>30</b>
<b>GB POLYP</b>	<b>2</b>	<b>6.7</b>
<b>CHRONIC CHOLECYSTITIS</b>	<b>11</b>	<b>36.7</b>
<b>ACC</b>	<b>8</b>	<b>26.7</b>

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In this bar diagram, 1 patient with carcinoma underwent Extended Cholecystectomy, 10 patients with suspicious carcinoma but benign histopathological reports underwent Anticipatory Extended Cholecystectomy and 19 patients with benign diseases underwent Laparoscopic cholecystectomy. In this bar diagram, comparisons between histopathological analysis and type of surgery were made. 1 patient the GBC

underwent EC, 2 patients with GB polyp underwent AEC, 1 patient with ICPTN underwent AEC, 6 patients with XGC underwent AEC.

FIGURE 6:

SURGERY TYPE	BENIGN	MALIGNANT	P VALUE
AEC	10(33.3%)		.000
EC		1(3.3%)	.000
LC	19(63.3%)		.000

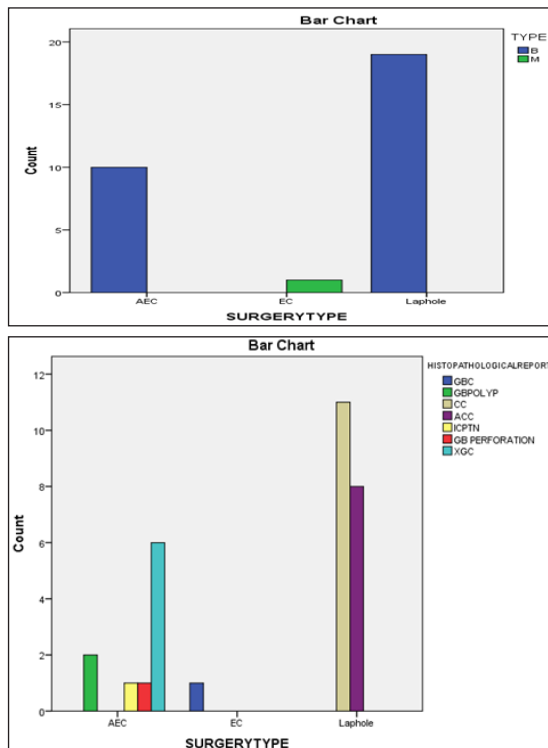


Figure 5:

SURGERY TYPE	GBC	GB POLYP	XGC	ICPTN	GB PERFORATION	CC	ACC	P VALUE
AEC		2(8.3%)	6(25%)	1(4.2%)	1(4.2%)			.000
EC	1(4.2%)							.000
LC						11(45.8%)	2(8.3%)	.000

In Figure 4, according to chi-square and Fisher's exact test p value is .000 which is significant to the given data. Frozen section biopsy showed 1(4.2%) with GBC, 2(8.3%) with GB polyp, 6(25%) with XGC, 1(4.2%) with ICPTN, 1(4.2%) with GB perforation.

**DISCUSSION:**

From the standpoint of a pathologist, a frozen section is no more than an imperfect and auxiliary diagnosis because the entire lesion cannot be examined by this method. Nevertheless, for surgeons, frozen section diagnosis is indispensable as a means of minimizing early postoperative recurrence or metastasis.

Although ultrasonography, computed tomography, and other imaging diagnostic techniques have yielded improved results for preoperative evaluation, there are limits to their ability to diagnose gallbladder cancer. Some typical cases in which gallbladder cancer is not diagnosed preoperatively are:

- (1) cases of flat-type cancer in which tumors are not formed,
- (2) cases in which the presence of gallstones makes it difficult to observe the gallbladder wall adequately,

- (3) cases in which it is difficult to distinguish cancer from cholecystitis when there is thickening of the gallbladder wall, and
- (4) cases of misdiagnosis due to the prominent presence of gallstones or inflammation.

The basic treatment for gallbladder cancer without liver metastasis or peritoneal dissemination is surgery. Treatment was successful with simple cholecystectomy alone in most of the cases but in suspicious cases of gallbladder carcinoma which includes thick walled gallbladder wall, single/ sessile polyp (>1cm) in size, pericholecystic ligament involvement, XGC, suspicious GBC, Anticipatory Extended Cholecystectomy is performed as a triage as the ability of diagnosis of frozen section is high. AEC involves removal of the GB with wedge of liver (but without lymphadenectomy) and frozen section histological examination. If frozen section reveals malignancy (GBC), lymphadenectomy is added to complete EC. The basic principle of hepatic resection is achieving a negative margin, while persevering maximal amount of liver parenchyma. The rationale of resection includes resection of liver invaded or likely to be invaded directly by the tumor, to remove micro-metastasis in segment IVB+V as a result of direct venous drainage of gallbladder through cystic vein to these segments and to resect en bloc Gilson's sheath because of potential invasion to hepatoduodenal ligament. The sensitivity and specificity of frozen section is 90% and 100% respectively. Extended cholecystectomy includes removal of the liver and lymphadenectomy. EC is curative if the tumor is confined to gallbladder wall and lymph nodes confined to the hepatoduodenal ligament. GB wall >3 mm on US is defined as TWGB. TWGB on US should be further evaluated with CT. Focal, non-uniform and irregular TWGB is highly suspicious of GBC and should be treated as such—by open surgery and EC. Diffuse, uniform and regular TWGB is usually benign (AC, CC or XGC) but can rarely be malignant (GBC). XGC mimics GBC not only on imaging (US and/ or CT) but even intraoperative and on gross examination of the resected specimen (GB); the two may also coexist. Preoperative FNAC may identify most GBC and some XGC (5) but a negative FNAC does not exclude GBC. EUS guided FNAC from TWGB has been reported but requires equipment and expertise which is not available easily and everywhere. Again, negative FNAC does not exclude GBC. Diffusion weighted MR imaging (DWI) may help to differentiate between benign and malignant TWGB but is not accurate. Tumor markers e.g., CEA, CA 19-9 and CA 125 have not been found to be useful to differentiate between XGC and GBC.

**CONCLUSION:**

The intraoperative frozen tissue diagnosis is fairly reliable as to whether lesions are malignant or benign; however, accuracy is low in patients with polypoid lesions of the gallbladder.

**Acknowledgments:** NONE

**Conflicts Of Interest:** NONE

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